Brendan T. Finucane
Ban C.H. Tsui
Editors

Complications of Regional Anesthesia

Principles of Safe Practice in Local and Regional Anesthesia

Third Edition

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Editors
Brendan T. Finucane, MB, BCh, BAO, FRCA, FRCPC
Department of Anesthesiology and Pain Medicine University of Alberta
Edmonton, AB, Canada

Ban C.H. Tsui, MSc (Pharm), MD, FRCPC
Department of Anesthesiology, Perioperative and Pain Medicine
Stanford University School of Medicine
Stanford, CA, USA

Originally published by Churchill Livingstone, New York City, 1999

ISBN 978-3-319-49384-8 ISBN 978-3-319-49386-2 (eBook)
DOI 10.1007/978-3-319-49386-2

Library of Congress Control Number: 2017933835

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

We would like to dedicate this edition of the book to our patients, our teachers, our students, and our families.

Brendan T. Finucane, MB, BCh, BAO, FRCA, FRCPC
Ban C.H. Tsui, MSc (Pharm), MD, FRCPC

Preface

We are now ready to publish the third edition of ***Complications of Regional Anesthesia*** which was first published 17 years ago. The title remains the same but we have added the subtitle, *Principles of Safe Practice in Local and Regional Anesthesia,* to stress the relatively new emphasis and importance on safety and prevention and to broaden our horizons to include some discussion about the practice and the administration of not just **Regional** but also **Local Anesthesia**.

We have made some significant changes to the book which we hope you approve. First of all this is a much more comprehensive edition going from 24 to 35 chapters, and we have also divided the book into seven separate parts based mostly on logic. In the opening part entitled **General** considerations, we started out with a chapter on the History of Regional Anesthesia which seemed like a good place to start. We also addressed the issue of Safety of Regional Anesthesia. It is difficult to discuss much about regional and local anesthesia without mentioning toxicity of local anesthetics which has been a problem with regional and local anesthesia since its inception more than 130 years ago, and we finished up that section with a good discussion of Outcomes comparing Regional and General Anesthesia. In the second part we addressed **Special** considerations, which includes a chapter on Mechanisms of Nerve injury, Infection, Catheter techniques, and the whole issue of regional anesthesia in the presence of neurologic disease and how to evaluate neurologic injury following regional anesthesia. We then dedicated several chapters to **Specific** blocks involving anatomic regions of the body specifically addressing safety and management of adverse events. We dedicated the next part to specific **Patient Populations**—the young, the old, the pregnant, obese, and those suffering from chronic pain. The next part is new territory for us and is entitled **Special Environments**. We invited a group of practitioners, mostly surgeons, who frequently use local anesthetics in their practices, to share their expertise and experiences with us. Among this group of specialists are dentists, ophthalmologists, emergency room physicians, orthopedists, and plastic surgeons. We have a lot to learn by sharing our experiences using local and regional anesthesia with specialists outside our own discipline and they from us. We dedicated a part to **Morbidity Studies** and this part includes writers from across the world adding an **International** flavor, as we are sometimes accused of being too insular in North America. We dedicated the final part to **Medical Legal Aspects** of Local and Regional Anesthesia, which we must realistically face in the modern world of this twenty-first century.

Labat, in the 1920s, was the first fully trained specialist in Regional Anesthesia, and he influenced the leaders of this new emerging specialty of anesthesiology to use regional anesthesia in their practices. Most anesthesiologists at that time opted for general anesthesia because of its predictability. Tremendous advances have been made in Regional Anesthesia in the past 30 or 40 years, so much so that most anesthesiologists in the modern era have become interested in regional anesthesia again because there is far more predictability in the practice of regional anesthesia than ever before. We can now actually see what we are doing instead of blindly seeking neural targets, based on our knowledge of anatomy. Most anesthesiologists fully appreciate the enormous benefits of regional anesthesia to patients especially in the postoperative period but also long term. However, despite good practice, we encounter problems

and unforeseen circumstances, so practitioners must be fully aware of the many pitfalls and complications associated with the practice of regional anesthesia even though we have made enormous advances in recent years.

This edition is much more comprehensive than our previous efforts and more inclusive and there are more pages, tables, diagrams, and colored illustrations. This text is also comprehensively referenced. As in previous editions, there is some repetition and that is inevitable. However, it is refreshing to compare anesthesia practitioners' experiences from around the world and from outside our own discipline. Local Anesthetic Systemic Toxicity (LAST) is a very common theme among all who practice Local and Regional Anesthesia, and we have learned a lot about prevention and treatment of this malady in the past 30 years. Fortunately most of the complications we have discussed are rare and all too often we appear to shoulder the blame for injuries that we did not cause in the first place.

Our main emphasis is on safety and prevention of injury in the practice of local and regional anesthesia, and we have called upon a great variety of experts from around the world to share their experiences with us. We hope you appreciate the changes we have and as always we welcome your critique and recommendations for improvement.

There is one other important change I have made in this edition and that is I have invited my colleague and friend from the Department of Anesthesiology and Pain Medicine from the University of Alberta to co-edit this edition of the text with me. He has contributed enormously to our knowledge of local and regional anesthesia in the past two decades and helped a great deal with this latest version.

Edmonton, AB, Canada — Brendan T. Finucane
Stanford, CA, USA — Ban C.H. Tsui

Acknowledgments

We would like to express our deep gratitude to all of the contributors to this text. We are impressed by the quality of the material presented and their willingness to abide by all of the rules imposed. We also wish to thank a group of students, medical students, fellows, and research assistants over the past 2 years, including Gareth Corry, Saadat Ali, and Jeremy Tsui, who assisted in organizing the written material. An investigator grant from the Alberta Heritage Foundation for Medical Research allowed Dr. Tsui to pursue this project by helping to support his academic work.

Acknowledgments

Brendan T. Finucane, MB, BCh, BAO, FRCA, FRCPC

I would like to acknowledge some special individuals who greatly influenced my career in anesthesia, academic medicine, and my passion for regional anesthesia. These are Dr. John Shanahan, Dr. Tom Bryson, Professors T Cecil Gray, John E Steinhaus, Evan Frederickson, Pritvi Raj, and Ben Covino.

Acknowledgments

Ban C.H. Tsui, MSc (Pharm), MD, FRCPC

To my wife, Eliza, and my children, Jenkin and Jeremy—the real loves of my life. Without their support and understanding, I could not have completed this demanding project. I would also like to dedicate this opus to my parents, Woon-Tak and Kau-Wan, for their love and guidance throughout my life.

Brendan T. Finucane
Ban C.H. Tsui

Contents

Contributors

George Arndt, MD Department of Anesthesia, University of Wisconsin Madison, Madison, WI, USA

Michael J. Barrington, PhD, MBBS, FANZCA Department of Anaesthesia and Acute Pain Medicine, St. Vincent's Hospital, Melbourne, Fitzroy, Melbourne, Australia

Faculty of Medicine, Dentistry and Health Sciences, Melbourne Medical School, University of Melbourne, Parkville, VIC, Australia

Dan Benhamou, MD Département d'Anesthésie et Réanimation, Groupe Hospitalier et Université Paris Sud, le Kremlin Bicêtre, Orsay, France

Robert B. Bolash, MD Department of Pain Management, Cleveland Clinic, Cleveland, OH, USA

Jörgen Bruhn, MD, PhD Radboud University Medical Centre, Nijmegen, Netherlands

Kelly Byrne, MBChB, FANZCA Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand

Yoo Kuen Chan, MD Department of Anaesthesiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Stephen Choi, MD, FRCPC, MSc Department of Anesthesia, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada

Michael Collins, MD Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA

Derek Dillane, MB, BCh, BAO, MMedSci, FCARCSI Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada

Karen B. Domino, MD, MPH Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA

F. Michael Ferrante, MD, FABPM Department of Anesthesiology, David Geffen School of Medicine at UCLA, Santa Monica, CA, USA

Brendan T. Finucane, MB, BCh, BAO, FRCA, FRCPC Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada

David Flamer, MD, FRCPC Department of Anesthesia, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

Andrea Fonner, DDS The Herman Ostrow School of Dentistry of the University of Southern California, Los Angeles, CA, USA

Kristen Gadbois, MD, FRCPC Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, ON, Canada

Steven J. Gaff, MBChB, FCARCSI, FANZCA Department of Anaesthesia and Perioperative Medicine, The Alfred Hospital, Melbourne, VIC, Australia

Sugantha Ganapathy, MBBS, FRCA, FRCPC Department of Anesthesiology and Perioperative Medicine, Western University, London, ON, Canada

Geert-Jan van Geffen, MD, PhD Radboud University Medical Centre, Nijmegen, Netherlands

Ferrante S. Gragasin, MD, PhD, FRCPC Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada

James D. Griffiths, MBBS, FANZCA, MEpi, PGCert CU Department of Anesthesia and Pharmacology, University of Melbourne, Royal Women's Hospital, Parkville, VIC, Australia

Matthew Harmelink, MD Division of Pediatric Neurology, Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA

Peter D. Hebbard, MBBS, FANZCA, PG Dip Echo Northeast Health Wangaratta, University of Melbourne, Melbourne, VIC, Australia

Andrew A. Herring, MD Emergency Department, Highland Hospital–Alameda Health System, Oakland, CA, USA

Department of Emergency Medicine, University of California, San Francisco, San Francisco, CA, USA

Quinn Hogan, MD Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI, USA

Terese T. Horlocker, MD Department of Anesthesiology, Mayo Clinic College of Medicine, Rochester, MN, USA

James L. Howard, MD, MSc, FRCSC Department of Orthopedic Surgery, Western University, London, ON, Canada

Andrea Kattula, MBBS, FANZCA Department of Intensive Care, The Austin Hospital, Heidelberg, VIC, Australia

Department of Surgery, The Austin Hospital, Heidelberg, VIC, Australia

Christopher Kent, MD Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA

Laura Kohl, MD Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, USA

Madison Radiologists SC, Madison, WI, USA

Don Lalonde Division of Plastic and Reconstructive Surgery, Saint John Regional Hospital and St Joseph's Hospital, Saint John, NB, Canada

Christine Lee, MD Department of Anesthesiology, David Geffen School of Medicine at UCLA, Santa Monica, CA, USA

Lorri A. Lee, MD Department of Anesthesiology, Vanderbilt University, Nashville, TN, USA

Hendrikus J.M. Lemmens, MD, PhD Department of Anesthesiology, Pain and Perioperative Medicine, Stanford University School of Medicine, Stanford, CA, USA

Ian M. MacDonald, MD, CM, FCCMG, FRCSC, FCAHS Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada

Robert William Andrew Machuk, BSc, MHA, MD Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada

Dean Y. Mah, MD, MSc, FRCSC Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada

Stanley F. Malamed, DDS Herman Ostrow School of Dentistry of U.S.C., Los Angeles, CA, USA

Belen De Jose Maria, MD, PhD Department of Pediatric Anesthesiology, Hospital Sant Joan de Déu, University of Barcelona, Barcelona, Spain

Colin J.L. McCartney, MBChB, PhD, FRCA, FRCPC Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, ON, Canada

Keith McCollister, MD Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, USA

X-Ray Consultants, Inc., South Bend, IN, USA

John W.R. McIntyre, MD Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada

Graeme A. McLeod, FRCA, FFPMRCA, MD Division of Neuroscience, Institute of Academic Anaesthesia, Medical Research Institute, Ninewells Hospital & University of Dundee School of Medicine, Dundee, Scotland, UK

John Mesa, MD Private Practice Plastic Surgeon, Livingston, NJ, USA

Adam D. Niesen, MD Department of Anesthesiology, Mayo Clinic College of Medicine, Rochester, MN, USA

Brian O'Donnell, MB, MSc, MD, FCARCSI Department of Anesthesia, Cork University Hospital, Cork, Ireland

ASSERT for Health Centre, University College Cork, Cork, Ireland

Michael O'Sullivan, MB, FCARCSI Department of Anesthesia, South Infirmary Victoria University Hospital, Cork, Ireland

Amanda Okundaye, DDS Department of Hospital Dentistry, UCLA, Los Angeles, CA, USA

Philip W.H. Peng, MBBS, FRCPC Department of Anesthesia, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

Mikko T. Pitkänen, MD, PhD Department of Anesthesia, Orton Invalid Foundation, Helsinki, Finland

Karen L. Posner, PhD Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA

Kenneth L. Reed, DMD New York University College of Dentistry, New York, NY, USA

Richard W. Rosenquist, MD Department of Pain Management, Cleveland Clinic, Cleveland, OH, USA

Albert H. Santora, MD St. Mary's Hospital, Athens, GA, USA

Rachael Seib, MD, FRCPC Humber River Hospital, Toronto, ON, Canada

John Shepler, MD Department of Anesthesia, University of Wisconsin Madison, Madison, WI, USA

Kari G. Smedstad, MB, ChB, FRCPC Department of Anesthesia, McMaster University, Hamilton, ON, Canada

Rizwan Somani, MSc, MD, FRCSC, ABO Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada

Rakesh V. Sondekoppam, MBBS, MD Department of Anesthesia and Pain Medicine, University of Alberta, Edmonton, AB, Canada

Peng Chiong Tan, MD Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Pekka Tarkkila, MD Department of Anesthesia and Intensive Care Medicine, Töölö Hospital/ Helsinki University Hospital, Helsinki, Finland

Bridgette Toy-Cronin Faculty of Law, University of Otago, Dunedin, New Zealand

Ban C.H. Tsui, MSc (Pharm), MD, FRCPC Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, USA

Luis O. Vasconez Birmingham Veterans Affairs Medical Center, Birmingham, AL, USA

Children's Hospital of Alabama, Birmingham, AL, USA

Brad Wakeman, BSc, OC(C) Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada

Denise J. Wedel, MD Department of Anesthesiology, Mayo Clinic College of Medicine, Rochester, MN, USA

Patrick B.Y. Wong, MD, FRCPC Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, ON, Canada

Part I

General Considerations

The History of Local and Regional Anesthesia

1

Brendan T. Finucane

Key Points

- The discovery of the local anesthetic properties of cocaine by *Koller* in 1884 was one of the most important discoveries in the history of Medicine and revolutionized the practice of Ophthalmology, Dentistry, Anesthesia, and Surgery.
- Chemists studied the pharmacological properties of cocaine and developed a series of synthetic local anesthetic compounds which were less toxic than cocaine and more predictable and efficacious.
- Systemic toxicity to local anesthetics continues to be an issue, but we have seen a significant reduction in the incidence of this problem and great advances in prevention and management.
- Spinal anesthesia was first introduced by *Bier* in 1884 and today remains one of the most reliable and safe techniques used in regional anesthesia more than 120 years after it was first introduced.
- *Bier* also introduced Intravenous Regional Anesthesia in 1908 (Bier Block) and this technique has also withstood the test of time and remains one of the most reliable techniques for short surgical procedures involving the upper extremity.
- A succession of leading figures in regional anesthesia have introduced and developed a number of safe and effective local and regional techniques, including epidural anesthesia and numerous peripheral nerve blocks. The lives of these great contributors to local and regional anesthesia are highlighted in this chapter, all of whom also wrote classic textbooks on the subject of regional anesthesia.
- The introduction of nerve stimulation more than 40 years ago represented a significant advance in the practice of regional anesthesia and the importance of this advance is emphasized in this chapter.
- The recent introduction of ultrasonography has transformed regional anesthesia practice, increasing safety and precision of nerve blocks.

Definitions

Regional anesthesia is defined as the selective blockade of a nerve or group of nerves supplying an area of the body such as a limb(s) or an eye, using local anesthetics, thereby allowing a surgeon to operate on a patient without the need for full general anesthesia. *Local* anesthesia is a non-selective blockade of a smaller area of the body by infiltrating with local anesthesia directly into the skin, subcutaneous, and deeper tissues, without any attempt to target a particular nerve. *Topical* anesthesia refers to anesthesia of the skin or mucous membranes which occurs following topical application of a local anesthetic.

A number of different approaches to regional anesthesia were tried before and after general anesthesia was introduced in 1846, but none of them were satisfactory. These included: nerve compression, refrigeration, alcohol injections, acupuncture, and ether sprays, but no real progress was made until the discovery of local anesthetics.

Of course in order to perform local and regional anesthesia, we must have a delivery system. Therefore, you should know that *Sir Francis Rynd* performed the first nerve block injection for the treatment of trigeminal neuralgia using morphine dripped through a cannula and this took place in the Meath Hospital in Dublin, Ireland, in 1844 [1]. *Alexander Wood* improved on this by producing a hollow needle in 1853 [2]. And the hypodermic syringe, known in Europe as the *Pravaz* syringe, was introduced in 1853 [3].

B.T. Finucane, MB, BCh, BAO, FRCA, FRCPC (✉)
Department of Anesthesiology and Pain Medicine,
University of Alberta, Edmonton, AB, Canada
e-mail: bfinucane6@gmail.com

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_1

The Discovery of Local Anesthetics

It has been known for centuries that the chewing of the coca leaf resulted in numbness of the tongue and lips. *Gaedeke* extracted the active principle of the coca leaf in 1855 and named it erythroxyline [4]. In 1858, the Austrian government sent the frigate Novara on an expedition around the world. A trade expert on board named Dr.Scherzer took samples of the coca leaf and upon return gave them to a knowledgeable chemist at the University of Gottingen in Germany, named Wohler. Dr.Wohler and his assistant *Niemann* isolated the crystal extract from the coca leaf and named the alkaloid cocaine [5].

Moreno y Maiz, a Peruvian army surgeon, saw the potential of sensory anesthesia with cocaine in a manual he wrote for the military in 1868 [6]. *Van Anrep* in 1879 observed the local numbing effects of cocaine on the throat and the dilation of the pupil upon local application to the eye, but he did not observe that the conjunctiva was anesthetized [7]. However, *Karl Koller* (Fig.1.1) put all this information together and discovered the local anesthetic properties of cocaine [8]. This happening deserves the full details.

Koller had studied cocaine in depth as a result of his friendship with *Freud* when they were in Vienna, so he was very knowledgeable about the compound. He was also highly motivated to find a suitable analgesic for patients undergoing eye surgery. General anesthesia was not used by ophthalmologists for cataract surgery because of severe post-operative nausea and vomiting frequently associated with its use, so most cataracts were performed without any anesthesia. Following is an extract from Koller's own writing on the topic:

> *The unsuitability of general narcosis for eye operations; for not only is the co-operation of the patient greatly desirable in these operations, but the sequelae of general narcosis-vomiting, retching and general restlessness-are frequently such as to constitute a grave danger to the operated eye; and this was especially the case at the time when narcosis was not skilfully administered as it is now, by trained experts. Eye operations were formerly being done without any anesthesia whatsoever* [9]

Fig. 1.1 Karl Koller (1857–1944). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

Following is a description of cataract surgery performed without anesthesia in 1882:

"*It was like a red-hot needle in yer eye whilst they was doing it. But he wasn't long about it. Oh no. if he had been long I couldn't ha' beared it. He wasn't a minute more than three quarters of an hour at the outside*"—an old man's description of his cataract operation to Thomas Hardy and his wife on their visit to Dorsetshire in 1882 [10].

Freud and *Koller* both worked at the same hospital in Vienna, and in the summer of 1884, *Freud* planned a trip to Germany and asked *Koller* if he would continue clinical research on cocaine in his absence. *Koller* agreed to do so. *Freud* had left some of the powdered cocaine to continue the experiments. *Koller* allowed one of his colleagues (Engel) to taste the cocaine and Engel said: "*how that numbs the tongue*". *Koller* immediately said: "*Yes that has been noticed by everyone that has eaten it' and in the moment it flashed upon me that I was carrying in my pocket the local anesthetic for which I had searched some years earlier.*"

Koller went straight to his laboratory and asked his assistant for a guinea pig for the experiment. This moment was observed by Dr.Gaertner, an assistant in Stricker's laboratory, who said the following. "*A few grains of cocaine were dissolved in a small quantity of distilled water. A large lively frog was selected from the aquarium and held immobile in a cloth, and now a drop of the solution was trickled into one of the protruding eyes. At intervals of a few seconds the reflex of the cornea was tested by touching the eye with a needle...After about a minute came the great historic moment, I do not hesitate to designate it as such. The frog permitted his cornea to be touched and even injured with out a trace of reflex action or attempt to protect himself, where as the other eye responded with the usual reflex action to the slightest touch. 'Now it was necessary to go one step further and to repeat the experiment upon a human being. We trickled the solution under the upraised lids of each other's eyes. Then we put a mirror before us, took a pin in hand and tried to touch the cornea with its head. Almost simultaneously we could joyously assure ourselves, "I can't feel a thing*".

This information was obtained from Koller's daughter who went through his papers after his death and found notes

her father had left about the actual discovery. This information was published in the Psychoanalytic Quarterly in 1963 some 20 years after *Koller's* death in 1944 [11].

Koller's discovery had an enormous impact immediately. Within 1 year of his discovery, cocaine was used in all parts of the developed world for cataract surgery. *Koller* was just 27 years of age when he made the discovery that led to the widespread use of local anesthetics all over the world. Local anesthetics are still among the most important and frequently used medications in Medicine, Surgery, and Dentistry and Anesthesia today. It is interesting to note that *Morton* gave his first public demonstration of etherization when he was 27 years old. By the turn of the twentieth century, General, Local, Regional, and Topical Anesthesia had all been discovered.

Evolution of Local Anesthetics

It soon became apparent that cocaine was a very toxic substance, and between 1884 and 1891, 200 cases of toxicity had been reported and as many as 13 deaths had occurred [11]. Cocaine was also an addictive substance. Chemists and pharmacologists studied the structure of cocaine and this led to the introduction of the first synthetic local anesthetic, novocaine [12], (later to be named *procaine*) in 1904. *Procaine* was an *ester* compound, and although much less toxic than cocaine, was not the most reliable local anesthetic, was quite short acting, and was somewhat unstable when sterilized and was associated with allergies. In the ensuing years, numerous local anesthetics were tested with variable results, but *procaine*, even with its limitations, was still considered to be the gold standard for almost 50 years. In the 1940s, *Löfgren* and *Lundqvist* from Sweden experimented with local anesthetic compounds and discovered *Xylocaine* (LL30), also known as lidocaine, an *amino-amide* compound which proved to be an outstanding local anesthetic [13]. Lidocaine was the prototype and quickly replaced procaine (novocaine) as the gold standard of local anesthetics. These compounds proved to be very stable and allergies occurred rarely. To this very day, *Xylocaine* is still considered the gold standard of local anesthetics and it is interesting that its discovery, like the local anesthetic effects of cocaine, was first uncovered by tasting! (*Löfgren* used taste to determine which local anesthetic compound was better than another—from the book entitled, "Xylocaine: a discovery, a drama, an industry," by *Lindqvist and Sundling* [14].)

Systemic toxicity was a problem with all local anesthetics from the very beginning and continues to be a problem to this day. The most serious reactions occur when local anesthetics are injected into the circulation (in error). Although the *amino-amide* compounds proved to be highly effective and relatively safe, the duration of action was a limiting factor with their use. The addition of epinephrine prolonged the duration of action of these compounds significantly, but the maximum reliable duration was only about 2–4 h for most major nerve blocks. The search continued for the ideal local anesthetic. In 1957, *Bo Af Ekenstam* introduced a new group of long-acting local anesthetics and these were the *pipecholylxylidine* compounds represented prominently by bupivacaine [15]. This group of compounds presented a new set of problems in that they were highly toxic not just to the central nervous system (CNS), but also to the cardiovascular system. Etidocaine and bupivacaine were the first *pipecholylxylidine* compounds used clinically and were approved for use in humans in the early 1960s, first in Europe and later in the United States. They were characterized by a markedly increased duration of action compared to lidocaine and were initially received with great enthusiasm. Etidocaine was much faster acting than bupivacaine because it was highly lipid-soluble, but was associated with profound motor blockade that sometimes outlasted the sensory blockade, which was very disturbing to some patients. This unusual problem was only one factor that led to etidocaine being relegated to the shelf. In 1979, *Albright* wrote a powerful editorial exposing the dangers of both etidocaine and bupivacaine[16]. Both of these local anesthetics were associated with numerous deaths in both the United States and the United Kingdom due to selective and lethal cardio-toxicity that did not come to light for more than 10 years after the drugs were first approved for clinical use. A number of the fatalities reported with these compounds occurred in healthy young patients and a high percentage of these fatalities occurred in young parturients. Unlike the *amino-amides* and *amino esters*, the *pipecholyl xylidine* compounds caused serious cardiac toxicity at blood levels close to those associated with CNS toxicity. Furthermore, treatment of both CNS and cardiac toxicity was very difficult and required prolonged and aggressive resuscitation as these compounds were highly lipid-soluble and attached firmly to both CNS and cardiac receptors. This episode led to a major investigation of these compounds by the FDA and restrictions were placed on the use of these compounds thereafter. The practice of regional anesthesia and use of local anesthetics was carefully scrutinized by the leaders in the field of regional anesthesia, which led to a series of safety guidelines published by the American Society of Regional Anesthesia. Furthermore, the academic anesthesia community was again challenged to produce a safe and reliable local anesthetic.

Just as the anesthesia community was recovering from the bupivacaine/etidocaine tragedy it was faced with another toxicity problem, this time associated with the use of 2-chloroprocaine (Nesacaine-CE). This ester compound was synthesized in 1949 and promoted by *Foldes* for obstetric anesthesia based on a greatly reduced potential for systemic toxicity [17]. *Ansbro* et al. estimated that the risk of systemic toxicity was 1/20 that of lidocaine when injected epidurally[18]. It became very popular in obstetric anesthesia because the risk to the fetus from trans-placental transfer was practically eliminated. In the early 1980s, there were reports of serious neural deficits following accidental subarachnoid injection of 2-chloroprocaine in

obstetric patients. The formulation of 2-chloroprocaine used contained preservatives (sodium bisulfite) and was not intended for subarachnoid use. The controversy continued for years afterwards as to whether the neural deficits were caused by the local anesthetic itself or the preservative. Eventually, a preservative-free chloroprocaine was introduced and is now being used for spinal anesthesia in ambulatory patients in some medical centers in the United States.

When all the controversy about systemic and neural toxicity of local anesthetics subsided, most clinicians agreed that, despite the toxicity potential of bupivacaine, it was otherwise an excellent local anesthetic.

This discussion brings us into the world of stereochemistry[19]. If we take a closer look at the chemistry of bupivacaine, we find that it is a *chiral* compound and can exist in two forms (enantiomers) depending on how each one responds to polarized light. Enantiomers have identical physical properties and have the same chemical formula and the only way they differ is in how they respond to polarized light. The enantiomer is dextrorotatory R (+) if polarized light is rotated to the right and levorotatory S (−) if rotated to the left. Bupivacaine is a racemic mixture containing equal parts of both enantiomers that neutralize each other and therefore do not rotate the plane of polarized light. In the process of studying stereochemistry, investigators learned that the S enantiomer of bupivacaine was less cardiotoxic. The S enantiomer was produced and marketed as levo-bupivacaine (Chirocaine) and proved to be less likely to cause cardiotoxicity. Ropivacaine was subsequently introduced after in-depth study and it too is the S enantiomer and theoretically even less toxic than levo-bupivacaine.

The pharmaceutical industry invested a huge amount of Research and Development funds into the development of the *chiral* compounds and it is unlikely that they will invest much more in this area of research at least in the near future. Yet there is a serious need for a good short-acting local anesthetic for spinal anesthesia in ambulatory surgery. There is still some discomfort among clinicians about using 2-chloroprocaine in spinal anesthesia. And after 50 years of apparent safe use, 5 % lidocaine is no longer acceptable as a spinal anesthetic as a result of reports of Transient Neurologic Symptoms in a significant number of patients following its use [20]. Also, more serious side effects have been reported with lidocaine 5 %, following subarachnoid injection through continuous micro-catheters.

Although the issue of systemic toxicity to local anesthetics continues to be a permanent risk, a great breakthrough has taken place recently in the treatment of this malady. Like many advances in medicine, it was accidentally discovered that systemic injections of lipids acted as a sponge which soaked up lipid-soluble medications and quickly and efficiently reduced the concentration of these toxic compounds in the circulation [21]. This is a brief summary of the history of local anesthetics without which we could not have Regional Anesthesia. Please refer to Chap. 3 for a more complete discussion of Local Anesthetics and Systemic Toxicity of local anesthetics.

The Birth of Regional Anesthesia

The same year that *Koller* discovered local anesthetics (1884), *Halsted* performed a brachial plexus block in a patient in the United States and so began the practice of Regional Anesthesia using injectable local anesthetics [22].

Leonard Corning (Fig.1.2), a neurologist from New York, was most likely the first person to perform spinal anesthesia, but apparently was not fully aware that he had done so at the time [23]. He described an experiment on a dog in which he injected 1.18 mL of 2 % cocaine hydrochloride into the space "situated between the spinous processes of two inferior dorsal vertebrae" with the result that the animal did not react for several hours afterwards if a stimulus was applied from a powerful faradic battery or through pinching or pricking the hind limbs. He did a similar experiment on a human with the same results and concluded the following: *Corning* actually believed that cocaine injected into the region between the two spinous processes was absorbed by the veins and 'then transferred to the substance of the cord and gave rise to anesthesia of the sensory and perhaps motor tracts of the same'. He said this in his own writings. *Corning* was more interested in relieving pain than he was of producing anesthesia. *Corning* was a prolific writer, and in 1894, he described 'The irrigation of the cauda equina with medicinal fluids…' "*I became impressed with the desirability of introducing remedies directly in to the spinal canal with a view to produc-*

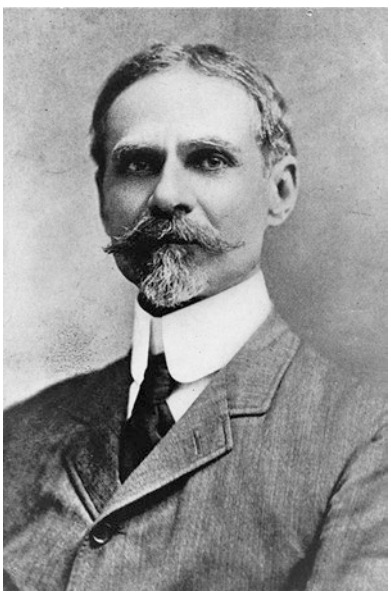

Fig. 1.2 James Leonard Corning (1855–1923). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

ing still more powerful impressions on the cord and more especially on its lower segment." Probably, the reasons why *Corning* did not make the connection between the injection of the local anesthetic and spinal anesthesia was that when he inserted a needle he always had a syringe attached to it. So he never saw CSF drip back and therefore perhaps did not appreciate that he was in the subarachnoid space on some of these occasions, which would explain some of his observations. However, he still deserves the credit for the first subarachnoid injection of a local anesthetic.

Corning published one of the first textbooks on Local Anesthesia in 1886 [24], and the first textbook on pain in 1894 [25], but nothing came of his suggested use of spinal anesthesia for surgery.

The Discovery of Spinal Anesthesia by Bier

Another dramatic breakthrough occurred in Regional Anesthesia in 1898 and that was the first recording of spinal anesthesia in a human by *August Bier* [26]. *Bier* was influenced by his senior mentor surgeon *Heinrich Quincke* who studied in depth the anatomy of the spinal canal and the spinal nerves and who pioneered the technique of lumbar puncture and treated patients with hydrocephalus and tuberculous meningitis by performing lumbar puncture as a therapeutic intervention [27]. Figure 1.3 shows a picture of *August Bier*, one of the great figures of surgery in Germany. He was born near Waldeck in Germany in 1861. He was educated in Berlin and Leipzig and graduated from medical school at Kiel in 1889 and dedicated his life to surgery and he worked as an assistant to the famous surgeon Professor *Friedrich von Esmarch* [28]. In 1898, Bier worked with *Heinrich Irenaeus Quincke*. He was also familiar with *Koller's* work with cocaine. It is likely that he put the two ideas together and developed the technique of spinal anesthesia, a technique that we perform today in much the same way it was performed by *Bier* 119 years ago. Bier anticipated that the injection of cocaine into the subarachnoid space would result in anesthesia of the lower body. He described his technique in 6 patients using 10–20 mg of cocaine and the first of these experiments occurred on August 16 1898. *Bier* was not happy with the initial results because the patients had intractable headaches and many of them were vomiting for days afterwards. *Bier* decided that he needed to experiment a little more before suggesting that this was a viable and safe technique. In his opinion, the results were not much better than those achieved with chloroform. *Bier* asked his colleague *Hildebrandt* to perform spinal anesthesia on him. *Hildebrandt* obliged but had trouble attaching the syringe containing the cocaine to the needle, and by the time he did so, most of the CSF had drained from the spinal canal and no anesthesia developed. *Hildebrandt* obliged *Bier* by inviting him to perform spinal anesthesia on him. *Bier* successfully performed a lumbar puncture on his colleague and then injected 5 mg of cocaine and obtained a very satisfactory spinal block, and to prove the success of this block, they performed a number of tests including pulling the pubic hair, hard pressure on and pulling of the testes, and a sharp blow with an iron on the shin! These experiments which began at 7.30 PM in the evening were followed by dinner, wine, and cigars. Both volunteers suffered headaches and nausea and vomiting for a day or 2 afterwards. *Bier's* symptoms of headache and dizziness were relieved when he lay down and could easily be attributed to leakage of CSF, and those of *Hildebrandt*, which included vomiting, suggest that meningeal irritation may have been the cause. *Bier* was quite discouraged by his observations and did not feel justified in continuing his work on patients without further animal work. *Bier* published the first paper on spinal anesthesia in 1899 and this was followed by another paper on this topic 3 months later by *Tuffier* in France [29]. *Tuffier* was more enthusiastic about his experiences and reports from America soon after supported this. One of the first reports of spinal anesthesia performed in the United States was written up by *Matas* et al. from Charity Hospital in New Orleans in the United States on December 18 1899 [30]. The technique was not widely practiced until newer and safer local anesthetics were introduced.

Fig. 1.3 Professor August Bier (1861–1949). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

While we can all agree that the discovery of local anesthetics truly heralded the dawning of regional anesthesia, the discovery of spinal anesthesia was a huge advance. As mentioned before, the novelty and enthusiasm of general anesthesia was waning especially when deaths were reported and so spinal anesthesia was greeted with great enthusiasm by the surgeons, who were not used to the profound degree of muscle relaxation associated with its use, especially when performing abdominal surgery.

Spinal anesthesia was the mainstay of regional anesthesia for the first 20 years or so of its use. During that time, great advances were made in the physiology and pharmacology of spinal anesthesia. The concept of baricity was introduced [31], new local anesthetic mixtures were used, and spinal anesthesia was found to be highly successful especially for procedures involving the lower abdomen, perineum, and lower extremity. Continuous techniques were used first using a malleable needle and subsequently continuous catheters were inserted for prolonged surgery. The great advantage of spinal anesthesia was the profound muscle relaxation associated with its use particularly for abdominal surgery. At the same time, the major drawback even today is the problem of spinal headache which, even with greatly advanced needle technology, continues to tarnish the reputation of a technique that has withstood the test of time.

Sir Robert Macintosh (Fig.1.4) was one of the great proponents of spinal anesthesia and wrote a remarkable handbook named *Lumbar Puncture and Spinal Anesthesia*, which has amazing illustrations and is still available today [32]. The fourth edition was published in 1978 by Lee and Atkinson and many more editions have been published since then. Spinal anesthesia was very popular in Great Britain until a very highly publicized tragedy involving spinal anesthesia was reported in the British Press (*Times*) in 1947 (*Wooley and Roe*) [33]. In this case, two patients in adjoining operating rooms remained permanently paralyzed following spinal anesthesia for relatively minor procedures. This report put an end to spinal anesthesia in the United Kingdom (UK) for the ensuing 50 years. *Sir Robert Macintosh* testified at the trial. The doctor involved in these cases was acquitted at trial. Spinal anesthesia came under serious scrutiny in the United States a few years later when a report by a prominent (former British) neurologist (*Foster Kennedy*) inferred that spinal anesthesia was associated with permanent paralysis, based on his observations in a series of 12 cases of paralysis following spinal anesthesia [34]. However, *Kennedy's* allegations were proven to be incorrect in a subsequent report by *Dripps and Vandam,* when they published one of the first major outcomes studies of spinal anesthesia involving more than 10,000 cases [35]. These authors definitively proved that spinal anesthesia was rarely associated with paralysis.

Fig.1.4 Professor Macintosh (1897–1989). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

Evolution of Regional Anesthesia

Regional anesthesia was greeted with great enthusiasm by surgeons at least initially because it gave them a sense of independence and autonomy because they did not have to rely on someone else to induce unconsciousness, which in those days could take as long as 30 min in the best of hands. The surgeon was now in control of his/her own destiny. This worked very well with spinal anesthesia, but not so well with other forms of regional anesthesia because the discipline of regional anesthesia was still in its infancy. Sometimes we forget that regional anesthesia was originally firmly in the domain of surgery.

Intravenous Regional Anesthesia (The Bier Block)

Bier's name is also associated with another remarkable regional anesthesia technique known as the *Bier* block [36]. *Bier* was mentored by *Friedrich von Esmarch*, a famous German surgeon who introduced the Esmarch bandage. One of *Bier's* other important discoveries was the use of passive hyperemia using the Esmarch bandage to treat tuberculous bones and joints in 1907. This likely led to his idea of intravenous regional anesthesia. This idea was not very practical initially because it required a venous cut-down at the elbow. Sixty years later, a simple modification of *Bier's* technique by *C Mck Holmes* established the *Bier* block as one of the most reliable regional anesthesia techniques for upper extremity surgery of short duration [37]. Instead of using a cut-down, *Mck Holmes* inserted a plastic cannula into the venous system and the local anesthetic was injected below an inflated tourniquet. *The Bier block* or intravenous regional anesthesia remains one of the most reliable forms of regional anesthesia of the upper extremity for procedures lasting 45 min or less. The technique can also be used for lower extremity surgery, but not as reliably or safely.

Regional Anesthesia-Pre-emptive Analgesia

One of the early enthusiasts of regional anesthesia in America was *George Crile*, the founder of the Cleveland Clinic [38]. His theory of "anoci-association" was quite advanced at that time.

He recognized that patients still responded to noxious stimuli under general anesthesia, but that this response was blocked in patients who had combined regional/general anesthesia. He theorized that by preventing the noxious stimuli from reaching the brain, he prevented "surgical shock" in some patients. This theory was formulated in 1908 and was the forerunner of a more recent theory of 'pre-emptive analgesia' put forward by *Woolf* et al. in 1993, proving in animals at least, that we can prevent or greatly reduce 'wind up', altering in a positive way the metabolic response to trauma and greatly reduce or prevent the risk of chronic pain following surgery [39].

Peripheral Nerve Blockade

Victor Pauchet (1869–1936) was another great pioneer of regional anesthesia in France in the early 1900s and wrote a text book on the subject of regional anesthesia and fostered the idea of using peripheral nerve blocks in surgery, including intercostal and paravertebral blocks in addition to spinal anesthesia [40]. *Gaston Labat* was one of Pauchet's trainees [41]. In 1920, *Charles Mayo* was visiting *Pauchet* in his hospital in Paris demonstrating some surgical techniques[42]. *Mayo* was quite impressed by *Labat's* skill set in regional anesthesia and invited him to Rochester, Minnesota in the USA, to teach regional anesthesia to his colleagues. *Labat* impressed a number of the doctors at Mayo, but his tenure there was short, but he did manage to publish an outstanding textbook entitled: *Regional Anesthesia-Techniques and Application* (on the basic principles of regional anesthesia) in 1922. This text book is still considered to be one of the classic textbooks ever published on the topic of Regional Anesthesia. *Labat* moved to New York to Bellevue hospital and worked with and taught *Emery Rovenstine* the principles of regional anesthesia. *Labat* was a great teacher of regional and his book was by today's standards a medical best seller with more than 10,000 copies sold during his lifetime. *Labat* had a significant following in New York and his enthusiasm as a teacher of regional anesthesia led to the formation of the American Society of Regional Anesthesia (ASRA) in 1923. This group consisted mostly of surgeons in the beginning, but with time specialists in anesthesia dominated the group. *Labat* was the first physician to dedicate his career solely to regional anesthesia. He was initially trained as a surgeon, but spent most of his career performing, teaching, and writing about regional anesthesia. *Labat* died from complications following a cholecystectomy in New York in 1934. ASRA was disbanded in 1939 and was reformed again in 1975 by *Alon Winnie*, *Don Bridenbaugh*, *Harold Carron*, *Jordan Katz*, and *Pritvi Raj* (Founding Fathers). *Labat's* name is memorialized by the annual award (Medal) given by the ASRA for outstanding contributions to Regional Anesthesia.

Epidural Anesthesia

Sicard and Cathelin injected cocaine into the epidural space caudally in 1901 [43, 44]. *Fidel Pages-Mirave* described the lumbar approach to the epidural space in 1923 [45]. *Dogliotti* popularized the technique in the 1930s when he described the "loss of resistance technique" [46] and *Curbelo* introduced continuous epidural anesthesia in 1949 [47]. *Hingson* popularized continuous caudal anesthesia in obstetrics anesthesia in the 1940s [48]. The progress of regional anesthesia was slow, but the technique of spinal anesthesia was always an important technique in the hands of most anesthesiologists.

There were a number of strong proponents of regional anesthesia in Europe and North America in the middle of the last century, but a few names deserve special mention. Regional anesthesia was one of those pursuits that required the most enthusiastic followers because, with the exception of spinal and epidural anesthesia, there were not many followers especially when it came to peripheral nerve blocks. Most practitioners preferred general anesthesia because it was far more predictable and easier to perform.

Development of Regional Anesthesia Post WW II

Danny Moore from the Mason Clinic published an outstanding textbook on Regional Anesthesia in 1953 entitled: *Regional Block* [49]. It was the most popular book on the topic of regional anesthesia since *Labat's* classic textbook was first published in 1922. In this book, *Moore* described how to perform most regional anesthesia nerve blocks and promoted regional anesthesia on a very broad scale. *Moore* also published a very good textbook on *Complications of Regional Anesthesia (1955)* [50]. He trained a large number of residents and fellows in regional anesthesia from around the world. He led the renaissance in regional anesthesia in the USA in the post-WW II for close to 50 years and was a legend in his own time.

John Bonica was another great proponent of regional anesthesia for Obstetric patients and published an outstanding book on this topic entitled *Principles and Practice of Obstetric Analgesia and Anesthesia* [51]. He also promoted the use of regional anesthesia for chronic pain therapy and wrote two definitive textbooks on these topics, both of which are anesthesia classics. In 1990, Pope John Paul II requested a copy of his book entitled *The Management of Pain* [52]. *John Bonica* was a pioneer in the discipline of chronic pain and was the leader in establishing one of the first multi-disciplinary Pain Centers in the world. He is also a founding member of the International Association for the Study of Pain (IASP).

Fig. 1.5 Professor Philip Bromage (1920–2013). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

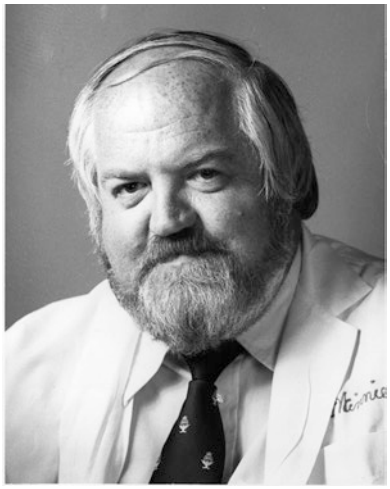

Fig. 1.6 Professor Alon Winnie (1932–2015). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

Although spinal anesthesia became obsolete in the UK in the 1950s, there was a great interest in epidural anesthesia and one of the outstanding pioneers of epidural anesthesia in the UK was *Philip Bromage* (Fig.1.5), who worked under the tutelage of *J Alfred Lee* in South-End-On-Sea in the UK. *Bromage* wrote the definitive textbook on epidural anesthesia and was a leading expert in epidural and regional anesthesia both in Europe and North America. His first text book was entitled *Spinal Epidural Anesthesia* [53]. *Bromage* moved to Montreal in 1956 and succeeded *Harold Griffith* as the Chair of Anesthesia at McGill University. He wrote the definitive textbook on *Epidural Anesthesia* in 1978 and it is today considered a classic[54]. He was very active in ASRA for many years, was a prolific writer, and a leading authority on the physiology and pharmacology of epidural anesthesia and the use of epidural and spinal opioids. He also deserves much credit for the promotion of epidural anesthesia for obstetric anesthesia in the 1960s. This new enthusiasm about epidural anesthesia for obstetrics attracted more interest in regional anesthesia also.

In the late 1960s, another great proponent of regional anesthesia emerged and that was *Alon Winnie* (Fig.1.6), who was an extraordinary teacher of regional anesthesia. Brachial plexus anesthesia was one of the great challenges to all enthusiasts of regional anesthesia. Even in the best of hands, most honest reporters could not achieve anything near 100 % success. *Winnie* described a new approach named the interscalene method and convinced most of us that the brachial plexus was contained in a single sheath, and if you could reliably place a needle in that sheath, you would have a high degree of success. His textbook entitled *Plexus Anesthesia: Perivascular Techniques of Brachial Plexus Block* is a classic and has the most spectacular illustrations [55]. *Alon Winnie* attracted a large number of new enthusiasts to regional anesthesia and he, *Don Bridenbaugh, Harold Carron, Jordan Katz*, and *Pritvi Raj* reformed the American Society of Regional Anesthesia (ASRA) and the first official meeting of that group occurred in 1975. In 2015, we celebrated 40 years of the newly formed ASRA (1975) during which tremendous advances were made in the discipline of regional anesthesia.

Pritvi Raj deserves special mention in the evolution of Regional Anesthesia. He popularized and promoted the idea of nerve stimulation to first identify the proximity of a needle to a nerve, and secondly, to actually identify which nerve was being stimulated based on a motor response. This was a major step forward because for the first time we had objective evidence indicating that a probing needle was in close proximity to a nerve based on the motor response. The first report about the use of nerve stimulation as an aid to regional anesthesia was published in 1973 [56]. The science of electro-location has evolved over the ensuing decades that it has been used and is still being used in some major anesthesia teaching centers in North America today. *Ban Tsui* has contributed enormously to our understanding of the science of electro-location today and was the first to use nerve stimulation to verify entry into the epidural space at any level. His textbook on ultrasound and nerve stimulation-guided regional anesthesia [57] is one of the most popular regional anesthesia textbooks published recently.

Nicholas Greene (Fig.1.7) was one of the great proponents of spinal anesthesia in the United States and his textbook entitled the *Physiology of Spinal Anesthesia* is one of the finest monographs ever published in the anesthesia literature and today remains a great resource in the understanding of all aspects of spinal anesthesia [58]. *Greene* was famous for his

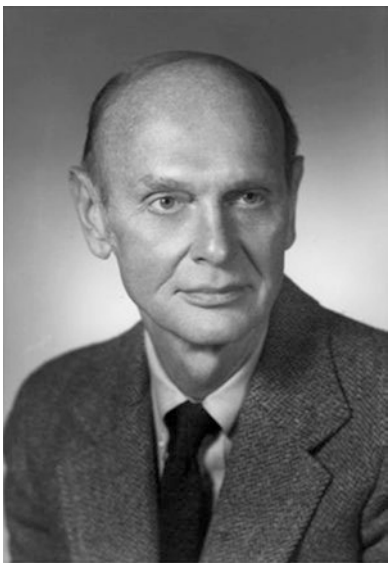

Fig. 1.7 Professor Nicholas Greene-(1922–2004). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

much quoted adage about spinal anesthesia when he said: "*position is everything in life, but especially in spinal anesthesia*". His lectures and publications on the topic of spinal anesthesia were outstanding and memorable experiences for those of us who were lucky enough to witness them.

The practice of regional anesthesia remained dormant in the UK for about 50 years after the *Wooley and Roe case*, but the French and Nordic countries were strong proponents of Regional Anesthesia. *Torsten Gordh* from Sweden was a leader in the use of regional anesthesia in his country and was among the first to test lidocaine clinically after *Löfgren's* discovery and demonstrated that lidocaine was a significant improvement on other available local anesthetics at the time [59].

Bruce Scott from Edinburgh deserves most of the credit for the revival of regional anesthesia in the UK and deservedly was named the founder and first President of the European Society of Regional Anesthesia in 1979 [60]. *Benjamin Covino* (Fig. 1.8), former Head of Research at ASTRA laboratories, was trained in regional anesthesia by *Bruce Scott*. *Covino* subsequently became one of the leading authorities on local anesthetics worldwide, and through his leadership, promoted research towards the introduction of newer, safer, long-acting local anesthetics. His textbook on local anesthetics is outstanding and concise and without a doubt is considered a classic today [61, 62].

Regional Anesthesia in the Modern Era

One of the greatest advances in regional anesthesia in recent years was the introduction of ultrasound technology to help identify peripheral nerves in regional anesthesia. This technology was first demonstrated in Europe and popularized in North America by *Vincent Chan* [63], and subsequently by *Ban Tsui* who recently published an outstanding publication entitled: *Atlas of Ultrasound and Nerve Stimulation-Guided Regional Anesthesia* [57]. The Regional Anesthesia Societies around the world(ASRA, ESRA, LASRA, AOSRA, AFSRA) deserve a great deal of credit also for hosting numerous workshops promoting the use of Ultrasound-guided regional anesthesia.

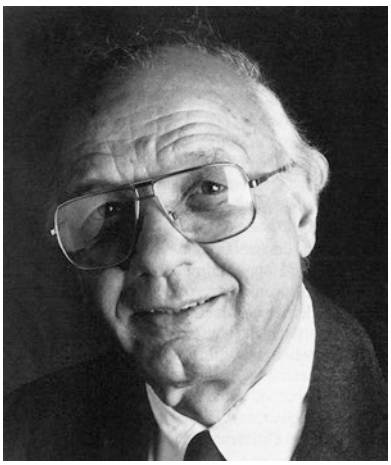

Fig. 1.8 Professor Benjamin Covino-(1931–1961). All images presented in this chapter are at the courtesy of the Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, USA

When one reflects on the progress that has been made in Regional Anesthesia since *Koller's* discovery of Local Anesthetics in 1884 just over 130 years ago, we realize how far we have come. When *Halsted* performed that first brachial block in 1884, he had the advantage of direct vision of the brachial plexus. For about 100 years, we inserted our needles blindly towards peripheral nerves based on knowledge of anatomy alone and that indeed was a very "hit and miss affair". Today, we can actually see the nerve that we wish to block and see the needle as it advances towards its target and then see and observe the results of the subsequent injection. One has to wonder how we can improve on that in the future. Without a doubt, there will be some improvement.

There are many other names that deserve mention in this brief history of local and regional anesthesia, but this chapter should be a good introduction to this fascinating subject. For a more complete history of local and regional anesthesia, we refer you to the definitive text on that topic entitled The Wondrous Story of Anesthesia [64].

Summary

The history of Local and Regional anesthesia is one of the most interesting chapters in the annals of the history of medicine and deserves special mention any time the

history of anesthesia is discussed. *Koller's eureka* moment in 1884 changed the practice of Ophthalmology overnight and sparked a new era in local and regional anesthesia in ophthalmology, dentistry, surgery, and anesthesia. Spinal anesthesia has changed very little in over 100 years of use and remains one of the most reliable techniques in anesthesia today. We have made great strides in recent years to relieve the scourge of acute postoperative pain by applying regional anesthesia techniques prior to and during surgery. We still have a long way to go before we develop reliable methods of relieving chronic pain, but we already know that the judicious use of local anesthetics, pre-emptively in some procedures, reduces the incidence of chronic pain following surgery.

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Regional Anesthesia Safety

2

John W.R. McIntyre and Brendan T. Finucane

Key Points

- A thorough preanesthetic patient history helps identify any risk factors related to the nervous, respiratory, cardiovascular, gastrointestinal, and hematologic systems. A thorough physical exam will identify any potential pitfalls or unforeseen surprises that could affect the ease and effectiveness of the nerve block.
- Use of well-designed equipment, which is appropriate for the procedure, can increase the success of regional blocks. Today's anesthesiologists have a wide range of needles, perineural catheters, nerve stimulators, ultrasound machines/probes, and monitoring devices at their disposal.
- Unique complications are associated with specific blocks and block procedures. These can occur during the block or appear during the postoperative period. Vigilance and knowledge on the part of the anesthesiologist and proper monitoring can help in identifying and addressing block-related complications perioperatively
- Prevention of complications is the key to safe and effective local and regional anesthesia practice. A preanesthetic checklist, good anatomical knowledge, patient selection, and technical skill are factors that can prevent adverse events during or after a block.

John W. R. McIntyre (deceased).

B.T. Finucane, MB, BCh, BAO, FRCA, FRCPC (✉)
Department of Anesthesiology and Pain Medicine,
University of Alberta, Edmonton, AB, Canada
e-mail: bfinucane6@gmail.com

Introduction

We are now in the third edition of this book and Professor McIntyre's observations are still very relevant today and more so in view of the fact that we are emphasizing safe practice of local and regional anesthesia. I updated the information in this chapter but the lion's share of the credit for the writing should still go to Dr. McIntyre (Fig. 2.1) posthumously.

Every patient wishes to receive anesthesia care that is safe, in other words, "free from risk, not involving danger or mishap; and guaranteed against failure" [1]. The anesthesiologist will present a more realistic view to the patient. The personal view of the hoped-for care will be one in which the clinical outcome is satisfactory and has been achieved without complication (defined as "any additional circumstances making a situation more difficult" [1]) because performance has deviated from the ideal [2]. By this standard, most deviations are trivial or easily corrected by a perfect process, and outcome for the patient and a reasonably stress-free life for the providers are objectives for all anesthesiologists. The general objective here is to provide information that helps the clinician to minimize complications that may occur during the course of local and regional anesthesia practice. This information is presented under the following headings:

- Complication anticipation
- Equipment
- Behavioral factors and complications
- Complication recognition
- Complications of specific neural blockades
- Complications in the postoperative period
- Complication prevention

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_2

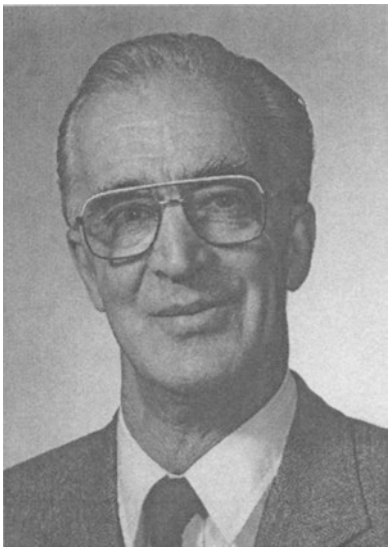

Fig. 2.1 Professor John W.R. McIntyre (1925–1998)

Complication Anticipation: Recognizing Precipitating Factors

The Preoperative Assessment: Patient History

Some anesthesiologists have a preconceived plan for regional anesthesia before they visit the patient; others gather information before considering what method of anesthesia is appropriate. The following paragraphs about the relationship between regional anesthesia and pathology are intended to aid recognition of potential complications for the patient under consideration and planning of anesthesia to avoid them.

The Nervous System

Fundamental issues to be settled during the preoperative visit are how the patient wishes to feel during the procedure and the anesthesiologist's opinion of how well the patient would tolerate the unusual sensations, the posture, and the environment. Whatever decision is made about pharmacologic support, it is absolutely essential that every patient has a clear understanding of reasonable expectations, once a plan has been made, and of the importance of revealing his or her own customary mood-altering medications. This is a convenient occasion to inquire about the patient's and relatives' previous experiences with local, regional, and general anesthesia.

Information should be sought regarding the presence of any degenerative axonal disease involving spinal cord, plexus, or nerve to be blocked and symptoms of thoracic outlet syndrome, spinal cord transaction, and lumbar lesions. Strong proponents of regional anesthesia have stated that a wide range of conditions—multiple sclerosis, Guillain–Barré syndrome, residual poliomyelitis, and muscular dystrophy—are unaffected [3], although difficulty in a patient with Guillain–Barré syndrome has been reported [4]. However, there are reports of permanent neurologic deterioration in patients with unidentified preexisting problems [5–7]. Spinal anesthesia is an effective way of obtunding mass autonomic reflexes in patients with spinal cord transaction above T5, but a mass reflex has been described in a patient with an apparently appropriate block [8]. It must be concluded that the uncertainty of outcome when regional anesthesia is used in patients with established neurologic disease demands that the technique be used only when it is clearly advantageous for the patient. It is prudent to seek out symptoms of unrecognized neurologic abnormality when planning which anesthesia technique will be used. Parkinson's disease and epilepsy are not contraindications to regional anesthesia, provided they are habitually well controlled by medications, which should be continued during and after the operative period. This topic will be discussed in much greater detail in Chap. 9.

Thus far, the concerns addressed have largely involved the possibility of long-term neuronal damage and uncontrolled muscle activity, but the rapid changes in intracranial pressure during lumbar puncture can be dangerous [9, 10]. The lumbar extradural injection of 10 mL of fluid in two patients increased the intracranial pressure from 18.8 to 39.5 mmHg in the first patient and from 9.3 to 15.6 mmHg in the second patient [11]. Among patients at risk are those with head injuries, severe preeclampsia, and hydrocephalus.

A history of sleep apnea is more a reminder of the need for meticulous monitoring than a contraindication to regional anesthesia. In any case, patients may not recognize their own sleep apnea experiences. They are more likely to know of snoring, daytime hyper-somnolence, and restless sleep.

The Respiratory System

Preoperative pulmonary function tests do not identify definitive values predictive of hypoxia during regional anesthesia, but for practical purposes, if there are spirometric values <50 % of predicted, risk is increased [12]. It is certainly so if the values are FEV < 1.0 L, FVC < 15–20 mL/kg, FEV/FVC < 35 %, PEF < 100–200 L/min, and PCO_2 > 50 mmHg. Avoidance of the airway manipulation associated with general anesthesia and preserving coughing ability are advantageous for the patient with asthma or chronic obstructive pulmonary disease. Unfortunately, that can be more than offset by a magnitude of motor blockade that decreases vital capacity, expiratory reserve volume, maximum breathing capacity, and the ability to cough, all of which can result from anesthesia for abdominal surgery. If for some reason

the patient is particularly dependent on nasal breathing, as infants are, a block that is complicated by nasal congestion due to Horner's syndrome will cause respiratory difficulty.

Clinical assessment determines the need for acid–base and blood gas measurements. Hypoxia and acidosis enhance the central nervous system and cardiotoxicity of lidocaine [13–15]. In neonates, these effects are accentuated by poor compensation for metabolic acidosis.

The Cardiovascular System

Cardiac disease has profound implications for regional anesthesia, as it has for general anesthesia. Among the systems classifying the degree of cardiac risk, Detsky's modification of the Goldman index is useful (Table 2.1) [16]. However, this risk assessment is not patient specific, and there are individual asymptomatic patients with significant coronary artery disease that is unlikely to be detected. Also, chronic and relatively symptom-free chronic valvular dysfunction may lead to sudden and severe circulatory collapse [17]. There are many potential causes of myocardial infarction in patients undergoing extra cardiac surgery, as there are for other cardiovascular complications [18]. The role of dipyridamole-thallium scintigraphy and ambulatory (Holter) electrocardiography (ECG) has attracted interest [19, 20]; however, physiologic changes that can occur in a patient during the operative period and subsets of patients to whom a specific test applies have yet to be identified with certainty [17].

Table 2.1 Detsky's modified multifactorial index arranged according to point value

Variables	Points
Class 4 angina[a]	20
Suspected critical aortic stenosis	20
Myocardial infarction within 6 months	10
Alveolar pulmonary edema within 1 week	10
Unstable angina within 3 months	10
Class 3 angina[a]	10
Emergency surgery	10
Myocardial infarction more than 6 months ago	5
Alveolar pulmonary edema ever	5
Sinus plus atrial premature beats or rhythm other than sinus on last preoperative electrocardiogram	5
More than five ventricular premature beats at any time before surgery	5
Poor general medical status[b]	5
Age over 70 years	5

Sources: Detsky et al. [16] Copyright 1986, American Medical Association. All rights reserved; Detsky et al. [17] Copyright 1986, Blackwell Publishing. All rights reserved with permission of Springer

[a]Canadian Cardiovascular Society classification for angina

[b]Oxygen tension (PO_2) <60 mmHg; carbon dioxide tension (PCO_2) >50 mmHg; serum potassium <3.0 mEq/L; serum bicarbonate <20 mEq/L; serum urea nitrogen >50 mg/dL; serum creatinine >3 mg/dL; aspartate aminotransferase abnormality; signs of chronic liver disease; and/or patients bedridden from noncardiac causes

When assessing the patient with cardiovascular problems for regional anesthesia and debating the addition, or perhaps sole use, of general anesthesia, the anesthesiologist must make predictions. These are the ability to satisfactorily control preload and afterload, myocardial oxygen supply, and demand and function. If one or more of these deviate from optimal limits, will the rate of change that may occur exceed the rate at which the therapeutic management can be developed?

The cardiac dysrhythmias of particular interest are the array of clinical disorders of sinus function (sick sinus syndrome). These are often associated with reduced automaticity of lower pacemakers and conduction disturbances. Local anesthetic drugs that diminish sinoatrial node activity, increase the cardiac refractory period, prolong the intracardiac conduction time, and lengthen the QRS complex will, in sufficient quantity, aggravate sinus node dysfunction.

It is important to realize that the pharmacokinetics of medications is influenced by certain cardiac defects. Patients with intracardiac right-to-left shunts are denied protection by the lungs, which normally sequester up to 80 % of the intravenous drug. If this is reduced, the likelihood of central nervous system toxicity is increased [21, 22].

The Gastrointestinal Tract

It is essential that the anesthesiologist obtain reliable information about the food and drink the patient has or will have taken preoperatively. A patient presenting for elective surgery will have received the customary institutional management, which may include one or more of the following: anticholinergic, histamine-receptor blocker (H2), antacid, and benzamide derivative. Based on knowledge up to 1990, the following proposals have been made. First, solid food should *not* be taken on the day of surgery. Second, unrestricted clear fluids should be permitted until 3 h before scheduled surgery [23, 24].

In a study of the effect of epidural anesthesia on gastric emptying, measured by the absorption of acetaminophen from the upper small intestine, it appeared that block of sympathetic innervation of the stomach (T6–10) did not affect gastric emptying [25]; however, epidural injection of morphine at the T4 level delayed emptying. Nevertheless, with the onset of high spinal anesthesia, antiperistaltic movements and gastric regurgitation may occur and the ability to cough is reduced during a high blockade. Thus, the value of peripheral neural blockade for a patient with a potentially full stomach cannot be overestimated: subarachnoid and epidural anesthesia do not protect patients from aspiration. Similarly, paralysis of a recurrent laryngeal nerve, a complication of

blockades in the neck region, predisposes patients to aspiration of gastric contents.

In a wide variety of abnormal circumstances, including trauma and near-term pregnancy, it is impossible to predict on the basis of the passage of time what the stomach contains. If the stomach is not empty, there are other vital considerations. In the presence of the blockade, the patient must be able to protect himself from aspiration; alternatively, in the presence of a failed blockade, it must be possible to administer a general anesthetic safely or to abandon the surgical procedure or delivery. Obstetric procedures usually brook no delay, and so it is mandatory that at some time well before the anticipated delivery date, the airway problems of pregnant patients be identified and plans made to cope with any eventuality.

The Hematologic System

Clotting Mechanisms

A regional anesthesia technique in which a hemorrhage cannot be detected readily and controlled by direct pressure is contraindicated in patients with a coagulation disorder, which might be attributed to diseases such as thrombocytopenia, hemophilia, and leukemia, or to drugs. Drugs having primary anticoagulant effects include unfractionated heparin, low-molecular-weight heparins, coumadin, and platelet inhibitors including aspirin, abciximab, clopidogrel, dipyridamole, anagrelide, ticlopidine, and tirifiban. Other drugs that to some degree influence coagulation are nonsteroidal anti-inflammatory medications, urokinase, phenprocoumon, and dextran 70.

Laboratory measurements determine the presence of a significant coagulation defect. Anticoagulation during heparin therapy is most often monitored by the activated clotting time. This method is not specific for a particular part of the coagulation cascade, and for diagnostic purposes, a variety of other tests are used: prothrombin (plasma thromboplastin) time, activated partial thromboplastin time, platelet count, and plasma fibrinogen concentration. Even in combination, however, these fail to provide a complete description of the status of the coagulation system. It is possible that viscoelastic methods are a convenient technique to monitor perioperative bleeding disorders [26].

Once a detailed history of drug use and laboratory measurements is available, a decision regarding the potential complications of central neural blockade, with or without catheter insertion, may be necessary, as may the influence of an anticoagulated state on postoperative developments.

Clinical experiences with these dilemmas have been comprehensively reviewed [27, 28], the conclusion being that performing epidural or spinal anesthesia in patients treated with drugs that may jeopardize the normal responses of the clotting system to blood vessel damage is a concern. It is clear that major nerve-blocking techniques can be used in some patients who have received or will be receiving anticoagulant drugs. This success is not only dependent on an appreciation of the properties of different anticoagulant managements and a skilled regional anesthesia technique but also very careful postblockade monitoring. Thus, the advantages of the regional block envisaged must be carefully compared with other anesthesia techniques for the patient and the overall patient care available.

"Histaminoid" Reactions

Histaminoid refers to a reaction whose precise identity—histamine, prostaglandin, leukotremia, or kinin—is unknown. Few patients would recognize that term, and it is wiser to inquire of "allergy or sensitivity experiences." This is particularly valuable information if the patient describes a situation that the anesthesiologist has contemplated repeating [29]. The patient's story should not be discounted by attributing the reported events to epinephrine or a misplaced injection.

The dose or rate of administration does not affect the severity of a histaminoid reaction. Additionally, many studies have shown that reactions occur more often in patients with a history of atopy [30], but that a history of allergy is not predictive of severe clinical anaphylaxis [31]. The patient's history, or lack of it, is important and may guide the anesthesiologist away from certain drugs; however, an unexpected reaction will challenge some anesthesiologists, somewhere, sometime, and that complication will demand immediate recognition and treatment.

Pseudocholinesterase Dysfunction

If a patient's red cell cholinesterase is deficient or abnormal, drugs metabolized by that enzyme, such as 2-chloroprocaine, will be broken down more slowly, lowering the toxicity threshold [32, 33].

Methemoglobinemia

Drugs predisposing to methemoglobinemia are aniline dyes, nitrites, nitrates, sulfonamides, and antimalarial medications. It may also be associated with hemoglobinopathies and glucose-6-phosphate dehydrogenase deficiencies. The local anesthetics benzocaine, lidocaine, and prilocaine can contribute to methemoglobinemia.

Muscle Disease

Inquiries about muscular dystrophy, myasthenia gravis, and malignant hyperthermia are part of the preanesthetic evaluation, regardless of the contemplated anesthetic technique. It has been stated that neither amide nor ester-linked local anesthetics are contraindicated in such cases [34], we now have a clear message from the Malignant Hyperthermia Association of the United States (MHAUS) that all local

anesthetics in common use today are safe to use in patients at risk of malignant hyperthermia [35].

If the patient has a muscular dystrophy it is important to know because of associated problems that may be present, such as ECG abnormalities, but regional anesthesia is not contraindicated and may indeed be the technique of choice.

Diabetes

Diabetic patients usually announce their disease, but some leave the anesthesiologist to find out. It is important that the anesthesiologist knows that a patient is diabetic, because although neural blockade may be the technique of choice in some respects, the peripheral neuropathy and autonomic dysfunction associated with the disease have implications, particularly if they are in the area to be blocked. Preanesthetic symptoms and signs should be carefully documented.

Notably, a central conduction block limits the normal physiologic response to hypoglycemia and a diabetic patient can be unduly sensitive to the normal insulin regimen. This may complicate postoperative care [36, 37].

Miscellaneous Medications

Neural blockade complications clearly caused by drug interactions are rare, but possibilities can be taken into account during anesthesia planning and in diagnosing any complications detected later.

Aspirin

Aspirin therapy, because of its antiplatelet activity, may increase the risk of bleeding, which in, association with central neural blockade, is potentially tragic. The effect of the drug on platelets is irreversible and lasts 7–10 days; thus, some assessment of platelet function should be made in aspirin-treated patients [38]. Today, measurement of the bleeding time is the only practical test of in vivo platelet function. It may return to normal 72 h after discontinuation of the drug, but in vitro platelet aggregation tests require much more time. If the bleeding time is 10 min or more, the clinician must weigh the relative disadvantages for that patient of other forms of anesthesia and analgesia.

Quinidine and Disopyramide

Laboratory studies showed that lidocaine metabolites and the metabolites of several antiarrhythmic agents had little effect on lidocaine protein binding. However, bupivacaine, quinidine, and disopyramide caused a significant increase in the lidocaine free fraction. These effects could cause unexpected drug-related complications [39].

Benzodiazepines

Diazepam enhances the cardiovascular toxicity associated with bupivacaine and verapamil [40]. Benzodiazepines mask the early signs of systemic toxicity, so that the first evidence of problems may be cardiorespiratory depression.

Verapamil

Verapamil increases the toxicity of lidocaine and bupivacaine in mice [41], and cardiovascular collapse in patients has been reported [42].

Nifedipine

Nifedipine increases the toxicity of bupivacaine in dogs [43].

The Preanesthetic Visit: Physical Examination

The routine preoperative examination for anesthesia is described in many textbooks. The following paragraphs address matters that, although interesting at any time, are particularly important for the anesthesiologist contemplating performing a neural blockade. Positive answers to the following questions are not necessarily contraindications to regional anesthesia; indeed, they may support its selection, but they do indicate matters that must be given particular consideration.

Positioning for the Block

- Is the patient so large or heavy that a dangerous strain may be placed on tables, stools, and assistants unless special precautions are taken?

Blood Pressure

- Is the patient hypertensive or hypotensive?

Oxygenation

- Is the patient hypoxic?

Blood Volume

- Is the patient hypovolemic?

Infection

- Is there dystrophic skin or infection at the site of needle entry or infection in the needle track?
- Is there systemic infection in the body?
- Is the patient febrile?

Previous Surgery

- Are there scars anywhere indicating previous trauma or surgery that the patient has not mentioned?

Abdominal Masses
- Is an abdominal mass present that could impair venous return or respiration?
- Is there a gravid uterus beyond the first trimester that could impair venous return and influence the spread of subarachnoid injections?

Venous Access
- Will venous access for medications or fluids be easily obtained?

The Upper Airway
- In an emergency situation, can the anesthesiologist easily take control of the patient's airway, ventilate the patient, and prevent aspiration?

Technical Difficulty Performing the Proposed Block
- Will arthritis, amputation, or obesity hinder positioning the patient?
- Does obesity obscure bony landmarks?
- Is arthritis likely to hinder neural access?
- Are spinal defects, abnormalities of vertebral fusions, or foreign bodies present to hinder neural access?
- Can the arm be moved into a suitable position?
- Is there a hindrance to positioning a tourniquet?

Lymph Glands
- Are there axillary or femoral lymph glands in the needle path for the proposed block?
- Evaluating the Hemodynamic Status of the Limb
- Will a cast or other hindrance prevent monitoring of peripheral blood flow in a limb?

Conclusion

Surprises for an anesthesiologist in the block room are usually stressful, potentially hazardous for the patient, and may delay the operating room schedule. It is cautionary to realize that, in complex processes, be they medical care or industry, dangerous situations result from a sequence of events. Failure to obtain a certain item of information at the preanesthetic visit can be compounded by related events in the surgical or dental suite and the recovery area. The preoperative visit is the opportunity to plan the patient's anesthetic, be it a technique of regional anesthesia, general anesthesia, or a combination. A structured interview and examination is one facet of safe regional anesthesia practice.

Equipment

The objective for any attempted neural blockade is to produce the anesthesia required, and thus a major complication is block failure. Neural blockade may fail for pharmacologic or pharmacokinetic reasons, because the anesthesiologist lacks mental imagery of the anatomy, manual dexterity, or tactile sensitivity. Well-designed equipment does not make the user skilled, but it can diminish the complication of "failed spinal" and other complications associated with needle placement. The following is a collation of published data criteria believed to influence successful identification of the location for the anesthetic and of the complications associated with these attempts. Ultrasound-guided needle placement has greatly enhanced success rates of regional anesthesia particularly those involving peripheral nerves, in recent years.

Spinal Needles

Clinical Reports

The size of needles ranging from 18 to 25 gauge do not affect the success rate for subarachnoid tap [44, 45], and Whitacre 25 and 27 gauge, Quincke 25 gauge, and Sprotte have been used satisfactorily [46–49]. Thinner needles (29 and 30 gauge) have a greater tendency to deviate during their passage through ligamentous tissues, and an introducer through which those needles can be passed is essential [50–52].

Cerebrospinal fluid (CSF) spontaneous flow through a 29-gauge needle appears extremely slowly, if at all, even if the hub is clear plastic instead of metal. Similarly, injection of fluid can be accomplished only slowly, and drug distribution may be affected [51].

Spinal anesthesia in children can safely be done with 22- or 25-gauge spinal needles or the hollow stylet from a 24-gauge Angiocath.

Headache is primarily a complication of spinal tap in adults. An extensive and critical analysis of clinical reports concluded that the smallest gauge needle with a noncutting tip reduces its likelihood [53, 54]. Thus, choice of needle gauge is a compromise because using a very fine needle is more difficult. It has been suggested that when avoiding headache is paramount, Quincke or Whitacre 27 gauge are the needles of choice [55]. Waiting times for the appearance of CSF, with the patient in a lateral position using these needles were 10.8 ± 6.9 and 10.7 ± 6.8 s, respectively.

Laboratory Reports

Laboratory reports address the technical problems about which clinicians speculate and some complications to avoid. The conclusions are summarized next.

Changing the Needle Direction During Insertion

Deliberate change of direction of a needle is customarily done by almost complete withdrawal and subsequent reentry, and inadvertent deviation during advancement is misleading. A laboratory model demonstrated the occurrence of needle deviation and the influence of needle point design and gauge [56]. It was least with pencil-point spinal needles and greatest with beveled spinal needles. The needle deviation with beveled needles was consistent in direction as well as degree, in contrast to pencil-point tip configurations. Thus, rotating a beveled needle during insertion and redirection may hinder future identification of the epidural or subarachnoid space.

Resistance to Penetration of the Dura Mater

The human dura mater is relatively resistant to penetration by a long, beveled 21-gauge (80 × 0.8 mm) Quincke-Babcock needle [57]. After entering the epidural space (anatomically believed to vary from 1 to 7 mm in depth), depending on the site of insertion, the needle advanced 7–13 mm within it. This tenting of the dura mater is believed to be a potential hazard in the thoracic and cervical region because the spinal cord could be impacted.

Detection Time for CSF After Dural Puncture

Features that determine the effective use of spinal needles include rapid detectability of CSF and low resistance to injectate. Experiments with a wide variety of needles revealed that all Becton-Dickinson needles had a zero detection time [58]. The Quincke "Spinocan" 26 gauge and Portex pencil-point had the greatest delay, which at an artificial CSF pressure of 20–50 cm H_2O was approximately 8 s. The calculated relative resistance to flow through the needles varied from 0.21 (Becton-Dickinson Whitacre 22 gauge) to 2.91 (Quincke, Spinocan 26 gauge).

Rate of CSF Leak Following Dural Puncture

The rate of CSF loss through a dural puncture site can be measured in an in vitro model, and experiments demonstrated that, although more force was required to pierce the dura, CSF leakage from pencil-point needles was significantly less than that from Quincke needles of the same external diameter [59]. The authors concluded that the Whitacre 27-gauge needle lacks a clear advantage over the 25-gauge needle, which may be easier to use.

Needle Orifice Shape and Unintended Extra Dural Injection

A needle whose distal orifice is partially in and partially outside the subarachnoid space may deliver CSF from the hub, but only part of the injectate will be delivered into the subarachnoid space. The 22-gauge Whitacre needle is preferable to long-orifice needles such as 22-gauge Sprotte, Quincke, and Diamond point [53, 60].

Epidural Needles

A suitable needle has the following characteristics: (1) easy penetration of ligaments, (2) minimally traumatic penetration, (3) minimal difficulty locating the epidural space, and (4) a lumen that facilitates epidural catheter placement. There are three needles that largely incorporate these features.

Tuohy Needle

The distal end is curved 20 degrees to direct a catheter into the epidural space. It must be introduced into the epidural space at least to the depth of the orifice. After a catheter has been inserted, it cannot be withdrawn without a serious risk of transaction.

Crawford Needle

This needle lacks a curved end and so must approach the epidural space obliquely if a catheter is to be inserted. It does not have to penetrate as deeply as the Tuohy needle into the space.

Whitacre Needles

Whitacre epidural needles have a blunt tip to reduce the likelihood of dural puncture. The eye of the needle is located laterally, so the distal end must be inserted well into the epidural space.

Needle sizes appropriate to the ages of children are as follows: [61] until 6–7 years, 20 gauge; from 7 to 10 years, 19 gauge; over 10 years, 19 or 18 gauge. A 16- or 18-gauge needle is customarily used in adults.

Combined Spinal and Epidural Techniques

The development of combined spinal and epidural (CSE) techniques since their inception in 1937 has been recently reviewed [62]. Various techniques, including conventional epidural, long spinal needles, catheters, and special devices, can be used. The double-segment technique involves the insertion of an epidural needle followed by a spinal needle inserted one or two segments below. The single-space technique (SST) requires an epidural needle insertion followed by a spinal needle insertion through its lumen once the epidural anesthesia solution has been injected. There are technical complications associated with the combined use of these devices as well as the individual ones, and sets specifically designed for SST have been designed.

Double-Lumen Needles

In this technique, a Tuohy needle has a parallel tube as a guide for a thinner spinal needle. There are two types—a bent parallel tube and a straight parallel tube. The bent parallel tube consists of a curved 20- to 22-gauge spinal needle of the same length as the Tuohy needle. The straight tube is fixed on the side of a Tuohy needle; the point of the guide is situated 1 cm behind the eye of the Tuohy needle. Spinal needles of normal length can be used. The double-lumen concept allows insertion of the epidural catheter before positioning of the spinal needle.

Another device is a conventional Tuohy needle to which has been added an additional aperture at the end of the longitudinal axis [52]. It is through this that a spinal needle on its way to the subarachnoid space will exit. Favorable clinical reports of CSE techniques have been supplemented by laboratory studies of flow characteristics of long spinal needles and the risk of catheter migration from the epidural space.

Flow Characteristics of Long Spinal Needles

The 120-mm, 26-gauge Braun Spinocan needle was compared in vitro with the 120 mm, 27-gauge Becton-Dickinson spinal needle. A pressure of 10 cm H_2O caused fluid to drop from the needle after 330 ± 14.8 and 129 ± 20.7 s, respectively. Clinical study findings were 33.5 and 10.85 s, respectively. The internal diameter of the 26-gauge needle is 0.23 mm and of the 27-gauge needle, 0.25 mm. The gauge value indicates the outer size, not the lumen [63].

Catheter Migration

An epiduroscopic study of cadavers demonstrated that the risk of epidural catheter migration through a dural puncture hole was very small. It was much less likely if the hole had been made by a 25-gauge spinal needle than with a Tuohy needle [64].

Complications Associated with Spinal and Epidural Catheters

1. *Insufficient length* to reach from the exit site to the shoulder.
2. *Venous penetration*. The lumen must be sufficient for aspiration. A stylet in the catheter must not project out of the tip.
3. *Dural penetration*. The lumen must be sufficient for aspiration. A stylet in the catheter must not project out of the tip. A closed round-ended catheter with side openings makes penetration less likely.
4. *Kinking*. This is less likely with currently manufactured catheters and with the redesigned version of the Racz catheter [65].
5. *Knotting*. Interval marking of the catheter is a useful guide to the catheter length within the subarachnoid or epidural space and discourages coiling.
6. *Difficult withdrawal*. A clinical study of forces necessary for lumbar extradural catheter removal (range 1.57 ± 0.96 to 3.78 ± 2.8 N) and literature review indicated that the original approach to the space was inconsequential. However, the withdrawal force required was greater with the patient sitting than in the lateral position. Thus, the flexed lateral position was recommended for removal [66, 67]. This opinion is controversial. It has been recommended that the patient be in the same position used for insertion when it is removed [68].

Devices for Peripheral Nerve Blockade

Complications of nerve blockade include intravascular injection, intraneural injection, and failure to locate the nerve to be blocked. Breakage at a weak junction between the hub and stem is unlikely with modern needles, although in some circumstances a security bead can be a useful precaution.

Intravascular needle placement may be impossible to detect by aspiration if the needle lumen is very fine, and a translucent hub is of little help. This has implications for resuscitation arrangements established for minor surgical or dental procedures performed in offices and clinics. Intraneural injection is unlikely, but needles with side ports provide some protection from that event.

Paresthesias are quite common and unwelcome during the conduct of a central neural blockade especially spinal anesthesia, but in the past peripheral nerves were often deliberately located by eliciting paresthesias with the needle. This crude method of identifying peripheral nerves is no longer necessary with the advent of neurostimulation and more recently, ultrasound-guided regional anesthesia techniques. The causal relationship between paresthesia elicited in this manner and neural damage is controversial, and no statistically significant clinical data indicate that such stimulation produces neuropathy [69]. The animal experiments upon which claims for potential neuropathy are based did not represent clinical practice, although a clinician can never be absolutely certain that the tip of the needle is not actually within a nerve. Indeed, the sterile flexible infusion line between syringe and needle is there to help immobilize the needle when it is in position.

Concerns about mechanically produced paresthesia popularized the introduction of nerve stimulation to locate and identify peripheral nerves. The needle should ideally be insulated by Teflon coating in order to enhance opportunities to place the needle tip close to the nerve. Paresthesias may occur when the instrument is in use, but its purpose is to elicit visible contraction in a muscle served by the nerve to be blocked.

Ideally, the nerve stimulator should have the following characteristics [70]:

1. Constant current output
2. Clear meter reading to 0.1 mA
3. Variable output
4. Linear output
5. Clearly marked polarity
6. Short pulse width
7. Pulse of 1 Hz
8. Battery indicator
9. High-quality alligator clips
10. High- and low-output settings

Instruments designed for testing neuromuscular transmission do not usually indicate voltage or current at the site of stimulation and so are disadvantageous because they control only voltage, whereas it is current that causes a nerve to depolarize [71]. It is possible to elicit a muscle response when the needle is some distance from the nerve unless the stimulus current is less than 0.5 mA [72]. The concept is attractive and popular with some practitioners, but definitive evidence of its superiority over other methods is lacking and the occurrence of serious complications has been reported [69].

Another technique to safely identify the site for injection is visualizing the anatomy by ultrasonography. Not only can this increase the likelihood of successful neural blockade, but it reduces the incidence of pneumothorax associated with the supraclavicular approach to brachial plexus blockade [73].

Resuscitation Supplies

Cardiovascular failure, with or without respiratory failure, is a rare complication of regional blockade whether for head, trunk, or limbs. If competent treatment is not *immediately* available, however, the result will be permanent cerebral damage or death.

ASRA guidelines require the following medications and equipment to be immediately available when performing any regional anesthesia procedure:

Intravenous access and fluids, a tipping trolley, an oxygen supply, and resuscitation drugs and equipment must be available. The equipment must include an anesthesia machine as a source of oxygen, a means of lung ventilation, a laryngoscope, oropharyngeal airways, cuffed endotracheal tubes, a stilette, and continuous suction. Benzodiazepine, propofol, suxamethonium, ephedrine, epinephrine, atropine, and Lipid Emulsion 20 % should be immediately available. For complete details, please refer to the ASRA Practice Advisory on Local Anesthetic Systemic Toxicity [74].

Those are the basic requirements of the caregivers trained to provide advanced cardiopulmonary resuscitation and must be present when neural blockade is attempted in the hospital, "block" clinic, or indeed anywhere. They are just as necessary in the office where a minor procedure is to be done under neural blockade. Not only must equipment be there, but the persons present should be trained to use it. In light of the magnitude of the potential tragedy, they should be able to communicate with extramural help while continuing their efforts at cardiopulmonary resuscitation. In other words, the anesthesiologist must always be accompanied by a trained assistant when performing regional anesthesia.

Behavioral Factors and Complications

The behavioral factors that lead to complications are of several categories. A lapse of safe habit is the routine failure to check effectively the identity and concentration of fluid to be injected. Another is the lack of a routine method of distinguishing between syringes. An unsafe habit could be the use of an air-filled syringe to identify the epidural space of a child. Other potential causes have been reviewed and in general are referred to as *vigilance decrement*, *vigilance* being a state of maximal and psychological readiness to react to a situation [75–77]. These can be the cause of temporarily breaking a safe habit or creating an unsafe habit or of missing evidence of a complication. It is an important feature of complication avoidance that anesthesiologists be aware of these behavioral pitfalls and to discipline themselves accordingly, while establishing safe work scheduling.

Effects of Sleep Deprivation

Sleep deprivation can dramatically impair performance of monitoring tasks, whether the signals are presented in an auditory or visual mode—and particularly if the task is not cognitively exciting. A cumulative sleep debt incurred over days has a detrimental effect; however, there are wide individual differences in responses to acute or chronic sleep loss. Ideally, anesthesiologists should objectively establish their own limitations because an anesthesiologist who has been working most of the night may feel remarkably awake, perhaps euphoric, in the morning, although studies have documented reduced performance, and in the afternoons the situation will have further deteriorated. Napping is not necessarily helpful, particularly if it occurs during a period of REM sleep.

A recommendation supported by evidence from a variety of subjects, including anesthesiologists, for the anesthesiologist who has been working most of the night and is scheduled for a full day's work is this: "Do not work [78]. If work is mandatory do not nap for only 2 h. If 4 h is possible, accept it but be prepared for some remaining performance decrement."

The Effects of Fatigue

Hours of continuous cognitively challenging work result in fatigue. The effects of fatigue are accentuated by sleep deprivation and influenced by the position of the activity in the individual's circadian rhythm. Published data support the contention that a fatigued anesthesiologist may be careless and less likely to detect perioperative complications or to respond optimally to evolving clinical situations [78].

The Hazard of Boredom

A task that is repetitious, uneventful, uninteresting, and undemanding is boring. In such a case, the anesthesiologist has too little work. It is a problem shared by many other real-life responsible tasks and results in inappropriate automatic behavior, vigilance decrement, inappropriate interest, and a general feeling of fatigue. Thus, the low-workload situation, similar to the high-workload state, can cause performance decrement, and thus complications, because evidence of their development is overlooked. Anesthesiologists periodically change their location in the operating room or converse with operating room companions, probably in an unconscious effort to maintain vigilance by increasing sensory input [76]. An unsedated patient under regional anesthesia is sometimes a highly entertaining and educational source of information and social commentary, thus keeping the anesthesiologist close by. During boring cases, the addition of occupations completely unrelated to patient care demand a time-sharing technique that must be learned, and even then their impact on an individual's vigilance for clinically important matters is variable and very difficult to predict. Thus, while reading or listening to personal music in the operating room is common behavior it is difficult to judge if these practices interfere with patient care.

The Influences of Physical and Mental Factors

An anesthesiologist is sometimes anxious in the operating room, but when this is compounded by personal anxieties, planning, decision making, and monitoring may be adversely affected. Substance abuse reduces vigilance and psychomotor performance and there is strong evidence that hangovers from alcohol and marijuana have similar effects. Recent work suggests that pilots should wait at least 14 h after drinking alcohol before flying, although it is constituent aromatic substances in some beverages that are more likely to cause a problem.

Work Environment

The physical environment for conducting hospital surgery under regional anesthesia is similar to that for general anesthesia in that monitor displays should be discernible from the variety of positions assumed by the anesthesiologist during the course of the procedure [76].

Recently, verbal communications were found to be responsible for 37 % of events that could have resulted in patient deterioration or death in an intensive care unit, supporting other anecdotal reports of communication errors [78]. This confirms the need for an established routine to check the identity and concentration of fluids to be injected in every hospital or clinic location where neural blockades are done or existing blockades reinforced.

Small clinics and professional offices may differ from the hospital environment in one significant respect. In an acute emergency, persons performing cardiopulmonary resuscitation may be unable to communicate with outside help without discontinuing their lifesaving activity, and in some countries or states such behavior is illegal. Protection of patients demands an arrangement that avoids such a situation by ensuring a communication system that can be instantly and conveniently activated.

The "mental environment" in which neural blockade and surgery are performed is as important as the physical environment. It is salutary that anesthesiologists, who are sometimes confronted with injured patients who have suffered because the response to industrial production pressures was to ignore certain defenses against injury, can find themselves faced with the same decision as the industrial worker—and even under similar production pressures. These pressures may be temptations for personal gain or generated by surgeons, dentists, or institutional managers. A recent study concluded that pressure from internal and external sources is a reality for many anesthesiologists and is perceived, in some cases, to have resulted in unsafe actions being performed [79]. The implication is that any effort to increase anesthesia and surgical productivity should be based on methods other than reducing safe practices. Any attempt to achieve it by introducing new technology should be accompanied by a careful analysis and, if necessary, education of the person using it [80].

Complication Recognition During Neural Blockade and Surgery

Sharing Human and Instrumental Monitoring

Regional anesthesia conducted expertly on the basis of a careful medical history and examination of the patient is safe, but complications can occur [81–93]. Signs and symptoms, listed by body systems, are matched with the human and instrumental monitoring techniques used for their detection in Table 2.2.

The role of the patient is included, as is the anesthesiologist's direct or monitor-assisted sensing. If heavy sedation or a supplementary general anesthetic is used, the clinical

Table 2.2 Complication recognition

Symptoms and signs to be detected	Detection methods
Nervous system events	
• Peroneal numbness and tingling	Patient: Assuming there is no language barrier, the patient may report any of these spontaneously but should be initially instructed to report any unusual sensation
• Dizziness, tinnitus	Anesthesiologist: Communication with the patient and observation
• Hearing impairment	Instrument: Instruments do not identify these sensations for the anesthesiologist
• Headache	
• Reduced vision	
• Diplopia	
• Taste in mouth	
• Dysphagia	
• Coughing and sneezing	
• Nausea	
• Throat numbness	
• Dysphasia	
• Pain and paresthesia	
• Faintness	
• Restlessness	
Postural pressure or tension on peripheral nerves	Patient: An unreliable source of information
	Anesthesiologist: Power of observation
	Instrument: Limited in application. A pulse oximeter at a limb periphery may indirectly indicate a threat to nerve or plexus
Horner's syndrome	Patient: Reports unusual feeling
	Anesthesiologist: Observation
	Instrument: –
Phrenic nerve paralysis	Patient: Reports unusual feelings
	Anesthesiologist: Observation
	Instrument: Spo_2 value may diminish
Recurrent laryngeal nerve block	Patient: Reports unusual feelings
	Anesthesiologist: Observation
	Instrument: –
Presence or absence of CSF in hub of needle or dripping from it	Patient: –
	Anesthesiologist: Observation. After dural puncture, the delay before the first drop of CSF appeared was approximately 11 s for a 27-gauge Becton-Dickinson spinal needle, and 33 s for a 26-gauge Braun needle [63]
	There is considerable variation among commercially available spinal needles [58]. Such details regarding needles used for blocks other than central neural blockade are unavailable
	Instrument: –
Loss of resistance to injection (epidural space detection)	Patient: –
	Anesthesiologist: Observation
	Instrument: Pressure variations in the injection system can be digitized and displayed to show an exponential pressure decline [94]
Blood reaching the hub of a needle and not pulsating	Patient: –
	Anesthesiologist: Observation. Note, blood will take substantially longer than CSF to pass through a spinal, or other, narrow bore needle
	There will be interpatient variability. Thus, a "bloody tap" is evidence that the needle is in a vein or hematoma, but absence of blood is not necessarily definitive evidence that drug will not be injected intravascularly
	Instrument: –
Cerebral function	Patient: Reports unusual sensation
	Anesthesiologist: Conversation or intermittent questioning of patient
	Instrument: –
Evidence of planned neural blockade	Patient: Report of unusual sensations
	Anesthesiologist: Questioning and examining the patient
	Instrument: Thermography and plethysmography

(continued)

Table 2.2 (continued)

Symptoms and signs to be detected	Detection methods
Evidence of unexpected neural blockade	Patient: Report of unusual sensations and/or motor function
	Anesthesiologist: Observation of blockade area and the patient
	Instruments: Sphygmomanometer, ECG, pulse meter
Vagal stimulation	Patient: Faintness or loss of consciousness
	Anesthesiologist: Observations
	Instruments: ECG, pulse oximeter, pulse meter, sphygmomanometer
Respiratory system events	Patient: Dyspnea may be reported but in general patients seem unaware of the significance of respiratory changes, and, if they have been sedated, unaware of them
• Respiratory rate changes	Anesthesiologist: Observations are valuable but are unlikely to assess function accurately or continuously
• Tidal volume change	Instruments: Pulse oximetry is a late indicator of respiratory dysfunction, relative to end-tidal capnography
• Apnea	The stethoscope in the operating room or PARR is now more of a diagnostic tool to identify such things as atelectasis and pneumothorax than a monitor of respiration but a paratracheal audible respiratory monitor has been described [95]
• Stertor	
• Respiratory obstruction	
• Dyspnea	
• Bronchospasm	
Erroneous gas delivery to patient	Patient: Comments may be made about odor
	Anesthesiologist: Observation of patient behavior
	Instrument: An Fio_2 monitor with functioning alarms is quicker and more reliable than patient or anesthesiologist
Cardiovascular system events	
Hypotension	Patient: –
Hypertension	Anesthesiologist: Sensing error is large
	Instrument: Automated direct or indirect measurement
Bradycardia	Patient: –
Tachycardia	Anesthesiologist: Accurate observation is possible but may be intermittent.
	Instruments: A variety is available to provide this information continuously
Cardiac arrhythmia	Patient: The patient may state their heart is beating irregularly
	Anesthesiologist: Clinical observation
	Instrument: Pulse oximeter and precordial stethoscope will indicate irregularity. The ECG provides continuous information upon which a diagnosis can be based
Asystole	Patient: –
	Anesthesiologist: Suspicion is aroused if at that moment the finger is on a pulse or a precordial stethoscope is in use
	Instrument: An ECG is a continuous and definitive indicator
	A pulse oximeter can raise a delayed but serious suspicion
Increased or decreased central venous pressure	Patient: Symptoms relative to cardiopulmonary function may be announced
	Anesthesiologist: Clinical events indicate a possibility
	Instrument: Central venous pressure measurement
Cyanosis	Patient: –
	Anesthesiologist: Visual acuity and environmental circumstances create an undesirable error of assessment
	Instruments: Pulse oximetry and blood gas measurements
Muscle events	
These range from twitching of facial muscles to convulsive movements of major muscle masses	Patient: –
	Anesthesiologist: Observations
	Instrument: –
Body temperature events	
Hypothermia	Patient: Patients are aware of cold sometimes but are often poor judges of their real body temperature. There is strong evidence that not only do spinal and epidural anesthesia impair central and peripheral regulatory controls but are not perceived by the patient [96–99]
	Anesthesiologist: The observations of the patient may be an unreliable assessment of temperature because shivering is not occurring and, depending on the area felt, the skin may feel warm
	Instrument: Thermometry

situation changes radically. The cost–benefit picture of a specific regional anesthesia plan must be estimated in light of these factors. This is followed by an account of the documented complications for different neural blockades. It would be possible to create monitoring algorithms for individual blocks, but in this author's opinion, such focusing of patient care would be detrimental to the patient's safety because unrelated events might be ignored, threatening though they might be. It is important to realize that, although monitoring devices are invaluable, an astute anesthesiologist will detect signs that are precursors to the resulting events detected by the device. This anticipatory information enables therapy to begin sooner.

Monitoring Devices

Contemporary recommendations for monitoring of patients under regional anesthesia include the cardiovascular and respiratory systems and body temperature. Whatever the combination of human and instrumental monitoring might be, its purpose is to recognize complications before damage to the patient is inevitable. A vital question is, during what period of patient care should monitoring be in progress? It may not be surprising that reported serious complications threatening patient outcome have occurred any time from the onset of attempted neural blockade until surgery has been in progress for several hours, or even when the patient is in the recovery area [90]. In some instances, a complication has been detected much later. Accordingly, it is prudent to monitor patients carefully from entry into the block room until the effects of the blockade have ended.

When instrumental monitors are used, they should be calibrated correctly and located so that there can be a planned balance of visual attention between patient and instruments, and access by audible alarms. If they are to be used optimally for the early detection of complications, however, the characteristics of these essential pieces of equipment must be appreciated. The following paragraphs concentrate on these limitations but should not undermine their clinical value for caregivers.

Pulse Oximetry [100–106]

Pulse oximeters require a pulse at the site of measurement and provide only a crude indication of peripheral perfusion. Blood flow is barely required. It has been shown that peripheral blood flow can be reduced to only 10 % of normal before the pulse oximeter has difficulty estimating a saturation [107]. It does not justify assumptions regarding cardiac output, arterial blood pressure, or cardiac rhythm, which must be assessed by other means. Regarding respiration, a normal saturation measurement when the patient breathes an increased inspired oxygen concentration does not confirm adequacy of ventilation. The hypoxemia that would otherwise accompany the rising carbon dioxide tension is masked. Most pulse oximeters make measurements and calculations that provide oxygen saturation. The more popular definition of O_2 saturation is functional saturation, which is the concentration of oxy-hemoglobin divided by the concentration of hemoglobin plus reduced hemoglobin:Functional saturation = $O_2Hb/(RHb + O_2Hb)$

The met or CO-Hb concentrations used in the algorithms are estimations for the population under consideration; however, the presence of a large percentage of those abnormal hemoglobin's can cause erroneous readings of saturation and mask serious hypoxia.

Regional anesthesia can produce profound changes of sympathetic nerve activity in different parts of the body. Evidence has been presented that pulse oximetry during lumbar epidural anesthesia gives falsely low readings when the sensor is placed on a finger [108].

Capnography [109–112]

Carbon dioxide production, pulmonary circulation, and ventilation are necessary to produce a normal capnogram. Change in the end-tidal carbon dioxide ($ETco_2$) value can have a cardiovascular or respiratory origin, but it is as a monitor of spontaneous breathing that the capnograph has its role in regional anesthesia.

End-tidal capnography sampling in the spontaneously breathing, unintubated patient may be from inside a plastic oxygen mask, a nasal cannula, or a catheter tip in the nasopharynx. The numeric value of the $ETco_2$ and its relationship to the arterial CO_2 pressure is influenced by oxygen delivery, ventilation–perfusion ratio, and sampling errors. The value of such monitoring, beyond respiratory rate indication and apnea detection, has been a contentious matter [113–115]. There have been very favorable recent reports of its use in adults and children, but certain provisos apply [116–120]. Small differences in sampling technique affect the accuracy of the values measured, so the technique requires expert evaluation where it is in use. A gas temperature–flow relationship in the nostril has been proposed as a monitor of respiration and refuted [121, 122]. Previous attempts to utilize such a relationship were unsuccessful.

Cardiac Rate and Rhythm

A normal ECG can be recorded from a patient who is profoundly hypotensive, hypoxic, or hypercapnic, so although it is valuable as an indicator of heart rate and rhythm, it is a

very late indicator of other threatening complications, even if the patient is conscious. Nevertheless, it provides potentially useful diagnostic information not provided by peripheral pulse-activated devices.

This information is more valuable for the diagnosis of arrhythmias than detection of myocardial ischemia, even if a modified V5 lead is used and the right arm electrode of lead I is placed over a position on the intersection of the left anterior axillary line and the fifth intercostal space and the ground electrode is placed on the left shoulder. The principal guides to cardiac ischemic complications are data gathered from monitoring and management of heart rate, mean arterial pressure, hemoglobin concentration, and saturation.

ECG monitoring should be used for major surgery and for patients at cardiac risk, but for routine cases the use of an ECG in preference to a pulse oximeter or capnograph is controversial. Many anesthesiologists favor pulse oximetry or capnography.

Systemic Arterial Pressure

The anesthesiologist predicts an acceptable blood pressure range for the patient and selects the methods of measurement on the basis of the anticipated margin of error. Invasive direct methods have their own sources of error but are more accurate than noninvasive techniques. Although invasive direct methods are possible during regional anesthesia and necessary for major surgery in very poor-risk patients, indirect methods are used for most patients.

Manual Indirect Measurement of Blood Pressure

Methods usually involve the application of a cuff (20 % larger than the diameter of the arm), applied snugly to the upper arm. After inflation to above the anticipated systemic pressure, it should be deflated, reducing the pressure at 2–4 mmHg per heartbeat. Detection of the returning pulse by palpation or oximeter provides a crude estimate, as do oscillations of aneroid manometers or mercury columns.

The Korotkoff method of detection requires a sensor under the cuff and over an artery, enabling the Korotkoff sounds to be heard. Although the pressures measured may differ from intra-arterial values by only a few millimeters of mercury, systolic, diastolic, and mean arterial pressures may be over- or underestimated by up to 30 % [123]. During anesthesia and surgery, the patient's cardiovascular status changes and the magnitude, and even the direction, of error may change [124].

Correlation with direct arterial pressure measurement is poor [125, 126]. Additionally, even if the blood pressure remains unchanged, alterations in the vascular tone in the limb, such as may be produced by vasopressor agents, alter Korotkoff sounds. When the patient is very vasoconstricted or hypotensive, Korotkoff sounds are difficult to detect and the palpatory method is reassuring rather than accurate [127].

Automated Oscillometric Measurement

The inflatable cuff functions as a sensor supplying a pressure transducer within the instrument. The varying oscillations and cuff pressures are analyzed electronically to determine systolic, diastolic, and mean arterial pressures. Comparisons with pressures in the aorta or a peripheral artery have been made [128–131], and these devices are accurate to ±10 mmHg. Another study demonstrated a good correlation only for systolic pressures [132]. Oscillometric diastolic pressures have been found to be higher; however, in a survey of six commercially available devices, errors ranged from −30 to +40 % for mean arterial pressures [124]. In general, low pressures were overestimated and high pressures were underestimated. If the patient has cardiac arrhythmia, results may be erroneous.

There is no doubt that automated sphygmomanometers are invaluable, providing blood pressure readings regularly and frequently, particularly when the patient is otherwise inaccessible. However, the anticipated accuracy of measurement does not always meet the anesthesiologist's requirements, and invasive methods are preferable, assuming they are conducted skillfully with the proper equipment. If electronic transducer-amplifier systems are not available, mean arterial pressure may be measured by a calibrated aneroid gauge [133].

Plethysmography

The finger arterial pressure device (Finapres) consists of a small finger cuff containing an inflatable bladder and an infrared plethysmograph volume transducer that can provide continuous monitoring. It seems that performance is better on a thumb than a finger [134], and studies have shown the Finapres to be as good as, if not better than, noninvasive oscillometric devices as compared with direct arterial pressure readings [135]. However, lacking precision, the instrument has not been recommended as a substitute for invasive arterial pressure measurement [135]. Since then, it has been shown that even small degrees of cuff misapplication contribute to measurement error as compared with intra-arterial cannulation. A comparative study of patients undergoing spinal anesthesia for lower segment cesarean delivery revealed many inconsistencies in some patients, and it was concluded that the Finapres was unsatisfactory for patients in whom sudden hypotension was a threat to outcome [136]. Problems with its use have been reviewed [137].

Thermometrography

The location of the sensor is important if it is to be used as a predictor of temperature at a site other than its location. The ideal place for a probe is the lower third to fourth of the esophagus, but this site, similar to the nasopharynx, tympanic membrane, and rectum, is uncomfortable for conscious or even mildly sedated patients. The axilla of an adducted area is a useful site for the patient under regional anesthesia, reading approximately 0.5 °C less than the oral temperature.

Liquid crystal skin thermometers have been evaluated and are potentially useful as trend indicators during surgery, because they can conveniently be applied to the skin. They are susceptible to drafts, and it is recommended that, before changing exclusively to such a device, it be standardized using a thermocouple method in parallel until adequate experience has been obtained in that working environment [138].

Conclusion

Conventional practice demands that certain monitoring devices be used routinely; however, funding for them competes in society with all the nonmedical and medical factors that contribute to health in that society. Accordingly, any application for funds and decisions on the dispensation of a global budget must be supported by a valid justification. These are challenging tasks. Outcome studies designed to predict individual risk of complications must be based on very large population [139, 140]. They are very expensive and can be confounded to a greater or lesser extent by learning contamination bias during their implementation [141]. Practitioners sometimes develop or improve clinical skills when using a device, and that change affects patient care when the device is not in use. The argument that once learning has occurred with the aid of a monitor the monitor is no longer necessary is invalid, because reinforcement of the learning will be necessary. Additionally, even if convincing studies demonstrating a lack of change in patient outcome were presented, the question of anesthesiologist outcome remains to be addressed. Do these simple monitoring devices render the task less stressful for anesthesiologists and enable them to be more effective members of the hospital personnel and better citizens, once the working day or night is over?

The template proposed for assessing the efficacy of diagnostic imaging [142] has been modified for the assessment of anesthesia technology [139] and has five components: (1) technical efficacy, (2) diagnostic efficacy, (3) diagnostic thinking efficacy and therapeutic efficacy, (4) patient outcome, and (5) societal efficacy. As new devices become commercially available, future studies will be based on the specific problems embraced by regional anesthesia.

Critical features of introducing any new device into the workplace are new educational requirements and the attitudes of the potential users, which will be strongly influenced by the design features, additional work, its perceived value, and health factors [80].

Complications of Specific Neural Blockades

The wide variety of symptoms and signs of complications associated with regional blockade have been described as, "When sorrows come, they come not single spies/But in battalions" (Hamlet: Act 4, Scene 5) so the anesthesiologist must be encouraged to take an overall view of the patient. Nevertheless, initially the emphasis is on the complications of the neural blockade under consideration, because of their role in determining the final anesthesia plan and the matters uppermost in the mind of the anesthesiologist while monitoring that procedure and diagnosing complications during its conduct. Some sources of complications are shared by all patients and will not be described repeatedly for each block (e.g., airway obstruction, drug toxicity, epinephrine side effects, and neural damage).

Airway Obstruction

Traditionally in some institutions, nurses familiar to the patient kept the patient comfortable during major surgery under regional anesthesia. The patient was wide awake, and this was considered an important feature; however, tolerance of the procedure and cooperation must be ensured, not only for the success of the procedure but for satisfaction of all concerned. The choices range from complete consciousness, through a mild state of cortical depression in which the patient is calm and tranquil, to a drug-induced sleep or even general anesthesia supplemented by the regional blockade. The last is usually necessary for infants and children; there are more options for adult patients.

From the anesthesiologist's point of view, some warning signs and symptoms are obtunded in unconscious patients. If the patient is heavily sedated, as opposed to tracheally intubated under general anesthesia, management of respiratory obstruction may be needed. In the awake state, the upper airway muscles help keep the airway patent. In the supine posture, airway patency increases in response to greater airway resistance. During normal sleep, muscle activity is reduced and can be supplemented by drugs such as alcohol, benzodiazepines, and barbiturates [143–145]. Thus, respiratory obstruction is a potential problem throughout the procedure that must be immediately recognized and successfully managed. This hazard is compounded in patients who normally experience episodes of sleep apnea, from the influence of deafferentation and central effects of the local anesthetic agent, including respiratory depression.

Local Anesthetic Focal Complications

In a conscious, unsedated patient, the first symptoms or signs of focal complications are drowsiness or light-headedness. As toxic activity increases, the characteristic sequence is circumoral and lingual numbness, tinnitus, visual disturbances, dysarthria, and restlessness. Muscular twitching, often facial, progresses to convulsions, coma, and respiratory and circulatory depression. The quantity of drug reaching activity sites and time after injection are influenced not only by distribution, elimination, and drug characteristics, but by the site of injection. Sometimes all the vital systems are depressed simultaneously. This dangerous situation is compounded by inability of the patient to report symptoms. In the case of pregnant patients at term, neonatal depression can occur and hypotonia has a prominent role [146–148]. Bradycardia, heart block, and ventricular tachycardia have been reported [149, 150].

Epinephrine Complications

Epinephrine complications in regional anesthesia are related to vasoconstriction at the site of the injected fluid. As such, they are more likely to be evidenced in the postoperative period. However, if absorbed into the general circulation at the time of neural blockade, temporary hypertension is associated with tachycardia or reflex bradycardia. Cardiac arrhythmias, including ventricular fibrillation, occur when the quantity entering the general circulation is sufficient.

Complications of Neural Blockade

The complications of neural blockade are directly related to the anatomy of the route of the needle and the body into which fluid or air has been introduced. Thus, the anesthesiologist with a good mental image of the relevant anatomy can predict events that may occur, particularly if the preoperative visit has been informative. Those events comprise a mix of the symptoms and signs outlined as complications to be recognized during neural blockade, surgery, and recovery. Risks depend not only on the skill and care of the anesthesiologist, but also on the drugs, equipment, the environment, and unanticipated scenarios. Their early detection and management depend on the competence of all those with care responsibilities and their performance. In view of this multifactorial situation, it is virtually impossible to know the chances of a specific complication for a specific patient, although low reported incidences can be an encouraging guide. Table 2.3 lists the complications that have been associated with various neural blockades and can be correlated with previous sections about detection methods. Complications associated with narcotics are described elsewhere in this volume. The complications identified have been gathered largely from references [61, 71, 72, 81–93].

Miscellaneous Neural Blockade Complications

Neural blockades are created at a wide variety of sites in the upper and lower limbs, the lumbar and sacral nerves, the scalp, and nerves supplying the mandible and maxilla. These complications are similar in character, and on occasion their development is sudden and severe.

- Vascular penetration and hematoma
- Vascular penetration followed by the local anesthetic focal complications (LAFC) that may culminate in cardiac and respiratory arrest
- Neural trauma
- Local vasoactive effects of epinephrine resulting in gangrene
- Cardiac arrhythmias produced by epinephrine
- Bradycardia

Complications in the Postoperative Period

Patients who have been neurally blocked or received centrally administered opioids require meticulous surveillance if complications are to be detected while therapy has an excellent chance of being effective. Specific training of personnel is necessary for these tasks.

Admitting the Patient: History and Physical Examination

The activities of caregivers in recovery rooms and intensive care units have much in common, and there is anecdotal as well as research evidence in intensive care units that a significant complication is failure of communication between physicians and nurses [78]. This complication can occur in recovery rooms as well. The nurse accepting responsibility for a patient from the operating room is entitled to a report of the baseline data about vital systems and other information that relates to the neurally blocked patient. Presented verbally with a completed written protocol, recovery room complications may be a continuation of intraoperating room or in-transit events on new developments. They manifest themselves in several categories.

Cardiovascular System

- Blood pressure, pulse rate, and cardiac rhythm: when vasopressor drugs were administered, and whether their waning effect will unmask residual sympathetic blockade or hypovolemia
- Details of any evidence of circulatory overload during surgical irrigation of the bladder

Table 2.3 Complications of neural blockade[a]

Orbital regional blockade	
Local effect by needle, catheter, or injected volume	Conductor blockade effects
• Venous penetration causing retrobulbar hematoma	• Brain stem anesthesia associated with optic nerve sheath penetration resulting in
• Arterial penetration causing a retrobulbar hematoma and local ischemia	• Increasing or decreasing cardiovascular vital signs, pulmonary edema, cardiac arrest, shivering, convulsions, hyperreflexia, hemiplegia, paraplegia, quadriplegia, contralateral amaurosis, contralateral oculomotor paralysis, facial palsy, deafness, vertigo, aphasia, loss of neck muscle power, loss of consciousness, vagolysis, respiratory depression, apnea
• Vascular occlusion of the central retinal artery	
• Optic nerve penetration	
• Penetration of the globe	
• Penetration of the optic stem	
• Oculo-cardiac reflex	
Cervical plexus blockade complications	
• Entry to epidural space	• High spinal anesthesia with cardiovascular and respiratory failure
• Entry to subarachnoid space	
• Intravenous penetration	• Aphasia and hemiparesis
• Intra-arterial penetration	• Blindness
• Penetration of esophagus (associated with the anterior approach to the ganglion)	
• Pneumothorax (especially on the patient's right side)	
• Nasal congestion	
Supraclavicular brachial plexus blockade complications	
• Vascular penetration of subclavian and axillary arteries or veins, the vertebral artery, and external jugular vein. Ischemic arm problems may develop, particularly in children	• Stellate ganglion block producing Horner's syndrome
	• Phrenic nerve block which in children impairs respiration
• Penetration of apical pleura, causing a pneumothorax	• Recurrent laryngeal in block causing hoarseness and possibility of aspiration
• Epidural space entry	• Epidural anesthesia with cardiovascular and respiratory depression
• Subarachnoid space entry	
• Nerve trauma	• Spinal anesthesia with cardiovascular and respiratory depression
• Vasovagal episodes in patients in the sitting position	
Infraclavicular brachial plexus blockade complications	
• Axillary artery puncture, sometimes with a brief vascular insufficiency	
• Venous penetration causing a hematoma	
• Apical pleura penetration and ensuing pneumothorax is possible but unusual	
Epidural blockade complications	
• Epidural vessel penetration	• Hypotension
• Epidural hematoma	• Respiratory depression failure
• Dural puncture	• Bradycardia
• Back pain	• Total spinal anesthesia
• Neural trauma	• Horner's syndrome
• Air embolism (especially in children) if an air-filled syringe has been used to locate the epidural space	• Trigeminal nerve paralysis
If a catheter has been inserted:	
• Subdural space catheterization	
• Intravascular catheterization	
• Infection	
• Headache associated with supplementary injections	
Caudal epidural blockade complications	
• Subcutaneous injection	• Accidental spinal anesthesia with cardiovascular and respiratory involvement
• Penetration of dura mater	

(continued)

Table 2.3 (continued)

Orbital regional blockade	
• Penetration into epidural vein	• Urinary retention
• Hematoma	
• Intraosseous penetration	
• Pelvic visceral penetration	
• Infection, particularly if a caudal-epidural catheter is in situ	
Subarachnoid block complications	
• Epidural vessel penetration	• Total spinal anesthesia
• Epidural hematoma	• Hypotension
• Neural trauma	• Respiratory depression/failure
• Headache	• Dyspnea
	• Bradycardia/asystole
Intercostal nerve blockade complications	
• Pneumothorax	• Hemodynamic depression
• Penetration of intercostal vessels	• Respiratory depression/failure
• Penetration of pleural space	• Depressed cough reflex
• Entry to paravertebral space	• Blockade of spinal nerves
• Entry to epidural space	
• Entry to subarachnoid space	
Intravenous regional anesthesia (IVRA, Bier's block) complications	
Local effect by needle, catheter, or tourniquet	Conductor blockade effects
• Tourniquet discomfort	
• Tourniquet leak	
• Tourniquet release less than 20 min after local anesthetic injection	
• Vomiting followed by aspiration of recent food or drink	
• Neural damage caused by prolonged tourniquet time, or the cuff too close to the elbow joint	
• Necrosis caused by ischemia created in an already injured limb	
Thoracic paravertebral anesthesia	
Local effect by needle catheter	Conductor blockade effects
• Paravertebral vessel puncture	• Hypotension
• Pneumothorax	• Respiratory paralysis
• Intrapleural catheter placement or migration	• Epidural analgesia
	• Horner's syndrome (possibly bilateral)
• Headache	• Phrenic nerve paralysis (possibly bilateral)
• Sepsis	
• Intercostal nerve trauma and pain	

[a]For an explanation of central effects, see the section Local Anesthetic Focal Complications

- Fluid balance
- Perfusion of peripheral vascular beds

Respiratory System

- Respiratory rate, tidal volume, and apparent oxygenation
- Administration of respiratory depressant drugs epidurally or by any other route, and any antidote administration
- Airway management in the operating room

Central Nervous System

- Sedative or analgesic drugs
- The likelihood that the patient will arouse before sensory and motor block have disappeared and then will become agitated
- State of consciousness and responses to sensory stimuli
- Analgesia preparations for recovery room sojourn
- Antinausea preparations administered

Peripheral Nervous System

- The existing neural blockade and when it is expected to have disappeared
- The nerves in an anesthetized area that need protection (e.g., ulnar or lateral peroneal nerves)
- An epidural or subarachnoid catheter in situ

Bladder Distention
- Presence of a urinary catheter, its drainage, and the state of the bladder
- Perioperative Anticoagulant Therapy
- The drugs administered and anticipated effects on prothrombin time or other measurements of coagulation

Endocrine Pathology
- Diabetes and its management in the operating room
- Steroid medications given in the operating room or elsewhere

Body Temperature
- Evidence of hypo- or hyperthermia

Muscle Activity
- Restlessness
- Shivering
- Muscle twitching

Monitoring the Patient

The demand for recognition of complications in the recovery room is similar in most respects to recognition in the operating room and as described in a previous section. It is a judicious combination of human and instrumental sensing, the former being the fundamental component of recovery room care. Analysis of recovery room complications in adults and children reveals that they were identifiable largely by clinical observation rather than instrumental monitoring [151]. Nevertheless, certain instruments are invaluable for recovery room care because they provide for patients at risk; they provide more precise information and supply the caregiver with continuous vital information. Instruments invaluable for recovery room care are an ECG, pulse meter, pulse oximeter, automated sphygmomanometer, thermometer, and stethoscope.

Complications monitoring include evaluation of respiration, hemodynamics, level of consciousness, adequacy of analgesia, degree of motor blockade, and other side effects on admission to the postanesthesia recovery room. There are certain complications for which early detection, followed by early diagnosis and treatment, reduces the chance of a permanent neurologic deficit. They are those associated with central neural blockade, and presenting symptoms include backache [152, 153]; pain in thighs, calves, or buttocks [153]; headache; muscle twitching; and increase in neural blockade or its failure to regress. The detection of these complications can be made difficult by postoperative sedation [154], and analgesia and the normal variation in block duration. Although these complications, indicative of a wide variety of pathology, are chronologically related to the neural blockade, they may be attributable to concomitant pathology [155], and headache accompanying epidural supplementation can be attributable to an increase in intracranial pressure during labor [156], trauma, or another intracranial lesion.

Discharging the Patient

Ambulatory patients are discharged home with a companion when the effects of the neural blockade have worn off and complications such as nausea, pain, and dizziness have been treated. Exceptions are patients who have had dental and very minor surgical procedures, for whom the residual effects of sedation determine fitness for discharge from the office or clinic, rather than the disappearance of neural blockade effects. Subsequent complications are detected by a follow-up call, visit 24 h later, or an emergency communication from patient or relative.

The situation for hospitalized patients who have often received a central neural blockade is somewhat different. When the neural blockade has worn off; pain and nausea have been treated; pharmacologic, neurologic, cardiovascular, and respiratory concerns resolved, the patient is transferred to a ward or intensive care unit. It is there that the delayed, but potentially permanent, complications occur 2 or 3 days later, whose outcome is determined by the time between detection and therapeutic intervention. The presenting symptoms and signs associated with different complications often include pain and evidence of increasing (rather than decreasing) neural blockade that may end in permanent disability. These complications are discussed elsewhere in this volume. It suffices to say that it is likely to be helpful if patient and caregivers are aware of the need to keep in touch regarding symptoms of these rare complications.

Complication Prevention

Complication reduction, and ultimate abolition, depends on consistent application of current knowledge and skills to patient care plus further development of expertise. In 1940, the leading article of the first issue of the *Journal of the American Society of Anesthesiologists* (today *Anesthesiology*) concluded with this statement: "The important decision is what man shall give the anesthetic [in contrast to the drug or technique]" [157]. The implications for training and practice remain.

The baseline competence reached at the inception of independent anesthetic practice is established by certifying authorities but the significant variation among certificants probably represents other training programs [158]. This is partly attributable to limited clinical experience and, particularly relevant for regional anesthesia, a possibly doubtful correlation between knowledge and skills [159–161].

Thus, any further move toward complication prevention must, among other things, include better regional anesthesia training. This is occurring on several counts. Virtual reality techniques that register in a three-dimensional manner on a computer screen can radically change the pattern of training [159]. Mental imagery of anatomy is an integral part of the anatomic reasoning while performing neural blockade. Three-dimensional computer-based methods of presenting anatomic relations have great potential for overcoming existing limitations of conventional teaching [162]. Last, more critical evaluation techniques can assess training methods and establish levels of competence reached in manual skills [163, 164]. However, improvement in the training of future anesthesiologists does little to reduce complications perpetuated by recently training and established anesthesiologists.

Contrasting characteristics of two competing perspectives of safe practice are presented in Table 2.4 [165].

Anesthesiologists' attitudes consistent with the same characteristics of normal accident theory have been documented [166]. These reflect certain problems facing persons who wish to implement factors supporting a high reliability theory, for example, the five hazardous thinking patterns: antiauthority, impulsivity, invulnerability, macho, and resignation.

Ever since anesthesia has been practiced, a variety of case reports and collations of mortality and morbidity have been published under the auspices of individuals, groups, or institutions. Nevertheless, controversy and democracy have remained preeminent, and resistance "on principle" to external imposition of medical practice was firmly entrenched until the last 25 years, when such independence was seriously challenged and many anesthesiologists perceived certain changes to be in their own interests as well as those of patients.

Table 2.4 Competing perspectives on safety

High reliability theory
• Complications can be prevented through good organization and management
• Safety is the priority of the organization
• Duplicating tasks and devices increase safety
• Continuous quality improvement with simulations creates and maintains safety
• Trial-and-error learning from complications can be effective
Normal accidents theory
• Complications are inevitable in any complex system
• Safety is only a competing objective, "We cannot necessarily do that here"
• Duplication encourages risks and reduces safety
• Discipline and socialization are incompatible with democratic values
• Organizations cannot train for the unimagined. "Intuition is better than algorithms"
• Learning efforts from critical incidents and complications are crippled by faulty reporting and denial of responsibility

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The Department of Anesthesia of Harvard Medical School, Boston, in 1986 published specific, detailed, mandatory standards for minimal patient monitoring during anesthesia [167]. These were to be implemented in its nine component teaching hospital departments and published for the interest of other practitioners, organizations, and institutions. The motivation was anesthetic complications that incurred substantial financial settlements and that were thought to have been preventable and strongly influenced by a report of critical incidents. Included in those standards were these references to regional anesthesia:

- An attending or resident anesthesiologist or nurse anesthesiologist shall be present in the operating room at all times during its conduct.
- The arterial blood pressure and heart rate shall be measured at least every 5 min, where not clinically impractical.
- The ECG shall be continuously displayed from the institution of anesthesia until preparing to leave the anesthetizing location, unless clinically impractical.

The effect of these standards on complications of regional anesthesia has not been published, but there has been a favorable association between the adoption of the standards and diminishing cost of malpractice insurance.

The Canadian Anesthesiologists' Society (CAS) has promoted its guidelines to the practice of anesthesia for close to 20 years [168]. A standard is a definite level of excellence or adequacy demanded by an organization. Clinical practice guidelines (CPGs) are systematically developed statements to inform practitioners about appropriate care in specific clinical circumstances. Implicit in this is planned avoidance of complications. The word *guidelines*, as opposed to *standards*, was used advisedly, because although mandatory requirements could be reasonable for a hospital or group of institutions, it was deemed inappropriate to address all Canadian anesthesiologists in such a manner. The Canadian guidelines promulgated for regional anesthesia in 1996 are as follows.

Patient Monitoring

The only indispensable monitor is the presence, at all times, of an appropriately trained and experienced physician. Mechanical and electronic monitors are, at best, aids to vigilance. Such devices help the anesthesiologist to ensure the integrity of the vital organs, and in particular the adequacy of

tissue perfusion and oxygenation. The healthcare facility is responsible for the provision and maintenance of monitoring equipment that meets current published equipment standards.

The chief of anesthesiology is responsible for advising the healthcare facility on the procurement of monitoring equipment and for establishing policies for monitoring to help ensure patient safety.

The anesthesiologist is responsible for monitoring patients receiving care and *must ensure* that appropriate monitoring equipment is available and working property. *A preanesthetic checklist* (*such as found in* Table 2.5 *or equivalent*) *must be completed before initiation of anesthesia*. Monitoring guidelines for standard patient care apply to all patients receiving regional anesthesia or intravenous sedation.

Monitoring equipment may be classified either as *required* for each anesthetized patient (i.e., the device is attached, or dedicated exclusively, to each patient) or *immediately available* (the device is available for the anesthetized patient without inappropriate delay).

Required Equipment

- Pulse oximeter
- Apparatus to measure blood pressure
- Stethoscope, precordial, esophageal, or paratracheal
- ECG monitor
- Capnograph for an intubated patient
- Apparatus to measure temperature
- Appropriate lighting to visualize the exposed portion of the patient

Table 2.5 Preanesthetic checklist

A. Gas pipelines	D. Vacuum system Suction adequate
Secure connections between terminal units (outlets) and anesthetic machine.	E. Scavenging system Correctly connected to patient circuit and functioning
B. Anesthetic machine	F. Routine equipment
1. Turn on machine master switch and all other necessary electrical equipment	1. Airway Functioning laryngoscope (backup available)
Line oxygen (40–60 psi) (275–415 kPa)	Appropriate tracheal tubes: patency of lumen and integrity of cuff
Line nitrous oxide (40–60 psi) (275–415 kPa)	Appropriate oropharyngeal airways
Adequate reserve cylinder oxygen pressure	Stylet
Adequate reserve cylinder nitrous oxide content	Magill forceps
Check for leaks and turn off cylinders	2. IV supplies
Flow meter function of oxygen and nitrous oxide over the working range	3. Blood pressure cuff of appropriate size
2. Vaporizer filled	4. Stethoscope
Filling ports pin-indexed and closed Ensure “on/off” function and turn off	5. ECG monitor
3. Functioning oxygen bypass (flush)	6. Pulse oximeter
4. Functioning oxygen fail-safe device	7. Capnograph
5. Oxygen analyzer calibrated and turned on functioning mixer (where available)	8. Temperature monitor
Attempt to create a hypoxic O_2/N_2O mixture and/or verify correct changes in flow alarm	9. Functioning low- and high-pressure alarm
6. Functioning common fresh gas outlet	G. Drugs
7. Ventilator function verified	1. Adequate supply of frequently used drugs and IV solutions
8. Backup ventilation equipment available and functioning	2. Appropriate doses of drugs in labeled syringes
If an anesthesiologist uses the same machine in successive cases, departmental policy may permit performing an abbreviated checklist between cases	H. Location of special equipment in each anesthetizing location
C. Breathing circuit	1. Defibrillators
1. Correct assembly of circuit to be used	2. Emergency drugs
2. Patient circuit connected to common fresh gas outlet	3. Difficult intubation kit
3. Oxygen flow meter turned on	
4. Check for exit of fresh gas at face mask pressurizes. Check for leaks and integrity at circuit (e.g., Pethick test for coaxial)	
5. Functioning high-pressure relief valve	
6. Unidirectional valves and soda lime	
7. Functioning adjustable pressure relief valve	

Immediately Available Equipment

- Peripheral nerve stimulator
- Respirometer (tidal volume)

It is recognized that brief interruptions of continuous monitoring may be unavoidable. Furthermore, there are certain circumstances when a monitor may fail; thus, continuous vigilance by the anesthesiologist is essential.

The use of agent-specific anesthetic gas monitors is encouraged.

Epidural Anesthesia During Childbirth

Experience since publication of the guidelines in the September 1986 issue of the CAS newsletter has shown that the incidence of major complications associated with continuous low-dose epidural infusion for obstetric analgesia is extremely low. Consequently, it is not necessary for an anesthesiologist to remain physically present or immediately available during maintenance of continuous infusion epidural analgesia. Instead, the following requirements suffice: (1) an appropriate protocol for the management of these epidurals is in place; (2) an anesthesiologist can be contacted for the purpose of advice and direction.

In contrast to continuous infusion epidural analgesia, bolus injection of local anesthetic into the epidural space can be associated with immediate life-threatening complications. In recognition of this, the CAS recommends the following:

- When a bolus dose of local anesthetic is injected into the epidural space, an anesthesiologist must be available to intervene appropriately should complications arise.
- The intent of the phrase *available to intervene appropriately* is that individual departments of anesthesiology shall make their own determinations of *availability* and *appropriateness*. This determination must be made after each individual department of anesthesiology has considered the possible risks of bolus injection of local anesthetic and the methods of dealing with any emergency situation that might arise from the performance of the procedure in their facility.

Practice of Anesthesia Outside a Hospital

The basic principles, training requirements, techniques, equipment, and drugs used for the practice of anesthesia are noted in other sections of the guidelines. The following guidelines are for certain aspects peculiar to anesthetic practice outside a hospital.

Patient Selection

Patients should be classified by physical status in a manner similar to that in use by the American Society of Anesthesiologists (ASA). Usually, only patients in the ASA classifications I and II should be considered for an anesthetic outside a hospital. Patients in classification III may be accepted under certain circumstances.

Preoperative Considerations

The patient must have had a recent and recorded history, physical examination, and appropriate laboratory investigations. This may be performed by another physician or anesthesiologist. The duration of fasting before anesthesia should conform to the previously stated guidelines. The patient should be given an information sheet with pre- and postanesthetic instructions.

Conduct of Anesthesia

The anesthetic and recovery facilities shall conform to hospital standards published by the Canadian Standards Association, as defined in other sections. The standards of care and monitoring shall be the same in all anesthetizing locations. The Canadian guidelines are comprehensive and include the organization of hospital anesthesia services, the responsibilities of the chief of anesthesiology, and anesthetic equipment and anesthetizing locations.

Intuitively, CPGs are useful for collaboration with lay persons in a managerial capacity and with physicians, and they have been generated for a variety of reasons [169], including quality assurance and the assistance of practitioners in their decision making. However, a cause-and-effect relationship between guidelines and anesthesia complications has been neither demonstrated nor sought [170]. Indeed, formal evaluation of CPGs in Canada is rare, and there is concern that CPGs, lacking policies to ensure compliance, will be ineffective. It is expected that guidelines unsupported by peer review and prominent personalities will be ignored; nevertheless, whether referred to as *audit*, *quality assurance*, *or continuous quality improvement* or CPG, developments continue. It is noteworthy that it was insistence of the government of the United Kingdom that motivated the Confidential Enquiry into Perioperative Deaths there, and pressures elsewhere for establishing actual standards of practice come from governments, insurers, and the general public. In a definitive analysis of guidelines [170], the need for a clear target if they are to be effective improvers of patient care is emphasized and that they must be oriented to practitioners, managers, and planners as well as other stakeholders. Achieving consensus is itself a difficult task, but guidelines for this process have been promulgated [171].

Conclusion

Safety—avoidance of complications—in regional anesthesia is dependent on the cooperative efforts of anesthesiologists, other care providers, and persons with management responsibilities. The deficiencies at any moment in time may be inadequacies in the state of the art or defects in what is a very complex system. It may be that differences between general and regional anesthesia detected in comparative studies are affected by factors in the patient care systems other than differences intrinsic to the techniques.

In 1858, the redoubtable John Snow published rules for chloroform administration. These were not rules in the regulatory sense but advice or recommendations from a respected figure. What would have been his views about competing perspectives on safety will remain unknown; however, his efforts for the greater good of patients can be emulated by taking advantage of superior opportunities to promote safe regional anesthesia practice, not only by improving training, practice, and research but by international dissemination of information.

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Local Anesthetic Toxicity: Prevention and Management

3

Derek Dillane

Key Points

- An unintentionally high blood level of local anesthetic results in an excessive concentration at the central nervous and cardiovascular systems. This may lead to a clinical spectrum of toxicity ranging from mild symptoms to cardiac arrest and death.
- Rate of absorption of local anesthetic into the bloodstream is a primary determinant of systemic toxicity and is influenced by local vascularity and extent of local tissue binding.
- Presentation and rapidity of onset of local anesthetic toxicity is variable and is dependent on the local anesthetic used and whether the patient is sedated/anesthetized.
- Intralipid emulsion is effective at reversing local anesthetic toxicity, although the underlying mechanism is poorly understood.
- CPR, ACLS, and low-dose epinephrine are the focus of treatment for local anesthetic toxicity-induced cardiovascular collapse.
- Preventative measures (safety checklists, monitoring, appropriate dosing) can help reduce the incidence of local anesthetic toxicity.
- Evidence from a large multi-center regional anesthesia database reports a reduction in local anesthetic systemic toxicity of 65 % when ultrasound guidance is used compared with peripheral nerve stimulation alone.

D. Dillane, MB, BCh, BAO, MMedSci, FCARCSI (✉)
Department of Anesthesiology and Pain Medicine,
University of Alberta, Edmonton, AB, Canada
e-mail: dillane@ualberta.ca

Introduction

Local anesthetic systemic toxicity is a potentially life-threatening result of either unintentional intravascular injection of local anesthetic or slow absorption of an inappropriately high dose of drug deposited perineurally. With the widespread adoption of ultrasound guidance as a nerve-seeking modality, there is reasonable evidence from large clinical registries that toxicity is occurring less frequently. Extensive whole animal and laboratory research have validated the usefulness of Intralipid emulsion as a treatment for evolving or established toxicity. Numerous case reports with several local anesthetic agents provide promising evidence that Intralipid is an invaluable element of the treatment protocol. It is now an established component of the American Society of Regional Anesthesia (ASRA) recommendations for the treatment of systemic toxicity to local anesthetic. Despite these advances, local anesthetic toxicity remains a very real and disquieting prospect. Constant vigilance, multiple preventive safety steps, education, and simulation may best serve the practicing regionalist.

Unintentionally, high blood levels of local anesthetics resulting in an excessive concentration of local anesthetic at the central nervous and cardiovascular systems encompass a clinical spectrum ranging from mild symptoms to cardiac arrest and death. Serious local anesthetic systemic toxicity (LAST) is a rare occurrence. Most available information comes from case reports and large clinical registries. Over the past decade, the widespread validation of ultrasound guidance as an aid to locating target nerves and vasculature has had a distinct effect on the success of peripheral nerve blockade. This, in conjunction with the serendipitous discovery of the utility of Intralipid emulsion for the treatment of LAST, has made regional anesthesia a safer prospect.

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_3

Incidence

There has been a dramatic and evolving change in the incidence of systemic toxicity to local anesthetics in the past 30 years. This is most perceptible for epidural anesthesia which had a cumulative frequency of systemic toxicity as high as 100 per 10,000 up to 1982 [1]. This is perhaps unsurprising given the large volumes of local anesthetic injected into a highly vascular epidural space. The utilization of multiple safety steps has benefited maternal morbidity and mortality more than any other group as evidenced by the substantial reduction in the incidence of epidural-associated systemic toxicity since 1982. At this time, in response to multiple case reports of fatal cardiac toxicity, emphasis was placed on epinephrine test doses, fractionated dosing, and withdrawal of 0.75 % bupivacaine for obstetric use. These safety measures eventuated a reduction in the incidence of epidural-associated toxicity to 1.2 to 11 per 10,000 [2].

Peripheral nerve blockade (PNB) has been subject to a similarly impressive reduction in the incidence of systemic toxicity, conceivably associated with the introduction and widespread use of ultrasound guidance as a means for locating the neural target. In the mid to late 1990s, the incidence of systemic toxicity associated with PNB was reported in the range of 7.5–20 per 10,000 blocks with an associated incidence of serious cardiac toxicity of 1 per 10,000 [2, 3]. Recent prospective clinical registries report frequencies of systemic toxicity for PNB of 0.8 to 8.7 per 10,000 blocks with no serious cardiac toxicity in either registry [4, 5].

History

From the coca leaf of the Peruvian Andes to the office of Viennese ophthalmologist Carl Koller, the early narrative of local anesthetic pharmacology stretches from Spanish Conquistadors to the psychoanalysts of the mid-nineteenth century. Cocaine (Fig. 3.1), isolated from the coca leaf in 1860 by the German chemist Albert Niemann, was used clinically for the first time by the Viennese ophthalmologist Carl Koller in 1884 when he performed the first surgical procedure using local anesthesia on a patient with glaucoma [6]. Two hundred cases of systemic toxicity and 13 deaths were assigned to the drug between 1884 and 1891, diminishing its initial widespread use as a local anesthetic [7]. Another German chemist, Alfred Einhorn, searching for a safer alternative to cocaine, synthesized the compound novocaine in 1904, later to be renamed procaine in the United States during World War I [8, 9]. Initially found to be safe, it became the local anesthetic of choice until it was found that it provoked allergic reactions in many patients and clinicians [10].

Lidocaine, the first amino-amide local anesthetic, was developed by Löfgren and Lundquist in 1943 and was first marketed in 1948 [11]. Lidocaine has been in clinical use for almost 60 years and it remains one of the safest and most efficacious local anesthetic agents ever manufactured. The short duration of action of lidocaine precipitated the search for a longer acting agent. Bupivacaine was synthesized by Bo af Ekenstam in 1957 and introduced into clinical practice 10 years later [12]. Bupivacaine, an amino-amide local anesthetic belonging to the family of the *n*-alkyl-substituted pipecholyl xylidines, was found to be long-acting and produced for the first time a dose-dependent separation between sensory and motor anesthesia. Initial safety reports were encouraging [13], but after 10 years of clinical use, serious concerns regarding associated cardiac toxicity were reported. In 1979, George Albright highlighted five anecdotal reports of cardiac arrest following regional anesthesia with bupivacaine [14]. These cases of almost simultaneous convulsion and cardiac arrest required prolonged and largely unsuccessful resuscitation following a presumed intravascular injection. In October 1983, Albright, in an address to the United

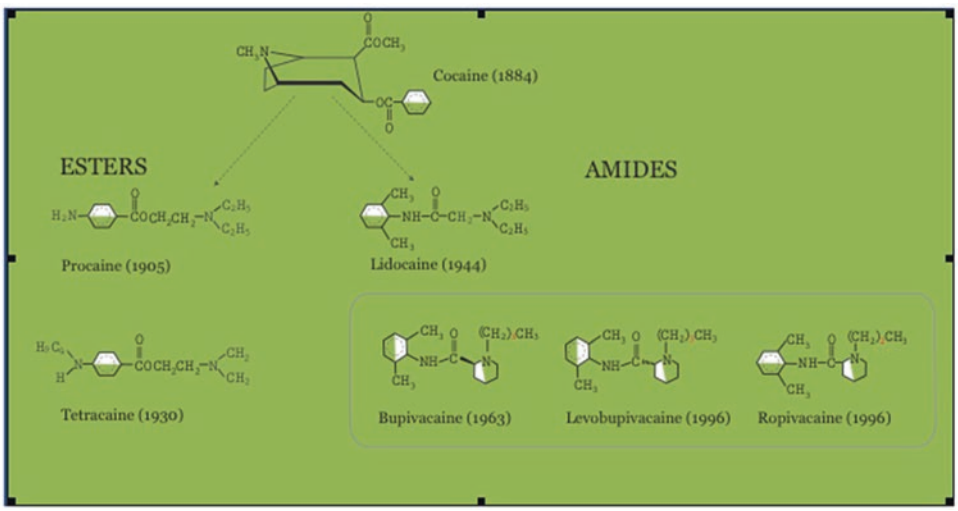


Fig. 3.1 Structure of local anesthetic molecule consisting of a lipophilic and a hydrophilic portion joined by a connecting hydrocarbon chain. The lipophilic portion is usually an aromatic ring which is responsible for the anesthetic activity. The hydrophilic portion is usually a tertiary amine. An ester (–C0–) or an amide (–NHC–) bond links the two moieties. The nature of this bond allows the molecule to be classified as an ester or amide local anesthetic

States Food and Drug Administration's Anesthetic and Life Support Advisory Committee, presented a series of 49 reports of cardiac arrest or ventricular tachycardia requiring cardioversion occurring over the previous 10 years [15]. Most of these cases involved obstetric epidural anesthesia using 0.75 % bupivacaine. This information led to the FDA-sanctioned withdrawal of 0.75 % bupivacaine for obstetric use in addition to the introduction of long overdue safety recommendations, including the use of an epinephrine test dose, fractionated dosing, and improved patient monitoring [16].

At the same time in the United Kingdom, the Council of the Association of Anesthetists of Great Britain and Ireland launched a campaign to discontinue the use of bupivacaine during Bier's intravenous regional anesthesia (IVRA) [17]. The agent of choice for IVRA up to this juncture, in which its use was considered relatively safe [18], was implicated in the deaths of 5 patients from 1979 to 1982. An editorial which appeared in the British Medical Journal in 1982 signified their comparability: all five were healthy patients being treated for minor conditions in emergency departments, and all five received bupivacaine during IVRA. Notwithstanding causative factors including cuff inflation pressure, time, or mechanical failure, the cardiac toxicity of bupivacaine was again demonstrated. In relatively modern times, though bupivacaine is no longer used for IVRA, this has not prevented deaths due to its intravenous administration. In the decade leading up to 2004, it has been directly responsible for the deaths of three patients in the United Kingdom as a result of accidental intravenous administration.

In the 1980s, the development of new long-acting amides took advantage of the fact that most of these molecules have a chiral centre determined by the presence of a carbon atom bound to four different molecules (Fig. 3.2). These three-dimensional stereoisomers have an identical chemical composition, but differ in their spatial orientation [19]. This is of significance for amide local anesthetics as it has been established that the levorotatory isomer (S−) has less potential for systemic toxicity than the dextrorotatory one (R+) [20]. This led to the development of the single stereoisomers levobupivacaine and ropivacaine, first approved for clinical use in North America in 1996.

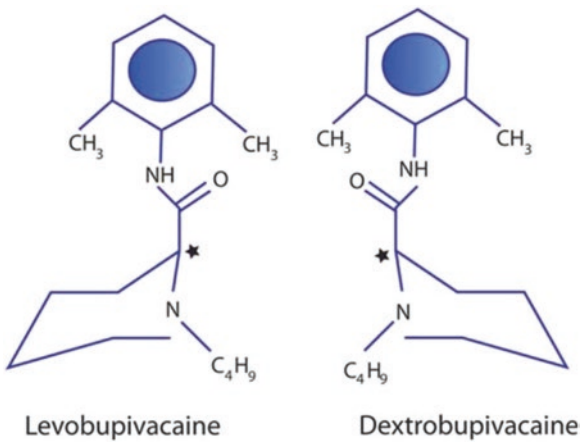


Fig. 3.2 Molecular structure of stereoisomers levobupivacaine and dextrobupivacaine. The *asterisk* denotes the presence of an asymmetric carbon atom

Structure and Properties of Local Anesthetics

All local anesthetics are weak bases. Their formula consists of a lipophilic aromatic ring connected to a hydrophilic residue by a hydrocarbon chain. They are clinically classified as amino-esters or amino-amides depending on the link between the lipophilic ring and the hydrophilic tertiary amine (Fig. 3.3). Amino-ester local anesthetics are hydrolyzed in the plasma by cholinesterases, whereas amides are metabolized in the liver by the cytochrome P450 enzyme system.

Onset of Action, Potency, and Duration

Local anesthetics as weak bases exist in solution as both ionized (water-soluble) and non-ionized (lipid-soluble) molecules but traverse phospholipid membranes in their non-ionized form only. The degree of drug ionization is determined by the dissociation constant (p*K*a) and the pH of the surrounding fluid. The dissociation constant (p*K*a) of a molecule represents the pH at which 50 % of the molecules exist in a lipid-soluble form and 50 % in a water-soluble form. Local anesthetic molecules with a p*K*a that approaches physiologic pH have a higher concentration of the non-ionized lipid-soluble form. As the p*K*a of a drug increases, a greater proportion exists in the ionized hydrophilic form at physiological pH. Commonly used local anesthetics have a p*K*a between 7.8 (lidocaine) and 8.1 (ropivacaine and bupivacaine) (Table 3.1). Drugs with a lower p*K*a (e.g., lidocaine) exist to a greater degree in a non-ionized form and diffuse more easily across cell membranes. This explains why lidocaine has a shorter *onset of action* than ropivacaine or bupivacaine. At physiological pH, a significant fraction of the drug is in a non-ionized form and readily crosses the membrane to the cytosolic side of the nerve cell. Excessively lipophilic drugs remain in the first membrane encountered. For the drug

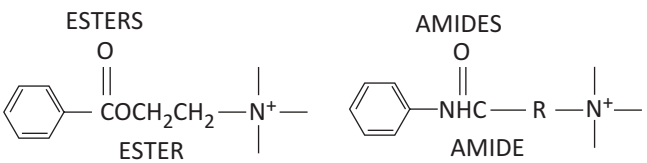


Fig. 3.3 Basic local anesthetic structure with lipophilic aromatic ring joined to a hydrophilic tertiary amine by an ester or an amide hydrocarbon chain

Table 3.1 Physicochemical properties of common amide linked local anesthetics

	p*K*a	Onset time	Plasma protein binding (%)	Duration of action	Lipid solubility (partition coefficient)	Potency
Lidocaine	7.7	Fast	64	Medium	304	Medium
Bupivacaine	8.1	Medium	95	Long	2565	High
Levobupivacaine	8.1	Medium	96	Long	2565	High
Ropicacaine	8.2	Medium	94	Long	775	Medium
Mepivacaine	7.6	Fast	75	Medium	90	Medium

Partition coefficient (octanol/buffer coefficient) Strichartz, G. R. et al. Fundamental properties of local anesthetics. II. Measured octanol: buffer partition coefficients and p*K*a values of clinically used drugs. Anesth Analg 1990;71:158–70

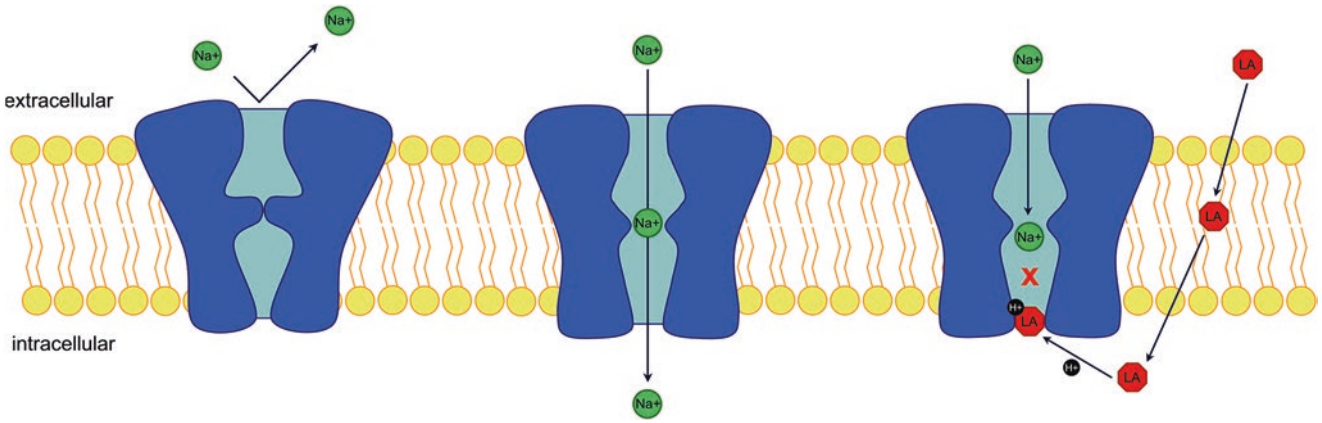


Fig. 3.4 Representation of sodium channels in various states of activation in a neuronal cell membrane. *Left*, the deactivated sodium channel is impermeable to sodium ion passage. *Middle*, the activated channel allows sodium ions to flow into the cell and ultimately trigger an action potential. *Right*, the sodium channel is blocked by local anesthetic. Local anesthetic crosses the phospholipid neural cell membrane in its non-ionized form only. Drugs with a low p*K*a, e.g. lidocaine, which exist to a greater degree in its non-ionized form at physiological pH, more readily cross the cell membrane, and have a faster onset time

to effectively block the sodium channel, it must become re-ionized on the cytosolic side of the membrane.

Potency is directly related to lipid solubility which is expressed as lipid/water partition co-efficient. Drugs with low lipid solubility need higher concentrations to produce a block of similar intensity to that produced by local anesthetics with higher lipid solubility (e.g. 2 % lidocaine vs. 0.5 % bupivacaine). *Duration of action* is largely determined by the degree of plasma protein binding.

Mechanism of Action

Local anesthetics prevent neural excitation and subsequent propagation of action potential by inhibiting passage of Na^+ ions through voltage-dependent Na^+ channels (Fig. 3.4). The sodium channel is a large, multimeric complex which exists in a closed, open, and inactivated state [21]. It contributes to the control of membrane excitability and is responsible for action potential generation. Local anesthetic molecules may access the Na^+ channel through the hydrophilic inner pore or traverse the hydrophobic cell membrane when the channel is closed. The local anesthetic must be re-ionized to prevent passage of Na^+ ions. Equilibrium exists between the ionized and unionized forms in the Na^+ channel.

Pharmacokinetic Considerations

Unlike many therapeutic agents, local anesthetics can be delivered directly to their site of action. Paradoxically, a relatively large volume of a high concentration of local anesthetic is injected during nerve blockade to ensure adequate anesthesia and analgesia. Ultrasound guidance now allows for more accurate deposition with a smaller volume and dose of local anesthetic. Historically, large volumes were utilized due to the relatively small number of local anesthetic molecules thought to reach the intended sodium channels. The nerve sheath or perineurium is a very effective diffusion barrier. Direct measurement in an animal model demonstrates that <2–3 % of an injected dose enters the target nerve. A large fraction of the delivered agent is absorbed by the surrounding tissue or is removed by the systemic circulation and distributed to distant organs according to their vascular density. More than 90 % of

an injected dose is taken up by the systemic circulation within 30 min of injection [22]. The rate of absorption into the bloodstream is a major determinant of systemic toxicity.

Absorption

For both central and peripheral blocks, the cephalic parts of the body have a more rapid rate of absorption [23]; for example, a cervical epidural leads to higher plasma levels of local anesthetic than a caudal epidural. Similarly, absorption decreases from head to foot for peripheral conduction and infiltration blocks due to the relative difference in vascularity between these areas [24, 25]. Absorption rates at different block sites are directly related to local blood flow and inversely related to local tissue-binding [26]. As a consequence, plasma uptake is faster from the more vascular intercostal space or the axilla than from the caudal space. Vascular uptake of local anesthetic after intercostal nerve block occurs more rapidly than with any other regional technique [27].

The main component of the epidural space is fat, which is an important determinant of local anesthetic systemic uptake. More lipophilic local anesthetic molecules will be retained to a greater degree by epidural fat leading to subsequent delayed absorption. It has been demonstrated in adults that after a single-shot epidural injection, 30 % of a dose of lidocaine and 50 % of a dose of bupivacaine remained in the epidural space for 3 h after injection [28]. The vasoconstrictive properties of ropivacaine may contribute to its prolonged absorption from the epidural space. After time to maximum plasma concentration (T_{max}) has been achieved, the rate of absorption slows down significantly so that it becomes longer than that of elimination, leading to a flip-flop effect in plasma drug concentration [23]. This continuous, protracted systemic absorption during the elimination phase, in combination with the buffering effect of plasma protein binding, limits the plasma concentration of unbound drug and is protective against toxicity.

Distribution

Local anesthetic is distributed to organs according to their vascular density. This accounts for the fact that highly vascular organs such as brain, heart, lung, liver, and kidneys are exposed to unmetabolized local anesthetic at peak concentration. The local anesthetic is taken up within each organ according to the tissue-plasma partition co-efficient (Table 3.2). The lungs play an important buffering role by taking the full impact of drug-laden venous blood. However, this buffering action of the lung is saturable.

Local anesthetics are distributed to the tissues and body fluid compartments after systemic absorption to the plasma. Volume of distribution (V_d) is the principal determinant of this step. This is a mathematical expression which depicts the distribution characteristics of a drug in the body and is a measure of the degree to which a drug is delivered by the plasma to the organs and tissues of the body. Drugs with a small calculated V_d have a high concentration of drug in the plasma, a low tissue concentration, and are more likely to accumulate to toxic levels. Drugs with a larger V_d are subject to slower elimination.

Table 3.2 Tissue-plasma partition coefficient for lidocaine in various organs

Organ	Tissue-plasma partition co-efficient (λ)
Spleen	3.5
Lung	3.1
Kidney	2.8
Stomach	2.4
Fat	2.0
Brain	1.2
Heart	1.0
Muscle	0.7
Liver	0.6
Skin	0.6
Bone	0.4–0.9

de Jong R.H.Local Anesthetics. Mosby-Year Book 1994: 165

Plasma Protein Binding

Local anesthetics bind tightly to serum proteins, greatly limiting the free fraction of available drug. This is clinically relevant as it is only the free or unbound fraction which is active (i.e., readily available to cross cell membranes to become active at the sodium channel). Volume of distribution is inversely related to protein binding, i.e. drugs which are highly protein-bound, have limited passage into tissues resulting in a high drug plasma concentration and a low V_d. In adults, lidocaine is up to 70 % protein-bound, while bupivacaine, levobupivacaine, and ropivacaine are over 90 % protein-bound [29].

Three principal blood components are involved in local anesthetic binding: the plasma proteins alpha-1-acid glycoprotein (AAG) and human serum albumin (HSA), and erythrocytes. Like most weak bases, local anesthetics bind mainly to AAG. It is a major acute phase protein, and its concentration rapidly increases in the first 24–48 h after surgery. AAG has a greater affinity for binding local anesthetic by an order of magnitude of 5000–10,000 compared to albumin [30]. Capacity for binding is relatively low, however, and saturation occurs at clinically relevant concentrations. Even though albumin is the most abundant plasma protein (50–80 times more abundant than AAG), it has a low affinity for amide local anesthetic drugs [23]. By virtue of its enormous bind-

Table 3.3 Select pharmacokinetic parameters of local anesthetics

Local anesthetic	Clearance (L/min)	Terminal half-life (min)	Hepatic extraction (ratio)
Lidocaine	0.95	96	0.72
Etidocaine	1.11	162	0.74
Mepivacaine	0.78	114	0.51
Bupivacaine	0.58	162	0.40
Ropivacaine	0.73	111	0.40
Levobupivacaine	0.47	108	0.67

de Jong R.H.Local Anesthetics. Mosby 1994: 67. Reproduced with permission from author. Data for ropivacaine from A. Lee et al.[117]

ing capacity (it is almost unsaturable), together with its abundance, the role of HSA becomes significant when AAG is saturated. Affinity for red blood cells is low and not saturable. This may be considered as a buffer system when toxic concentrations occur.

Hepatic Metabolism

Most absorbed local anesthetic is cleared from the liver. Hepatic clearance is a function of the hepatic extraction ratio which in turn is dependent on the ratio of free to protein-bound drug. Lidocaine, being moderately protein-bound, has a high hepatic extraction ratio (70–75 %). Clearance is therefore flow-limited and is reduced by factors that limit hepatic blood flow, e.g. cardiac failure, intravascular volume depletion, and upper abdominal surgery. Bupivacaine and ropivacaine, being highly protein-bound, are cleared by less than 50 % per pass; their clearance depends on free drug concentration (Table 3.3). It follows therefore that factors which influence hepatic extraction and plasma protein binding of local anesthetic must be acknowledged when determining the total dose of local anesthetic to be administered.

Renal Excretion

Only a small fraction of unmetabolized amide local anesthetic is excreted in the urine. Thus, renal dysfunction affects local anesthetic clearance less than hepatic failure, notwithstanding the accumulation of potentially harmful metabolites [20]. The clearance of one of the main metabolites of ropivacaine, 2, 6-pipecoloxylidide (PPX), is decreased in uremic patients. Its cardiotoxicity in rat studies is reported as half that of bupivacaine.

Clinical Presentation

The presentation and speed of onset of LAST are extremely variable. In a review from Vasques et al., of all published LAST cases since the publication of ASRA treatment recommendations and guidelines, 26 % of toxicity presentations

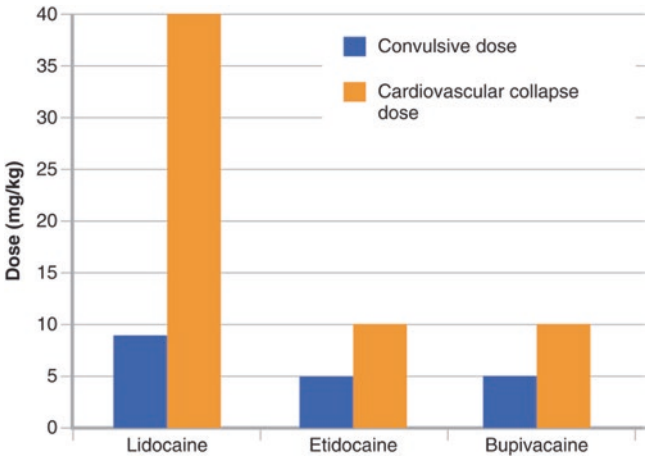


Fig. 3.5 Ratio of convusion:cardiovascular collapse dose. Lidocaine has a far greater margin of safety, i.e. seizures can be taken as a timely warning. Cardiovascular collapse may rapidly follow seizure for bupivacaine toxicity. Covino BG. Pharmacology of local anesthetic agents. Adapted from: Rogers MC, Tinker JH, Covino BG et al.(Eds). Principles and Practice of Anesthesiology. St Louis: Mosby Year Book; 1993; 1235–57

after single shot blockade occurred within 1 min and 48 % became apparent within 5 min of injection [31]. Twenty-two percent did not manifest symptoms or signs of toxicity until 30 min or more had elapsed. Isolated cerebral toxicity occurred in 50 % of cases, combined cerebral and cardiac toxicity was reported in 36 % of cases, and 14 % of cases exhibited cardiac toxicity alone.

The major toxic effects are on the cardiovascular and central nervous systems. Neurologic toxicity occurs at lower concentrations followed by cardiac toxicity at higher concentrations. This is not always true for bupivacaine, which has a narrower margin between the dose that produces cerebral and cardiac toxicity (Fig. 3.5). Early signs of cerebral toxicity are subjective (dizziness, drowsiness, and tinnitus). These will not be related by the heavily sedated or anesthetized patient. Moreover, general anesthesia itself raises the cerebral toxicity threshold, and neuromuscular blockade will preclude the onset of generalized tonic-clonic seizures. Consequently, the first manifestation of an accidental intravascular injection or rapid absorption may be cardiovascular collapse.

Central Nervous System Toxicity

Local anesthetics readily cross the blood–brain barrier to disrupt cerebral function. The central toxic response is specifically related to plasma levels of local anesthetic in the central nervous system (CNS) and their effect on the complex interplay between excitatory and inhibitory pathways that facilitate neurotransmission. Initially, there is a generalized excitatory phase, as manifest ultimately by seizure activity. This initial phase appears to be the result of blocking inhibitory pathways in the amygdala, which allow excitatory neurons to function unopposed. Early clinical prodromal signs of CNS toxicity include light-headedness, dizziness, blurred vision, and tinnitus. Vasques et al. report that prodromal manifestations, i.e. confusion, dizziness, tinnitus, dysarthria, limb twitching, tremor, and eye movement abnormalities were reported in 40 % of all LAST cases reported since 2010 [31]. With increasing plasma concentrations, muscle twitching and tremors involving facial musculature and distal parts of the extremities are often observed. As blood and brain levels of local anesthetic concentration increase, generalized tonic-clonic reactions occur [21]. Seizure was the commonest reported sign of CNS toxicity in Vasques' series (54 % of reported LAST cases) [31]. When levels of local anesthetic in the CNS increase further, both inhibitory and excitatory pathways (being more resistant to the effects of local anesthetic toxicity) are inhibited, leading to CNS depression, a reduced level of consciousness, and eventually coma.

Cardiac Toxicity

Cardiotoxicity typically follows a two-stage pathway. In the early stages, sympathetic nervous system activation during the CNS excitatory phase indirectly leads to hypertension and tachycardia.A direct myocardial depressant effect occurs at higher concentrations epitomized by ventricular arrhythmias, myocardial conduction delays, and profound contractile dysfunction ultimately leading to cardiovascular collapse. Blockade of potassium and calcium channels may also contribute to cardiotoxicity signifying up to three sites of action [32]. Inhibition of cardiac potassium and calcium channels appears to occur at a concentration greater than that at which binding to sodium channels is maximal.

Most available information on this subject comes from whole animal and in vitro studies and case reports. The principal mechanism relates to the binding and inhibition of myocardial voltage-dependent sodium channels by local anesthetic molecules leading to an increase in the PR interval and QRS duration, provoking a dose-dependent prolongation of conduction time and eventual depression of spontaneous pacemaker activity. Persistent sodium channel blockade predisposes to re-entrant arrhythmias. Subtle T-wave changes on the electrocardiogram may progress to ventricular arrhythmias. These arrhythmias may subsequently be followed by ventricular fibrillation. Alternatively, profound bradycardia may ensue, followed by asystole [23]. These electrophysiological effects are compounded by a direct negative inotropic effect of local anesthetic drugs.

Clarkson and Hondeghem, when comparing lidocaine to bupivacaine in guinea pig ventricular muscle, developed the concept that lidocaine blocks sodium channels in a "fast-in fast-out" fashion, whereas bupivacaine blocks these channels in either a "slow-in slow-out" manner in low concentrations or a "fast-in slow-out" manner at higher concentrations [33]. The dissociation constants for the R(+) and S(−) bupivacaine enantiomers demonstrate that the dextrorotatory isomer is seven times more potent in blocking the potassium channel than the levorotatory isomer [34]. The levorotatory isomer (S−) of bupivacaine has less potential for cardiac toxicity than the dextrorotatory one (R+) or racemic mixture of both [20]. This led to the development of the single stereoisomers levobupivacaine and ropivacaine. Ropivacaine blocks sodium channels in a "fast-in medium-out" fashion [35]. In fact, the dissociation constant (between ligand and receptor) for bupivacaine is almost ten times longer than that of lidocaine resulting in a prolonged and near irreversible cardiac depressant effect [33]. There is a positive correlation between local anesthetic lipid solubility and inhibition of cardiac contractility, further evidence for the clinically relevant finding that ropivacaine is less toxic than bupivacaine (Table 3.1). If ropivacaine and levobupivacaine are accepted as being the safest options, the obvious question is, how do they compare to each other? Existing evidence from animal studies and one volunteer study has demonstrated both reduced cardiotoxicity and neurotoxicity of ropivacaine when compared to levobupivacaine [36]. This may be related to the reduced potency of ropivacaine or, as suggested by Groban et al., due to its smaller molecular size and piperidine-free structure [36].

The true equipotency ratio between the enantiomeric agents has been the subject of much conjecture. Results from a number of animal and clinical studies would suggest a rank order of potency of ropivacaine < levobupivacaine < bupivacaine [19]. This suggests that any theoretical cardioprotective benefit derived from ropivacaine would be negated by the clinical need for higher doses due to its lower potency. The difference in potency does not appear to be clinically relevant for surgical blocks (both peripheral and epidural) when the newer agents are used at concentrations of 0.5–0.75 %, with the clinical profile of the nerve block being similar to that obtained with racemic bupivacaine. However, the lower potency of ropivacaine becomes relevant when used for post-operative analgesia with both epidural and continuous peripheral nerve blockade. For this application,

0.2 % ropivacaine appears to be as effective as 0.125–0.15 % levobupivacaine, which in turn is identical to racemic bupivacaine [19].

Treatment of Toxicity

While the widespread use of ultrasound guidance may be the defining hallmark of regional anesthesia in the last decade, the discovery of the usefulness of Intralipid emulsion (ILE) for resuscitation from LAST has been no less instrumental in improving overall safety. Nonetheless, ILE is meaningless without vigilant monitoring and a high index of suspicion. This is especially important for the 'ultrasound generation' of regionalists who may not have had first-hand experience of local anesthetic-induced cardiac toxicity. Conversational contact with the patient is prudent on many levels. All patients subject to a regional anesthesia procedure must have electrocardiography, pulse oximetry, and blood pressure monitoring.

Immediate intervention at the earliest sign of toxicity improves the chances of successful treatment (Fig. 3.6). Prominent display of a treatment checklist in locations where regional anesthesia nerve blocks are frequently performed may be helpful (Fig. 3.7). Extensive laboratory and animal research suggest that important nuances exist between the general supportive measures of Advanced Life Support Guidelines (ACLS) and more specific measures directed at local anesthetic toxicity.

Acute morbidity from seizure activity is due in large part to airway complications. Hypoxia, hypercarbia, and acidosis all worsen prognosis. Consequently, airway control must be achieved prior to management of seizure activity. This was recognized by Moore and Bridenbaugh over half a century ago when they reported no instances of death attributable to LAST induced cardiac collapse among 103 cases of severe toxicity with mask ventilation and oxygenation [37].

Seizure control is optimally achieved with benzodiazepines, e.g. midazolam (0.05–0.2 mg/kg). Small doses of propofol may be used in the absence of immediately available benzodiazepine if there are no signs of cardiovascular instability. However, propofol can produce cardiovascular depression which may be harmful in the setting of evolving cardiac compromise.

Intralipid Emulsion

Experimental animal studies, and more recently, numerous clinical case reports document the dramatic reversal of the toxic effects of local anesthetics by intravenous Intralipid emulsion (ILE) [38–41]. Intralipid emulsion is an FDA-approved hyper-alimentation source comprised of soybean oil, glycerol, and egg phospholipids. The mechanism of action of lipid emulsion in the reversal of local anesthetic toxicity is contentious. It may have a scavenging effect by acting as a circulating lipid sink extracting lipophilic local anesthetic from plasma or tissues [40]. It also has the direct effect of improving cardiac output in the absence of toxicity and this also contributes to the rapid recovery from toxicity [42–44]. Indeed, a recent study of LAST in a rat model demonstrated that the direct cardio-tonic effect of ILE was

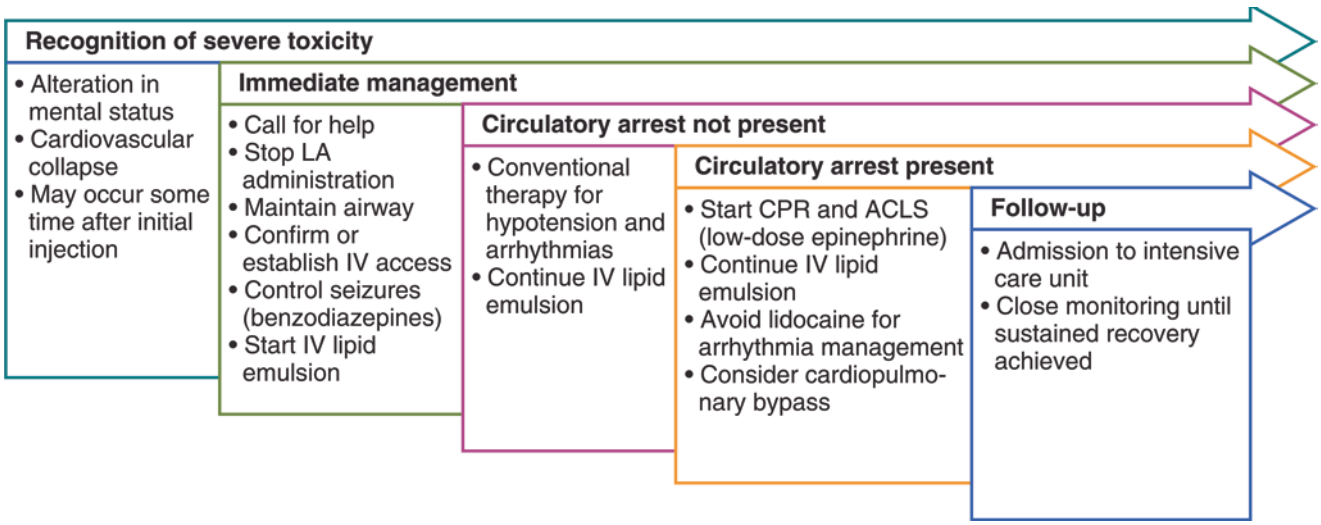
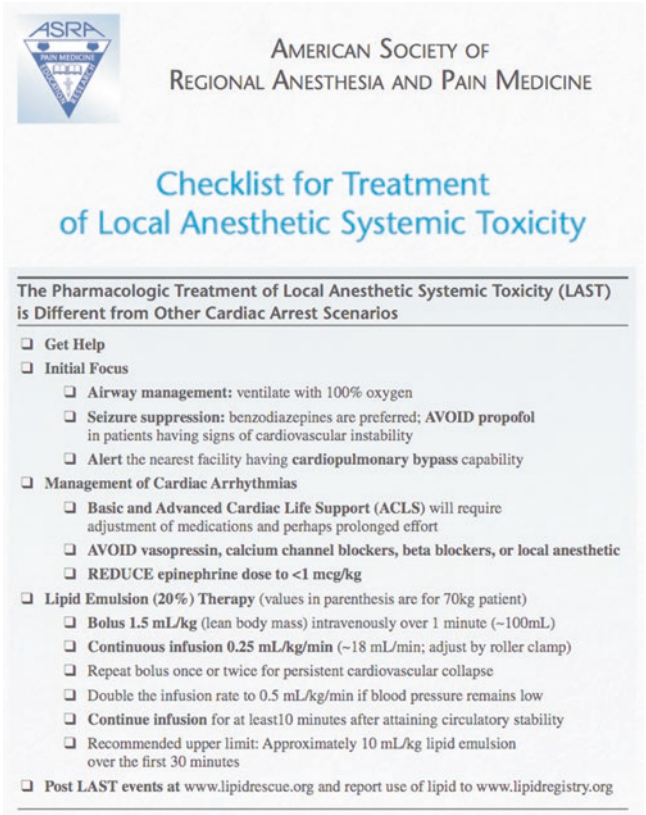


Fig. 3.6 Algorithm for management of LAST. Early recognition and intervention are vital to ensure a successful outcome. The generally accepted order of care is airway control and oxygenation followed by seizure control preferably with benzodiazepine. ILE should be initiated at the first sign of cerebral or cardiac symptoms. Adapted from: Vadi, M. G. Local anesthetic systemic toxicity after combined psoas compartment-sciatic nerve block: analysis of decision factors and diagnostic delay. Anesthesiology. 120(4) 987–96


American Society of Regional Anesthesia and Pain Medicine

Checklist for Treatment of Local Anesthetic Systemic Toxicity

The Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST) is Different from Other Cardiac Arrest Scenarios

- ❑ Get Help
- ❑ Initial Focus
  - ❑ **Airway management:** ventilate with 100% oxygen
  - ❑ **Seizure suppression:** benzodiazepines are preferred; **AVOID propofol** in patients having signs of cardiovascular instability
  - ❑ **Alert** the nearest facility having **cardiopulmonary bypass** capability
- ❑ Management of Cardiac Arrhythmias
  - ❑ **Basic and Advanced Cardiac Life Support (ACLS)** will require adjustment of medications and perhaps prolonged effort
  - ❑ **AVOID vasopressin, calcium channel blockers, beta blockers, or local anesthetic**
  - ❑ **REDUCE epinephrine dose to <1 mcg/kg**
- ❑ **Lipid Emulsion (20%) Therapy** (values in parenthesis are for 70kg patient)
  - ❑ **Bolus 1.5 mL/kg** (lean body mass) intravenously over 1 minute (~100mL)
  - ❑ **Continuous infusion 0.25 mL/kg/min** (~18 mL/min; adjust by roller clamp)
  - ❑ Repeat bolus once or twice for persistent cardiovascular collapse
  - ❑ Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
  - ❑ **Continue infusion** for at least10 minutes after attaining circulatory stability
  - ❑ Recommended upper limit: Approximately 10 mL/kg lipid emulsion over the first 30 minutes
- ❑ **Post LAST events at** www.lipidrescue.org and report use of lipid to www.lipidregistry.org

Fig. 3.7 ASRA checklist should be prominently displayed in any location where regional nerve blocks are performed

primarily responsible for the rapid recovery from bupivacaine-induced toxicity with an apparent secondary effect from the lipid sink [42]. Weinberg and colleagues conducted the original research involving the successful resuscitation of rats in whom cardiovascular collapse was induced with intravenous bupivacaine [45]. These findings were successfully repeated in a canine model of bupivacaine toxicity [40]. The first clinical case report of the successful use of lipid emulsion in the treatment of bupivacaine-induced cardiac toxicity appeared 8 years after publication of the original animal studies [39]. Its successful use has subsequently been reported for the treatment of toxicity induced by ropivacaine, levobupivacaine, and mepivacaine [46–48].

ILE should be administered as a bolus of 1.5 mL/kg over 1 min followed immediately by an infusion at a rate of 0.25 mL/kg/min. Two further boluses of 1.5 mL/kg with 5 min between boluses may be considered if the initial response is inadequate. The infusion may be continued until hemodynamic stability is restored. The rate may be increased to 0.5 mL/kg if blood pressure remains low. The infusion should be continued for at least 10 min after attaining hemodynamic stability. In light of the current evidence, it would appear prudent to ensure immediate availability of ILE in areas where regional anesthesia is performed.

At what stage during a developing case of toxicity should ILE be administered? Though minor differences exist between various guideline recommendations, the general approach involves establishing airway control and oxygenation followed by seizure control and then intravenous ILE administration. ILE appears to be relatively safe and no serious clinical complications have been reported after its use in the treatment of drug-induced toxicity. This, in conjunction with the potential devastating consequences of toxicity, connotes that administration of ILE should be considered at the earliest signs of toxicity.

Advanced Cardiac Resuscitation

The focus of treatment of cardiovascular collapse is recovery and/or preservation of coronary perfusion. Reports of successful reversal of severe LAST with return to normal cardiac function support the hypothesis that local anesthetic-induced cardiac collapse does not lead to irreversible damage to cardiac myocytes [49]. CPR and ACLS (modified to low-dose epinephrine and, of course, the exclusion of lidocaine) should be commenced if circulatory arrest is present. High-quality chest compressions are a prerequisite to circulate ILE to the coronary vasculature. It should be borne in mind that resuscitation has been successful in the past after prolonged periods of cardiac collapse. Cardiopulmonary bypass has been used successfully in the resuscitation of bupivacaine-induced cardiac arrest [50].

Though contentious as to its effect on long-term survival, epinephrine has been recommended for the treatment of cardiac toxicity [51]. However, careful titration is required with individual boluses of less than 1 μg/kg in order to avoid ventricular fibrillation or tachycardia. Although standard dose epinephrine (1 mg) may initially restore circulation and improve systolic blood pressure, it is highly arrhythmogenic and does not necessarily lead to improved long-term outcomes. Animal studies of bupivacaine-induced cardiac arrest demonstrated that epinephrine over a threshold of 10 μg/kg impaired lipid resuscitation [52]. There is also evidence from a rat model of bupivacaine toxicity that epinephrine should be given immediately after ILE bolus completion to achieve optimal success [53]. Vasopressin is contraindicated for the treatment of local anesthetic-induced cardiovascular collapse; moreover, it has been removed entirely from the ACLS Adult Cardiac Arrest Algorithm, as it shows no benefit as an alternative or in combination with epinephrine. Similarly, beta-blockade and calcium channel blockers must be avoided.

Medical management of LAST should not be determined by the variability of whatever comes to mind based on empirical experience and education. The merits of a systematic, practiced approach incorporating both cognitive and behavioral components during anesthesia emergencies have

Table 3.4 Common pediatric blocks and dosing

Route of administration	Recommended agent	Maximum dose single shot (mg/kg)	Maximum dose re-injection	Maximum dose continuous
Caudal epidural	Bupivacaine[a]	2	Not recommended	
	Bupivacaine with epinephrine	2.5		
Lumbar epidural	Bupivacaine with epinephrine	1.25–1.75	0.75–1 mg/kg	Infants 1 month–1 year 0.2–0.25 mg/kg/ h
	Bupivacaine			
Peripheral blocks	Lidocaine	6		As for lumbar epidural
	Lidocaine with epinephrine	8		

[a]Use bupivacaine-equivalent doses (i.e., 1:1) for ropivacaine and levo bupivacaine

Table 3.5 Dose recommendations for commonly used local anesthetics

Local anesthetic	Concentration (%)	Maximum dose (mg/kg)	Maximum dose with epinephrine (mg/kg)	Onset time (min)	Duration (h)
Lidocaine	0.5–2	4–6	6–8	10–20	0.75–2
Bupivacaine	0.125–0.5	2	3	15–30	2.5–8
Ropivacaine	0.2–1	2–3	–	10–20	2.5–8
Mepivacaine	0.5–1.5	6–8	10	5–10	1–1.5
2-Chloroprocaine	2–3	10	15	5	1

been promoted for a number of years under the aegis of crisis resource management [54]. Due to the rarity of a life-threatening episode of LAST, management of LAST may be practiced and reinforced using simulation. Use of the ASRA guideline checklist (Fig. 3.7) has been shown to significantly improve performance during simulated episodes of LAST [55].

Prevention of Toxicity

Considering the potential severity and refractory nature of local anesthetic toxicity, it is perhaps best to employ a cautious and preventive approach. Unintentionally, high blood levels of local anesthetic lead to a spectrum of neurologic and cardiac complications with possible devastating sequelae. This may be prevented by careful observation of a number of safety steps. Strong evidence exists to support the use of checklists as part of healthcare safety processes [56]. Implementation of a formalized checklist for the performance of regional nerve blockade may be prudent to ensure immediate availability of resuscitation equipment and medications [57].

Often overlooked but impossible to overemphasize is the significance of monitoring. All patients undergoing a regional anesthesia technique should have electrocardiography, blood pressure monitoring, and pulse oximetry. This is especially important when regional anesthesia is practiced in so-called 'block rooms' outside the immediate operating room environment. Oxygen therapy remains a prerequisite.

Slow, incremental injection of an appropriate dose (Tables 3.4 and 3.5) of a safe agent is recommended. The dose is determined by age and lean body mass and modified according to pathophysiological concerns. Higher plasma concentrations may occur after injection into a vascular area. The highest plasma levels have been widely reported after intercostal nerve blocks, followed by caudal, epidural, brachial plexus, femoral, and sciatic blockade. Of note, in their review of published cases of toxicity since publication of the ASRA guidelines on LAST management in 2010, Vasques et al. report that interscalene block was the technique most commonly associated with toxicity (23 % of all published cases) followed by epidural/caudal (16 %) [31]. Twenty-two percent of cases were associated with field infiltration anesthesia. Whether these data are an accurate reflection of block-specific risk is of course subject to publication bias.

The use of a vasoconstrictor will serve to reduce the rate of uptake in addition to prolonging the block. The author's preference is for the addition of epinephrine (1:200,000) to a dextrose solution, the primary purpose of which is ultrasonographic observation of spread of injectate. This is used in 0.5–1 mL increments as a test dose prior to injection of local anesthetic. A rise in heart rate of ten beats per minute or more is indicative of intravascular injection. Electrocardiographic evidence of T wave elevation with combinations of a small dose of bupivacaine and epinephrine is mainly caused by epinephrine. However, research in neonatal pigs shows that a higher dose of bupivacaine alone can also cause T wave elevation (Fig. 3.8) [58]. Subsequently, T wave elevation is not a reliable

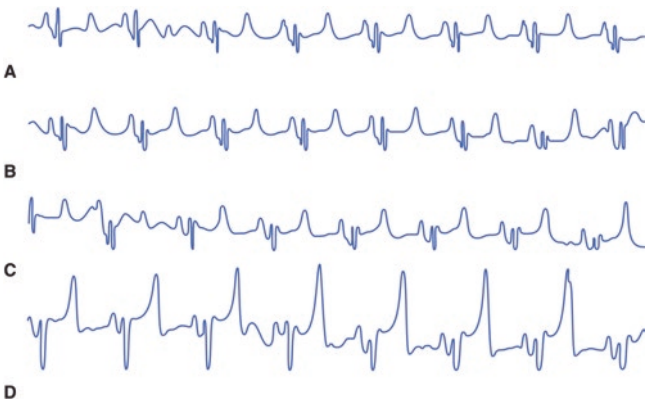


Fig. 3.8 Electrocardiographic T-wave elevation caused by increasing concentrations of bupivacaine. (**a**)No bupivacaine, (**b**)1.25 mg/kg, (**c**)2.5 mg/kg, (**d**)5 mg/kg. IV bupivacaine without epinephrine can cause T-wave elevation. Adapted from: Mauch J et al. Electrocardiographic changes during continuous intravenous application of bupivacaine in neonatal pigs. Br J Anaesth. 105 (4) 437–41

indicator for *early* detection of toxicity and may in fact be a precursor to impending cardiovascular compromise.

The use of ultrasound-guided regional anesthesia may be as important for local anesthetic systemic toxicity as the pharmacological advances of previous decades. It is now possible to visualize the target neural structure, potential vascular hazards, and the spread of local anesthetic solution. This allows for more accurate deposition of smaller volumes of local anesthetic. For instance, successful interscalene brachial plexus blockade has been reported with volumes as low as 5 mL of 0.5 % ropivacaine [24]. Interestingly, this did not translate into a measureable reduction in the risk of LAST for several years after the popularization of ultrasound as a nerve seeking modality [59, 60].

Large single- and multi-center regional anesthesia databases are useful indicators of estimate of risk for infrequently occurring events such as LAST. The largest registry in the ultrasound era (over 25,000 peripheral nerve blocks in multiple institutions) reports a reduction in local anesthetic systemic toxicity of 65 % when ultrasound guidance is used compared with peripheral nerve stimulation alone [4]. An unrelated large single center registry (9062 dual ultrasound-nerve stimulator-guided blocks and 5436 nerve stimulator-guided blocks) similarly demonstrated a significant reduction in the incidence of LAST when ultrasound was used. The use of ultrasound does not negate the need for the more conventional safety mechanisms. After all, the ultrasound image must be interpreted appropriately. The importance of maintaining a persistent view of the needle tip, especially when performing out-of-plane techniques, cannot be overstated. Injection of local anesthetic solution must be immediately stopped if spread of injectate is not clearly visible. Cases of inadvertent vascular puncture during ultrasound-guided nerve blockade with subsequent systemic toxicity have been reported in the literature [61].

Dosing

Recommendations for maximal doses are widely available in many anesthesia textbooks and in the monographs provided by pharmaceutical companies. Examples for both adult and pediatric practice are provided in Tables 3.4 and 3.5. These have largely been extrapolated from animal research, clinical case reports, and measured blood concentrations during routine clinical use. Maximal recommended doses are neither evidence-based nor site-specific. Differential absorption from injection site leads to a large variation in peak blood levels. Modification of total dose of local anesthetic in the presence of relevant pathophysiological states, e.g. cardiac, hepatic, or renal failure, is essential. Similarly, it would be unwise to adhere to these recommendations in the obese population as dosing should be performed using lean body mass. Finally, these recommendations have been developed for the normal non-intravascular injection of local anesthetic and are meaningless after unintentional intravascular injection.

A number of recent studies indicate that total mass (concentration ×volume) rather than concentration or volume alone may be the most important determinant of peripheral nerve block onset and duration [62]. Furthermore, investigations looking at the minimum effective anesthetic volume (MEAV) and concentration (MEAC) for a variety of regional anesthesia techniques suggest that improvements in onset time, block intensity, and duration may plateau beyond a threshold dose [24, 63].

A combination utilizing a local anesthetic with a fast onset/short duration, e.g. lidocaine with a slow onset/long acting agent, e.g. bupivacaine, is a common practice in an effort to maximize the favorable characteristics of both. This may have the benefit of reducing the plasma concentration of the longer acting potentially cardio toxic agent and has been demonstrated for lidocaine /bupivacaine and lidocaine/ropivacaine combinations [64]. A limited number of animal studies indicate that local anesthetic toxicity can be additive, i.e. an equipotent mixture of lidocaine and bupivacaine is as toxic as the individual compounds [65].

Abdominal Wall Blocks

Transversus abdominis plane (TAP) and rectus sheath blockade are frequently used as part of a multimodal strategy to optimize post-operative analgesia after a wide variety of surgical procedures [66–68]. These techniques are frequently used as ‘a low risk’ alternative to epidural analgesia for abdominal wall incisions. However, when compared with epidural blockade, a much larger dose of local anesthetic is frequently used for TAP and rectus sheath blockade. This is due in part to a lack of consensus with

regard to the minimum effective anesthetic concentration and volume for these blocks. Secondly, these blocks are frequently bilateral. A number of case reports serve to highlight the potential risk of toxicity with abdominal wall blocks [69–71]. These serve as a cautionary reminder that a large volume of local anesthetic injected into a neurovascular plane will be absorbed by blood vessels and surrounding highly vascular musculature. Two recent investigations of plasma ropivacaine concentration after single shot [72], and continuous TAP blockade [73], found potentially toxic plasma concentrations with wide variability between patients. This serves to reinforce the need for individualized dosing and close monitoring of patients receiving TAP and rectus sheath blockade.

Intravenous Lidocaine Infusion

The potential benefits of systemically administered lidocaine have been well-documented. Its value as a systemic analgesic was first described in 1954 in a study of over 2000 patients [74]. Several other studies involving patients undergoing colorectal surgery were collated in a meta-analysis demonstrating rapid resumption of bowel motility, shortened length of stay, and reduced nausea and vomiting [75]. No local anesthetic toxicity was observed apart from a single episode of transient arrhythmia. However, the safety of intravenous lidocaine has yet to be established in large clinical trials.

Sustained Release Local Anesthetic Formulations and Myotoxicity

Microscopic liposomal vesicles containing bupivacaine are used as a drug delivery vehicle for the slow release of the encapsulated drug, ostensibly avoiding high plasma levels while prolonging the duration of the block. These preparations are used primarily for infiltrative field blocks, but 'off-label' use for peripheral nerve blockade has been described [76]. Early reports of its safety for peripheral nerve blockade are reassuring with a similar safety and side-effect profile to that of bupivacaine and normal saline [76]. Similarly encouraging was a report from Bergese et al. on analyses of pooled safety data from 992 subjects who received liposomal bupivacaine infiltrated into the surgical site [77]. There have been reports of local inflammation, myotoxicity, and neurotoxicity with encapsulated formulations in both animal and human studies, which have prompted concerns that myotoxicity may be an unavoidable consequence of increased concentrations or prolonged exposure to local anesthetic [78].

Summary

The recognition of the usefulness of cocaine as a local anesthesic by Koller more than 130 years ago was one of the greatest medical advances ever made. It revolutionized the practices of ophthalmology, dentistry, surgery, and anesthesia. The only blemish that tarnished this revelation was, and continues to be, the risk of systemic toxicity. However, we have made enormous progress in the prevention, diagnosis, and management of this problem. We have seen improvements in the quality of local anesthetic agents and equipment that we use today. In the early days of regional anesthesia, anesthesiologists depended on their knowledge of anatomy to predict nerve location as they blindly advanced a needle towards its target. Today, using ultrasound guidance, we can visualize the needle trajectory as it courses towards the target nerve. We can identify and avoid blood vessels in our path and we can deposit local anesthetic solution more accurately in proximity to the nerve. These achievements have taken place over a century of outstanding research and clinical practice. However, we continue to be challenged by the ever-present risk of potentially fatal local anesthetic toxicity.

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Outcome Studies Comparing Regional and General Anesthesia

4

Brian O'Donnell and Michael O'Sullivan

Key Points

- Outcome studies of regional anesthesia are hindered by sample size issues and the possibility of selection bias; however, overall, regional techniques appear to offer benefits in the postoperative period.
- Neuraxial anesthesia and analgesia provide significant reduction in pain following major surgery, but to date, its effects on mortality, morbidity, cardiovascular/respiratory complications, and postoperative delirium/cognitive dysfunction are inconclusive.
- Results of studies investigating the effects of regional anesthesia on cancer recurrence are inadequate, although several prospective trials are currently underway.
- The limited data available comparing regional anesthesia and general anesthesia suggests benefits for the former with respect to pain management, postoperative comfort, and discharge readiness.

B. O'Donnell, MB, MSc, MD, FCARCSI (✉)
Department of Anesthesia, Cork University Hospital, Wilton Road, Cork, Ireland

ASSERT for Health Centre, University College Cork, Cork, Ireland
e-mail: briodnl@gmail.com

M. O'Sullivan, MB, FCARCSI
Department of Anesthesia, South Infirmary Victoria University Hospital, Cork, Ireland
e-mail: miosul06@yahoo.com

Introduction

Amid the growing complexity and cost of delivering and organizing healthcare, the role of outcomes research has grown substantially over the past 20–30 years [1]. Outcomes research can be defined as, "the study of the end results of health services that takes patients' experiences, preferences, and values into account—(outcomes research) is intended to provide scientific evidence relating to decisions made by all who participate in healthcare" [2]. Outcomes research seeks to inform medical decisions by focusing on the safety, effectiveness, efficiency, and patient-centeredness of medical interventions and health strategies. Although outcomes measurements include a wide variety of patient-related assessments (including functional health status, patient satisfaction, and economic measurements), anesthesiologists have traditionally focused on clinically related patient outcomes, in particular, mortality and major morbidity [3].

Regional anesthesia has been associated with favorable outcomes in patients undergoing a wide range of surgeries. Beneficial effects have been demonstrated in terms of postoperative respiratory and cardiovascular endpoints [4, 5], 7-day survival [6], time to ambulation and hospital discharge [7, 8], and postoperative analgesia [9, 10]. Many of the advantages attributed to regional anesthesia are thought to be associated with the provision of high-quality analgesia and the attenuation of the surgical stress response. The stress response to surgery is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system, which can affect cardiovascular, immune, and coagulation function with potentially negative impacts on patient outcome [11]. Regional anesthesia attenuates the stress response to surgery, thus providing the conceptual framework for improved outcome after regional anesthesia compared to general anesthesia.

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_4

A number of factors make the interpretation of outcome studies in regional anesthesia challenging. One such factor is the poorly defined line between the use of regional techniques for anesthesia and/or analgesia [12]. The quality of postoperative pain relief offered by regional analgesic techniques is well established [9, 10, 13–15]. However, these studies compare the use of regional techniques with systemic analgesics (e.g., opioids) and do not strictly compare regional *anesthesia* with general anesthesia. While analgesic outcomes are important for obvious reasons, these studies do not address the question of outcomes based on anesthetic technique. Another consideration is the fact that many large outcome studies examining the role of regional anesthesia have focused on the use of neuraxial anesthesia in comparison or in addition to general anesthesia. The study of peripheral nerve blocks in either large prospective or retrospective studies has been relatively neglected. Therefore, most of the available data on patient outcomes relate to neuraxial block. It cannot be assumed that results attributable to central neuraxial block might be similarly attributed to peripheral nerve block and vice versa; in other words, not all 'regional anesthetic' techniques are equal. This consideration has been alluded to in several Cochrane reviews [16, 17]. There is, therefore, a growing need to develop a robust nomenclature and evidence base that reflects the differences inherent between neuraxial and peripheral techniques in outcomes research.

Outcomes research comparing regional anesthesia with general anesthesia essentially consists of one of the following types of studies: prospective randomized controlled trials (RCTs), meta-analyses, and retrospective database research. Each study design has inherent advantages and disadvantages when attempting to compare regional anesthesia to general anesthesia. Before exploring individual studies on the topic of outcome following general or regional anesthesia, it is worth commenting briefly on the influence of study design on our current understanding.

Randomized controlled trials are regarded by many as the 'Gold Standard' method to evaluate the effect of an intervention on patient outcome. This study design permits hypothesis testing on a primary outcome measure (e.g., 30-day survival), in a controlled environment and on a carefully selected, randomly allocated, statistically powered study population. Anesthesia-related mortality and major morbidity is extremely uncommon. The number of patients required to detect differences in mortality between patients randomly allocated to receive either general anesthesia or regional anesthesia would be enormous, potentially necessitating the inclusion of tens of thousands of patients. A randomized controlled trial to evaluate the effect of such a very rare outcome, with multiple confounding variables, would be extremely difficult if not impossible to conduct. Potential solutions include increasing the size of the study population by conducting the study at multiple sites. Multicenter trials are possible, and potentially increase the size of the study sample frame; however, protocol deviations, inconsistencies with data management, and institutional differences in clinical practice may affect the study results [3]. Additional challenges with RCTs include the cost, time, and the potential for bias. One such example of bias is blinding. It would be impossible to blind a patient as to whether they received general or regional anesthesia. Studies comparing general anesthesia with regional anesthesia are at best observer blinded only. Therefore, current RCTs are hopelessly underpowered to evaluate major morbidity and mortality outcomes, are difficult to perform, and subject to significant bias and confounding.

Meta-analysis is a statistical approach to combine the data derived from a systematic review. This approach seeks to ascertain the best estimate of a treatment effect based upon all of the available evidence. Meta-analysis involves strict criteria for the inclusion and weighting of data from carefully selected studies. This facilitates the use of pooled data from small, underpowered studies to explore treatment effect size. This method of data analysis has been particularly popular in comparing regional anesthesia with general anesthesia, where many of the individual studies were underpowered. Meta-analyses have, however, several inherent disadvantages such as the inclusion of studies with heterogeneity of study population, study design, and outcome measures. Such potential sources of bias will adversely influence the quality of the individual studies and therefore influence the quality of the data used for pooled analysis. Publication bias is an additional problem in interpreting meta-analyses. Studies with positive outcomes are more likely to be published, while those with negative outcomes are either not submitted by investigators or rejected by the peer review process. This creates an environment whereby a systematic review of the literature is likely to discover a greater proportion of positive outcome studies for inclusion in a weighted pooled analysis. Hence, although meta-analysis can prove a useful tool to assess the effect of a treatment from pooled data, these data should be interpreted carefully as they are subject to considerable bias.

Retrospective database research has become increasingly popular in recent years to compare outcomes after regional anesthesia with general anesthesia. This method of research has the ability to employ very large populations for analysis, and thus can facilitate the assessment of infrequent outcomes. These studies are generally less expensive and less time consuming than equally large RCTs, and the information derived from databases reflects typical clinical practice. Disadvantages of database research include the essential retrospective nature of the data. The quality and type of data available is highly dependent on the initial purpose and historical context of the database. As such retrospective data may be both inaccurate and unreliable. Thus, this type of research can propose associations but not confirm causation.

Retrospective database research is therefore useful to identify associations, generate hypotheses, and estimate effect size to inform further research.

The perioperative management of patients has changed considerably over the past 20 years, with an increased emphasis on minimally invasive and ambulatory surgery. As a result, the historical benefits of regional anesthesia (e.g., decreased thromboembolism) may not apply to contemporary perioperative care. As perioperative care has become complex and integrated, it is difficult to isolate the effect of a single component from other facets of the perioperative pathway.

In this chapter, we will attempt to summarize some of the key outcome studies comparing regional and general anesthesia. A significant proportion of these studies will relate to neuraxial anesthesia, reflecting the greater attention this mode of regional anesthesia has received compared to peripheral nerve blocks. We will highlight recent large, population-based database studies to shed light on this controversial subject, and we will focus our attention particularly on areas of current interest: orthopedic surgery (in particular, hip fracture surgery), postoperative cognitive dysfunction/delirium, and cancer recurrence after surgical excision.

Neuraxial Blockade for Major Surgery

During the 1990s, several small RCTs were published which supported the beneficial effects of central neuraxial blockade on postoperative outcome for major surgery [18, 19]. However, none were sufficiently powered to provide conclusive evidence. In 2000, Rodgers et al. published a landmark meta-analysis on this subject which included 141 RTCs with 9559 patients across several surgical disciplines [20]. All studies included were performed before 1997 and a substantial number before 1985. This meta-analysis demonstrated that the use of epidural or spinal block (with or without general anesthesia) resulted in a 30 % reduction ($P = 0.006$) in overall 30-day mortality after surgery (OR 0.70; 95 % CI 0.54–0.90). Furthermore, neuraxial blockade lessened the odds of deep vein thrombosis by 44 %, pulmonary embolism by 55 %, transfusion requirements by 50 %, pneumonia by 39 %, and respiratory depression by 59 % (all $P < 0.001$). Also identified were improvements in the incidence of perioperative myocardial infarction and renal failure. This paper was regarded as a key, seminal paper at the time in establishing the beneficial role of regional anesthesia in postoperative outcome. Subsequently, however, this meta-analysis has been heavily criticized. Many of the trials included were outdated at the time of publication, had methodological flaws, and did not represent contemporary perioperative management [21]. Several studies reported an unusually high mortality rate of up to 27 % in the control group [14, 22–25]. Furthermore, on subgroup analysis, neuraxial anesthesia only improved mortality in patients undergoing orthopedic surgery and not in patients undergoing general, urologic, or vascular surgery.

Three meta-analyses, mainly including studies in vascular surgery, suggested a significant reduction in cardiac morbidity with epidural techniques [9, 26, 27]. In patients undergoing open abdominal aortic surgery, Nishimori et al. reported a significant relative risk reduction of 0.52 (CI, 0.29–0.93) for myocardial infarction (MI) in the presence of thoracic epidural analgesia [9]. Beattie et al. included pooled data from 17 studies comprising 1173 patients who underwent major vascular, open aortic, or abdominal surgery [26]. They found a nonsignificant risk reduction of 0.56 (confidence interval [CI], 0.30–1.03, $P = 0.06$) for MI. On post hoc subgroup analysis of only patients who received thoracic epidurals, a significant MI risk reduction was identified (odds ratio of 0.43 (CI, 0.19–0.97)) [27]. However, the results of these three studies critically depended on inclusion of a single study by Yeager et al.; this study reported an unusually high incidence (76 %) of adverse events in the nonepidural group (19 of 25 patients) [28]. When data from this study is excluded, no statistically significant effect on MI prevention can be identified. Two further meta-analyses and two RCTs, including high-risk cardiac surgery, also failed to identify a beneficial effect of epidural analgesia on cardiovascular complications [29–32].

The influence of epidural analgesia on respiratory complications has been the subject of much debate. The Multicentre Australian Study of Epidural Anesthesia (MASTER trial) [32] recruited 915 high-risk patients undergoing major abdominal operations or esophagectomy and randomized them to receive either intraoperative epidural anesthesia with general anesthesia or general anesthesia and systemic opioids. In an intention-to-treat analysis of 888 patients, no difference in 30-day mortality or major morbidity was identified. The occurrence of respiratory failure was, however, significantly reduced by epidural techniques from 30.2 % to 23.3 % ($P = 0.02$). A RCT on the effect of epidural analgesia on postoperative outcomes by Park et al. failed to identify any protective effect on respiratory complications [31]. Pooled data in the form of meta-analyses of epidural related outcome following major abdominal, vascular, and cardiac surgery provide conflicting results [4, 29, 30, 33].

Most recently, Guay et al. performed a review of all Cochrane reviews that assess the effects of neuraxial anesthesia on perioperative rates of death, chest infections, and myocardial infarction [34]. They included all Cochrane systematic reviews that compared neuraxial anesthesia to general anesthesia alone for the surgical anesthesia, or neuraxial anesthesia plus general anesthesia to general anesthesia alone for the surgical anesthesia. Compared with general anesthesia, neuraxial anesthesia reduced the 0- to 30-day mortality (risk ratio [RR] 0.71; 95 % confidence interval

[CI], 0.53–0.94) based on 20 studies that included 3006 participants. Neuraxial anesthesia also decreased the risk of pneumonia (RR 0.45; 95 % CI, 0.26–0.79) based on five studies that included 400 participants. No difference was detected in the risk of myocardial infarction between the two techniques (RR 1.17; 95 % CI, 0.57–2.37; $I_2 = 0$ %) based on six studies with 849 participants. When neuraxial anesthesia was combined with general anesthesia, there was no difference in 30-day mortality or risk of myocardial infarction, compared to general anesthesia alone, though there was a reduced risk of pneumonia (RR 0.69; 95 % CI, 0.49–0.98).

Clearly the evidence for outcome benefit of neuraxial blockade in major general surgery is contradictory and remains a source of controversy in current clinical practice. Neuraxial analgesia and anesthesia may have a role in reducing pulmonary complications in high-risk patients undergoing intrathoracic procedures, but a conclusive reduction in overall mortality or major cardiovascular and pulmonary complications has not been definitively established. Alterations to perioperative care, including minimal access surgery and the use of routine thromboprophylaxis, have led to a reduction in postoperative pneumonia and deep venous thrombosis (DVT) in recent years. Thus, the potential protective benefits of neuraxial blockade on cardiovascular and respiratory complications may be diluted by the modern perioperative environment [21]. It is worth noting, however, that even in the studies which failed to demonstrate improvements in morbidity and mortality, neuraxial techniques were associated with a significant reduction in postoperative pain [9, 31, 32]. This finding alone may be sufficient justification to the continued appropriate use of epidural analgesia following major surgery.

A word of caution is appropriate at this point. Data from the third National Audit Project of the Royal College of Anesthetists (UK) (NAP 3) provides sobering insight as to the potential morbidity burden associated with central neuraxial block (CNB) [35]. Using a denominator of over 700,000 CNBs performed in the United Kingdom during the study period, it was calculated that the incidence of 'paraplegia or death' directly attributable to CNB is 1.8 (1.0–3.1) per 100,000 blocks performed. Given the absence of evidence demonstrating a survival benefit in those receiving CNB, the cost of better analgesia at a population level is potentially high.

Neuraxial Blockade for Hip or Knee Surgery

Keen interest exists in the potential for regional anesthesia to improve outcomes in the orthopedic population, particularly in patients undergoing hip or knee arthroplasty surgery. As previously mentioned, subgroup analysis of Rodgers et al.'s influential meta-analysis in 2000 suggested improved mortality only in the orthopedic population who underwent regional rather than general anesthesia [20]. Lower limb arthroplasty surgery is amenable to the use of neuraxial anesthetic techniques. The patient population is elderly, and many have significant comorbidities which increase their risk of adverse cardiovascular and pulmonary events following surgery. Our aging population is an expanding group of patients with an ever-increasing impact on healthcare economics. Hip fractures, in particular, are a global public health issue, and their incidence is anticipated to grow rapidly as the population ages. Approximately 5 % of hip fracture patients die during hospitalization, while up to 10 % die within 30 days of fracture due to associated cardiovascular and pulmonary complications [36–39].

A Cochrane review in 2004 examined the subject of anesthesia for hip fracture surgery [17]. This review included 22 trials involving 2567 patients which compared neuraxial anesthesia (spinal or epidural) to general anesthesia, with mortality as the primary outcome measure. Regional anesthesia was associated with a borderline statistically significant reduction in mortality at 1 month: 6.9 % versus 10.0 % (RR 0.69; 95 % CI 0.5–0.95), but at 3 months no difference in mortality existed. There was no significant difference between the two groups in most other perioperative outcomes (e.g., length of operation, hypotension, and transfusion requirements). Acute confusional state was reported in a small number of studies, and summation of the limited results demonstrated a significant reduction in the regional anesthesia group (9.4 % vs. 19.2 %; RR 0.50, 95 % CI 0.26–0.95). The authors of this review acknowledged that all trials included had methodological flaws that probably did not reflect contemporary anesthetic practice, and that overall there was insufficient evidence to rule out clinically important difference between the two groups.

Subsequently, a meta-analysis compared neuraxial anesthesia with general anesthesia for elective total hip replacement [40]. This study included ten trials involving 330 patients under GA and 348 patients under neuraxial block. A lesser risk of both DVT (OR 0.27, 95 % CI 0.17–0.42) and PE (OR 0.26, 95 % CI 0.12–0.56) and intraoperative blood loss (275 mL/case) was identified in the neuraxial block group. This study suggested significant outcome benefits of neuraxial anesthesia versus general anesthesia for THR, but significant criticism of this paper derives from small numbers of patients and the fact that most included studies were prior to 1990, and therefore might not represent current practice.

In 2009, a comprehensive systematic review examined the effect of regional anesthesia on outcome after total knee arthroplasty (TKA) [41]. The authors only included RCTs, comparing general anesthesia and/or systemic analgesia with regional anesthesia and/or analgesia for TKA, from 1990

onward to reflect contemporary practice. Twenty eight studies involving 1538 patients were identified, though only 11 of the 28 were considered to provide level I evidence, and the sample sizes of the included studies were relatively small (varying from only 20 to 262 patients). Overall, the authors felt there was insufficient evidence to conclude that the anesthetic technique influenced mortality, cardiovascular morbidity, or the incidence of DVT/PE. However, regional anesthesia/analgesia improved patient postoperative pain experiences, lessened morphine consumption and opioid-related side effects, and facilitated better postoperative rehabilitation.

In recent years, there has been a renewed interest in the use of large population-based databases to address the issue of potential impact of anesthesia type on postoperative outcomes. This method of research allows the analysis of large populations, thus facilitating the assessment of infrequent outcomes, while the information derived from databases typically reflects actual clinical practice. As already discussed, past clinical trials suffered from small sample sizes and exclusion of important patient groups (e.g., dementia); therefore, the use of large-scale observational data may enhance the validity of comparisons between anesthesia type for hip fracture surgery.

In 2012, Neuman et al. published the results of a large observational study of over 18,000 patients who underwent surgery for hip fracture in 126 hospitals in New York between 2007 and 2008 [42]. The primary outcome analyzed was inpatient mortality, while secondary outcomes included pulmonary and cardiovascular complications. Twenty nine percent of patients received regional anesthesia. Regional anesthesia was associated with a lower adjusted odds of mortality (OR 0.71, 95 % CI 0.541–0.932) and pulmonary complications (OR 0.752, 95 % CI 0.637–0.887) relative to general anesthesia. There was no difference in the odds of major inpatient cardiovascular complications according to anesthesia type.

Subsequently, White et al. published the results of an observational review of over 50,000 patients who underwent surgery for hip fracture, from the National Hip Fracture Database (UK) [43]. However, this study revealed no significant difference in either cumulative 5-day (2.8 % vs. 2.8 %, $p = 0.991$) or 30-day (7.0 % vs. 7.5 %, $p = 0.053$) mortality between 30,130 patients who receive general anesthesia and 22,999 patients who received spinal anesthesia.

In 2013, Memtsoudis et al. published a large observational study of nearly 400,000 patients undergoing THA or TKA [44]. Data from approximately 400 hospitals in the USA between 2006 and 2010 were included. Patients were allocated to subgroups by anesthesia technique: Neuraxial (11 %), Combined Neuraxial-General anesthesia (14.2 %), and General anesthesia (74.8 %). Multivariate analysis was performed for THA and TKA separately. This study found no difference in severity-adjusted mortality according to anesthesia type among THA patients, but noted statistically significant increases in 30-day mortality among TKA patients in the General anesthesia group compared with the Neuraxial or Neuraxial–General groups (adjusted odds ratio [OR] of 1.83, 95 % CI 1.08–3.1, $P = 0.02$; OR of 1.70, 95 % CI 1.06–2.74, $P = 0.02$, respectively). Incidence rates of in-hospital complications were generally lower among the Neuraxial and Combined Neuraxial-General anesthesia groups versus the General anesthesia group, including for PE, pulmonary compromise, pneumonia, cerebrovascular events, renal failure, and prolonged length of stay. There was no significant difference in the rate of cardiac complications across the three groups. When controlling for covariates, general anesthesia was associated with higher odds for most systemic complications and resource utilization (including need for postoperative critical care services). The following year, some of the same group published an even larger study of almost 800,000 patients who underwent THA or TKA performed across approximately 500 hospitals in USA between 2006 and 2012 [45]. In this study, patients were categorized by age (<65 years, 65–74 years, >75 years) as well as by presence of cardiopulmonary disease. A multivariate logistic regression analysis was performed to assess the independent influence of the type of anesthesia on complications within each patient subgroup (including cardiac complications, pulmonary complications, prolonged length of stay, ICU utilization). The incidence of major complications was highest in the oldest patient group with cardiopulmonary disease (26.1 %) and lowest in the youngest group without cardiopulmonary disease (4.5 %). Neuraxial anesthesia was associated with decreased odds for major complications and resource utilization after joint arthroplasty for all patient groups, irrespective of age and comorbidity burden, with patients of advanced age potentially having the greatest benefit from choice of neuraxial technique. Overall the effects of anesthesia were strongest when comparing neuraxial anesthesia with general anesthesia; effects were less pronounced in the combined neuraxial-general group versus general anesthesia group.

Postoperative Delirium and Postoperative Cognitive Dysfunction

Over the last decade, postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) have been identified as significant adverse outcomes following anesthesia and surgery, with the elderly being most at risk [46]. Postoperative delirium is an acute neurological disorder characterized by inattention and disorganized thinking.

It is an important postoperative complication as it is very common, affecting up to 70 % of patients over the age of 60 undergoing major surgeries. It is associated with serious adverse outcomes including mortality and persistent cognitive decline [47]. Postoperative cognitive dysfunction refers to deterioration in cognition temporally associated with anesthesia and surgery, though its diagnosis is controversial as there is no International Classification of Disease Code for POCD. It is only detectable with comparison between appropriate pre- and postoperative neuropsychological tests. Recent studies have demonstrated that up to 50 % of elderly patients undergoing both cardiac and noncardiac surgery experience persistent POCD [48, 49]. Steinmetz and colleagues of the International Study of Postoperative Cognitive Dysfunction (ISPOCD) Group demonstrated that POCD is associated with increased risk of mortality, of leaving the labor market prematurely, and dependency on social transfer payments [50]. Evidence has emerged recently that preventing excessive depth of general anesthesia using processed EEG may decrease the incidence of POD and/or POCD in vulnerable patients [51–53]. Conceptually, therefore, one might expect regional anesthesia to be associated with a lower incidence of POD and POCD than general anesthesia.

Rasmussen and colleagues from the International Study of Postoperative Cognitive Dysfunction (ISPOD) group randomly assigned 438 elderly patients undergoing major noncardiac surgery to either general or regional anesthesia [54]. This study demonstrated no difference in POCD after 3 months between the general anesthesia group compared to the regional anesthesia group (14.3 % vs. 13.9 %, $p = 0.93$). Subsequently, three separate systematic reviews on this subject failed to demonstrate a benefit from regional anesthesia in decreasing the incidence of POD and/or POCD [55–57], though it is acknowledged that the interpretation of the literature on this subject is controversial due to numerous methodological limitations such as underpowered studies, variations in the number and range of neuropsychological tests used, and different definitions of POCD.

Cancer Recurrence Postsurgery

Regional anesthesia attenuates the neuroendocrine stress response and reduces the requirements for opioid and volatile anesthetic agents. These factors may, in theory, preserve perioperative immune function and potentially reduce the incidence of cancer recurrence [58]. Over the last decade, several retrospective studies suggested a role for regional anesthesia in improving disease-free survival following primary surgery for malignant cancer [59–63]. However, other retrospective studies during this period did not demonstrate such benefit [64–67]. Many of these retrospective analyses consisted of small numbers of patients and, as with all retrospective studies, are susceptible to selection bias.

In 2014, a Cochrane review was published regarding the issue of anesthetic technique potentially influencing the risk of cancer recurrence [68]. This review included four studies, all of which were secondary data analyses of previously published prospective RCTs. All studies compared general anesthesia alone with combined general and epidural anesthesia [69–72]. The primary outcomes analyzed were overall survival, disease-free survival, and time to tumor progression. One of the included RCTs was a long-term follow-up analysis of the previously discussed MASTER Trial [32]. This multicentre prospective study was the first to provide long-term follow-up of patients prospectively randomly assigned to general anesthesia plus opioid or general anesthesia plus epidural blockade [71]. This study showed a median time to recurrence of cancer or death of 2.8 (95 % CI 0.7–8.7) years in the control group and 2.6 (95 % CI 0.7–8.7) years in the epidural group ($P = 0.61$); the recurrence-free survival was similar in both epidural and control groups (hazard ratio 0.95, 95 % CI 0.76–1.17; $P = 0.61$). Overall, this Cochrane review graded the quality of available evidence as either low or very low. The authors concluded that, at present, the evidence suggesting a benefit of regional anesthesia on tumor recurrence is inadequate. Recently, an expert group issued a consensus statement supporting that position and called for randomized clinical trials to evaluate the effect of anesthetic technique for primary cancer surgery on cancer recurrence or metastasis [73]. Currently, there are several such RCTs ongoing, which should significantly clarify the issue in the future.

Peripheral Nerve Blockade and Ambulatory Anesthesia

Large multicenter RCTs comparing outcomes after surgery performed under general anesthesia versus peripheral nerve blockade (PNB) are lacking. In general, where RCTs on this subject exist, the numbers of patients analyzed are small, and therefore, definitive conclusions are lacking. Theoretically, by providing site-specific analgesia while facilitating ambulation, PNBs potentially could offer several advantages over general or neuraxial anesthesia [74]. Liu et al. performed a meta-analysis of trials comparing regional anesthesia (neuraxial or PNB) with general anesthesia in the ambulatory surgery setting [75]. Fifteen studies (1003 patients) comparing neuraxial with general anesthesia, and seven studies (359 patients) comparing PNB with general anesthesia were identified that met the inclusion criteria. Compared to general anesthesia, both neuraxial anesthesia and PNB were associ-

ated with lower VAS pain scores (−9 and −24 mm, weighted mean difference) and decreased need for analgesics (OR 0.32 and 0.11) in the postanesthesia care unit (PACU). With regard to the other outcomes, there was little difference between neuraxial anesthesia, while, in contrast, PNB was associated with a greater ability to bypass PACU (OR 14), a shortened time spent in PACU (24 min, weighted mean difference), and a higher patient satisfaction rating (OR 4.7). While significant limitations in this meta-analysis existed, not least the nonhomogenous nature of the patients included from different studies, it suggested a more comfortable recovery and better patient satisfaction when PNB was used in the ambulatory setting.

Conclusion

In summary, the anesthesia literature has shown that the use of regional anesthetic techniques provides better analgesia and enhances patient experiences in the immediate postoperative period. With regard to CNBs in combination with general anesthesia, better analgesia, however, does not appear to translate into fewer cardiovascular or respiratory complications on a population basis. This is either because of a genuine absence of beneficial effect or due to the nature and methodological flaws of outcomes research to date. Where CNBs can be used instead of general anesthesia, for instance, major lower limb joint arthroplasty, there is evidence of beneficial effects in terms of lessening both cardiovascular and respiratory complications.

Data on comparing PNB to general anesthesia is very limited. In the ambulatory setting there appears to be a beneficial relationship between PNB use and measures of pain, nausea and vomiting, ambulation, and discharge readiness. Large multicenter studies are required to ask appropriate outcomes-based questions to ascertain the true (if any) influence of PNB on important clinical outcomes following surgery.

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Part II

Special Considerations

Nerve Injury Resulting from Intraneural Injection When Performing Peripheral Nerve Block

5

Rakesh V. Sondekoppam and Ban C.H. Tsui

Key Points

- A neuronal injury can be explained using an epidemiological triad model as an interaction between an injurious agent (local anesthetic/needle or pressure injury), a susceptible host (inadequately protected nerve), and a hazardous working environment (poor supervision/guidance for locating needle; unsafe practices, unintended exposure). In theory, elimination of one of the triad's components should prevent the occurrence of the event.
- Long-term neurologic complications (lasting more than 6 months) are rare following peripheral nerve blocks while the short-term neurologic symptoms although more common are known to resolve within a few weeks to 3 months.
- Most of the evidence regarding needle, pressure, and local anesthetic-related injuries comes from animal studies.
- In clinical practice, it is difficult to stay extraneurally all the time and intraneural injections do occur while performing PNB.
- To minimize the risk of neurological injury, one must evaluate the patient properly (preprocedural examination to ensure no preexisting neuropathy/risk factors), select equipment appropriately (needle gauge, type), and administer local anesthetic accordingly (lower concentration for nerves susceptible to insults).
- Allow a sufficient follow-up period particularly if paresthesia is noted during the procedure.
- Utilize all available guidance methods if possible for the performance of PNB including US, injection pressure monitoring, and neurostimulation.

R.V. Sondekoppam, MBBS, MD (✉)
Department of Anesthesia and Pain Medicine,
University of Alberta, Edmonton, AB, Canada
e-mail: vijayash@ualberta.ca

B.C.H. Tsui, MSc (Pharm), MD, FRCPC
Department of Anesthesiology, Perioperative and Pain Medicine,
Stanford University School of Medicine,
300 Pasteur Drive, Stanford, CA 94305-5640, USA
e-mail: btsui@ualberta.ca

Introduction

Neurologic injuries following peripheral nerve blocks (PNB) are rare, ranging between 2.4 and 4 per 10,000 blocks, but they can be debilitating and, at times, devastating [1–6]. From a health perspective, a rare event can be defined as any event that occurs infrequently (≥1/10,000 to <1/1000) [7]. Rare events do not occur in a predictable pattern; thus, trying to deduce event rates may prove to be erroneous. Predicting neurologic complications following PNBs is subject to the same issues affecting other rare events, such as multiplicity of sources, difficulties in data collection, and variation in statistical analysis. The incidence of the event may be impacted further by any change in the target population or the definition of the problem. Unsurprisingly, no studies to date have investigated neurologic complications following regional anesthesia from a rare event perspective, likely due to the complex interactions of known and unknown factors that influence these complications. Although the use of ultrasound (US) has been shown to reduce the incidence of vascular puncture, LA systemic toxicity [7], and block success [8] we have yet to demonstrate improvements with the introduction of US.

Neurologic injury following PNB is complex and includes needle trauma, pressure injury [9], damage to the vasa nervosum resulting in hematoma formation or ischemia, and finally LA [10] or adjuvant-related toxicity. Other important factors also include patient characteristics [11, 12], type of surgery [13], and the anatomical location of injections. Given the complexity of possible interactions among various factors in regional anesthesia, the complication may be best explained using the same epidemiological principles of disease causation (Fig. 5.1).

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_5

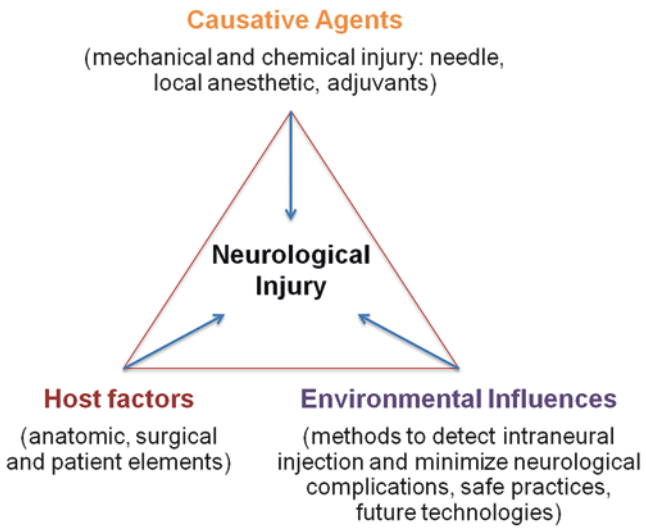

Fig. 5.1 Epidemiologic triangle demonstrating relationship between causative agents, host factors, and environmental influences on neurological injury

Epidemiological principles have been used to determine and study the interrelationship of various factors on the suspected cause of diseases so that control measures can be identified and implemented to prevent and minimize the disease. Typically, the event (complication) is said to occur when there is interaction among an injurious origin (causative agents), a susceptible host (host factors), and suitable circumstances (environmental influences) known popularly as the epidemiological triad [14, 15]. Using this model, risk factors can then be broadly classified to the host (anatomical and biological factors), the injurious agent (mechanical, pressure, and neurotoxic insults), and the environment (guidance techniques, supervision, safety culture). The neurological injury may represent the final result from the interaction between these risk factors. Elimination or minimization of one of the triangle's component may potentially, in theory, interrupt the interaction and prevent the event from occurring.

In fact, any discussion of epidemiology would be incomplete without mentioning John Snow, a pioneer anesthesiologist, who is also known as the "father of epidemiology" due to his well-known first epidemiological studies conducted in the 1850s [16]. In his studies, Snow used logic and common sense to study the interaction of factors causing disease and to develop preventative measures in ending the cholera outbreak. This work classically illustrates the effective use of epidemiological principles used even today to investigate and control disease and outbreaks. In this chapter, we, therefore, have performed a systematic review to evaluate the pertinent clinical and pathophysiological aspects of neurological complications following PNBs from the perspective of the epidemiological triangle."

Search Strategy and Selection of Studies

A systematic review of the medical literature (MEDLINE, OVID, and EMBASE) was performed during Nov–Dec 2015 using the search strategy described later. The MEDLINE search used a combination of the following medical subject headings: nerve injury, neurologic injury, peripheral nerve injury, neurologic deficit, paresthesia, neurologic sequelae, pathology, ultrastructure, anatomy, transient neurologic deficit, transient neurologic symptoms, paralysis, nerve block, peripheral nerve block, local anesthetic, local anesthesia, conduction anesthesia, and regional anesthesia. Subsequent searches combined the keywords intraneural injection, epineurium, subepineurial injections, perineurium, intrafascicular injection, extrafascicular injection, injection pressure, ultrasound, neurostimulation, and needles. EMBASE and OVID database searches were performed for the period 1975–2015. We started from the year 1975 since the very first investigations, looking into the factors important to the causation of nerve injury following regional anesthesia in a systematic way, began in 1977 [17].

Both human and animal studies were included in the review. Additional database searches included Cochrane, LILACS, DARE, IndMed, ERIC, NHS, HTA via Centre for Reviews and Dissemination (CRD; York University), which did not produce any additional unique results. The bibliographies of publications included for analysis were also reviewed manually for additional material that may have been missed by the database searches.

Literature Selection

The full text of all articles obtained from the searches was retrieved for critical appraisal. References of all articles were examined to ensure that no original research studies were missed. We included closed claimed analyses, meta-analyses, systematic reviews, randomized controlled trials (RCTs), controlled studies without randomization, observational studies, retrospective studies, comparative studies, and case series for this review. For the purposes of this review, RCTs were defined as such only when they included human subjects; randomized studies of animal subjects were not classified as RCTs. We did not include correspondences, pediatric population, or conference abstracts with incomplete data sets in this review.

Evidence Evaluation

Relevant full-text articles were separated based on literature type (database reviews, human and animal studies) and were subsequently reviewed independently in duplicate. Data

Table 5.1 Oxford Centre for Evidence-Based Medicine levels of evidence and grades of recommendation (adapted from www.cebm.net)

Level	Description
1a	Systematic review of RCTs or of prospective cohort studies
1b	Individual RCT or prospective cohort study with good follow-up[a]
1c	All or none studies
2a	Systematic review of cohort studies
2b	Individual cohort study (including retrospective)
2c	"Outcomes" research
3a	Systematic review of case–control studies
3b	Individual case–control study, nonconsecutive cohort study, or limited population
4	Case series
5	Expert opinion without explicit critical appraisal or based on physiology, bench research, or "first principles"
Grades of recommendation	
A	consistent level 1 studies
B	consistent level 2 or 3 studies *or* extrapolations[b] from level 1 studies
C	level 4 studies *or* extrapolations from level 2 or 3 studies
D	level 5 evidence *or* inconsistent or inconclusive studies of any level

[a]Defined as >80 % with adequate time for alternative diagnoses to emerge (e.g., 1–6 months acute; 1–5 years chronic)
[b]Where data is used in a situation that has potentially clinically important differences than the original study situation

were classified based on the epidemiologic triangle: (1) host factors (anatomic, surgical, and patient-specific elements), (2) damage-causing agents (needle, local anesthetic, adjuvants, pressure injury), and (3) environmental factors (methods to detect intraneural injection, safe practices, future technologies). Additionally, data relating to nerve injury and the incidence of unintentional intraneural injection were evaluated separately.

Data were extracted and entered into a database (Microsoft Excel, Microsoft Corp., Redmond, WA). Level of Evidence (Table 5.1) and Grades of Recommendation (Table 5.2) developed by the Oxford Centre for Evidence-Based Medicine were assigned to each study.

Furthermore, RCTs included in the current review were assigned Jadad scores (0–5) [18] while case reports were graded by Pierson scale [19] to assess scientific quality. Nonrandomized studies were not assessed for quality. Animal and cadaveric tissue studies were given a lower grade (Level of evidence 5; Grade D) irrespective of the study design.

Selected studies: A total of 3328 abstracts were retrieved from the MEDLINE, OVID, and EMBASE databases. After elimination of 62 duplicates, 3266 articles were screened for eligibility, 206 of which were selected for full-text review. Seven additional articles identified from a manual search of references from relevant articles were included. Seventy nine studies were excluded based on the criteria earlier, leaving 134 full-text articles for review (Fig. 5.1).

A total of 43 animal [9, 17, 20–59] studies (Table 5.2), 60 human [1–6, 60–113], and 8 cadaver/laboratory studies [114–121] (Tables 5.3 and 5.4) 21 case reports/case series (Table 5.5) [122–143] were included for this review. The statement of evaluated outcomes has been summarized in Table 5.6.

Among animal studies, eight studies evaluated the impact of needle design on nerve trauma, while seven studies reported on the injection pressure, 21 studies evaluated neurotoxicity of LA/adjuvants, and seven studies evaluated guidance methods such as neurostimulation/US. Of the human studies, six studies evaluated the incidence of unintentional intraneural injections while four studies evaluated the impact of deliberate intraneural injections. A total of 38 studies reported on neurologic complications in relation to PNB, while the remaining 9 reported on methods to detect or avoid intraneural injection.

Incidence of Neurologic Complications Following PNB

Transient neurologic dysfunction following PNBs are more common than long-term dysfunction and usually resolve with time (*LOE 1b*; *Grade A*). *Long-term postoperative neurologic dysfunction is rare following peripheral nerve blocks* (*LOE 1b*; *Grade A*). *Procedure-induced paresthesia may increase the risk of postoperative neurologic dysfunction* (*LOE 1b*; *Grade A*). *The safety of performing PNB under general anesthesia and its impact on neurologic outcomes is currently unknown* (*LOE 2b*; *Grade C*).

Retrospective reviews tend to under-report the incidence of neurologic complications due to selection, information, and recall bias, whereas the medico-legal databases may overestimate the incidence due to over-reporting and a lack of denominator for the incidents (Table 5.4). Early attempts to determine the incidence of neurologic sequelae following regional anesthesia came from ASA closed claims analyses [69, 88]. The first closed claims analysis included spinal anesthesia, ophthalmic blocks, and chronic pain blocks, while the latter looked specifically for neurologic complications following PNB. Closed claims analyses of PNBs have shown a trend toward a rise in nerve injury claims over the years (31–51 %), but only a few are thought to be related to the PNB itself [88, 89]. This ambiguity necessitated several prospective studies of block-related neurologic sequelae.

Prospective studies estimate the incidence of long-term neurologic injury following peripheral nerve blocks to be in the range of 2.4–4 per 10,000 blocks [2, 65–68, 144]. Transient neurologic deficits lasting up to 2 weeks occur more frequently following PNB, with an incidence varying

Table 5.2 Assessment of animal studies investigating neurological injury

Study	Animal model	Number of blocks/ attempts	Block type	Key findings	LOE[a]
Hadzic et al. [9]	Dog	14	Sciatic	• Perineural injections required low injection pressure (<4 psi) while 4/7 intraneural injections required high injection pressure (>25 psi)	5
				• High injection pressures resulted in severe persistent motor deficits throughout the study period (7 days) and histological changes of nerve injury	
Selander et al. [43]	Rabbit	20	Sciatic	• Intrafascicular injection required higher injection pressures (>600 mmHg) and showed a rapid longitudinal spread within the fascicle	5
				• Rupture of the perineurium occurred at pressures between 125 and 900 mmHg	
Selander et al. [16]	Rabbit	30	Sciatic	• Nerve fascicles slid or rolled away easily from the needle tip, especially with short-bevel needles	5
				• The most severe fascicular injuries occurred more frequently with long-bevel (14°) than with short-bevel (45°) needles	
Macias et al. [37]	Rat	12	Sciatic	• The nerve trunk rotated and slipped at the time of contact with the needle more frequently with a short bevel than with a long bevel	5
				• Four animals in the short bevel group showed a decrease in movement and flexion tendency	
Steinfeldt et al. [44]	Pig	40	Brachial plexus	• Nerve damage (hematoma and myelin damage) and injury scores were greater with larger needle diameter after intentional nerve perforation	5
Maryuama et al. [36]	Rabbit	90	Sciatic	• All needles caused axonotmesis and interruption of myelin sheath. The mean number of transected axons was significantly less for tapered needle than for the beveled needle	5
				• The number of damaged axons was reduced significantly by inserting the beveled needle parallel to the nerve fibers	
Steinfeldt et al. [45]	Pig	58	Brachial plexus	• No significant difference with regard to incidence of intraneural hematoma or myelin damage after both needle injuries	5
				• Myelin damage was 40 % with both Sprotte and Tuohy needles, and hematoma was 55 % with the Sprotte needle compared to 60 % with the Tuohy needle	
Rice et al. [41]	Rat	63	Sciatic	• After deliberate intrafascicular needle insertion, short-bevel needles caused more axonal damage and neuronal edema compared to long-bevel needles	5
				• The structural (axonal degeneration and neuronal edema) and functional changes after short-bevel needle insertion persist for a long time and result in disorganized regeneration	
Kapur et al. [33]	Dog	30	Sciatic	• High injection pressures during intraneural injection may be indicative of intrafascicular injection and usually result in functional and histological changes indicative of nerve injury	5
				• Intraneural injections with low pressure resulted in significantly longer duration of sensory motor blockade	
Gentili et al. [25]	Rat	140	Sciatic	• Nerve damage seems to be highest with 1 % tetracaine and 2 % procaine. Damage seems to recover with time and was minimal by 9–12 days	5
				• Damage by lidocaine with or without epinephrine was mild and least with bupivacaine and mepivacaine without epinephrine	

Yang et al. [58]	Rat	16	Sciatic	• Local anesthetics cause Schwann cell death in vitro in a time- and concentration-dependent manner	5
				• Prolonged exposure of nerves in vivo to continuous infusions of bupivacaine causes damage to myelin as well as infiltration and activation of macrophages	
Lupu et al. [35]	Pig	20	Median	• Nerve expansion seen on ultrasound during intraneural injection of a clinically relevant volume of local anesthetic results in histological evidence of nerve injury but does not necessarily translate into functional neuropathy	5
Iohom et al. [27]	Rat	52	Sciatic	• Intraneural injection of ropivacaine at concentrations routinely used in clinical practice had no deleterious effect on sciatic nerve motor function	5
Myers et al. [39]	Rat	48	Sciatic	• Epinephrine reduces nerve blood flow (NBF) significantly; this effect is more pronounced after addition of lidocaine. The reduced NBF is not reversed with washout in local anesthetic groups	5
Bouaziz et al. [22]	Rat	48	Sciatic	• All local anesthetics studied decrease NBF	5
				• The greatest decrease was noted with ropivacaine followed by levobupivacaine (0.75 %) and then by the rest	
				• Addition of epinephrine did not result in further decrease in NBF	
				• Although significant, the reduction in NBF did not result in subsequent histopathological changes of neurotoxicity	
Partridge et al. [21]	Rat	90	Sciatic	• Epinephrine + lidocaine causes dose-dependent reduction in NBF which continues after washout	5
				• Bupivacaine causes dose-dependent improvements in NBF and is reversed by washout	
				• Tetracaine results in no significant change in NBF	
Whitlock et al. [54]	Rat	54	Sciatic	• Ropivacaine is capable of inducing demyelination and Wallerian degeneration when administered directly into or placed onto an exposed nerve, but the extent of injury is always less than that of phenol, and nerve regeneration is near normal at 2 weeks	5
Williams et al. [57]	Cultured rat neurons	n/a	n/a	• Ropivacaine (2.5 mg/mL) is more neurotoxic than high concentrations of preservative-free adjuvants, clonidine, buprenorphine, dexamethasone, and midazolam	5
				• Midazolam increased the neurotoxic potential of ropivacaine	
Tüfek et al. [49]	Rat	40	Sciatic	• Total antioxidant status of sciatic nerve was almost equal between sham, saline, dexmedetomidine, and bupivacaine + dexmedetomidine groups but was significantly lower in the bupivacaine group	5
				• No difference in total oxidant status between the sham, saline, and dexmedetomidine groups but significant increase in the bupivacaine group	
Chan et al. [23]	Pig	28	Brachial plexus	• Threshold current was variable [0.43 mA (range: 0.12–1.8 mA)] with the threshold being 0.5 mA in 45 % and 1 mA in 5 %	5
				• Intrafascicular injection occurred in 2/24 injections	
Tsai et al. [173]	Pig	40	Sciatic	• Type I motor response was obtainable only when needles were positioned 0.1 cm from the nerve or closer.	5
				• Distance: current: frequency was 0.1 cm: 0.92 ± 0.33 mA: 70 %	
				• On epineurium = 0.39 ± 0.33 mA: 95 %; Intraneural = 0.56 ± 0.54 mA: 100 %	
Altermatt et al. [19]	Pig	24	Brachial plexus, femoral	• The diameter increased by more than 50 % compared with preintervention images	5
				• The current required to elicit a motor response was variable (0.2–3.3 mA)	
				• Minimum current threshold was ≤0.5 mA in 75 % of cases and >1.0 mA in 17 % of cases	

(continued)

Table 5.2 (continued)

Study	Animal model	Number of blocks/ attempts	Block type	Key findings	LOE[a]
Wiesmann et al. [55]	Pig	50	Brachial plexus	• Nerve contact and intraneural needle placement showed similar threshold current intensities (≤0.2 mA), irrespective of the pulse duration	5
				• No significant difference between needle–nerve contact and intraneural needle tip positions	
				• Control nerve stimulation required significantly higher threshold current, regardless of applied pulse duration	
Vuckovic et al. [53]	Rat	24	Median	• All injections were characterized by an initial rise in pressure, which was followed by a similar but lower pressure. The majority of intraneural injections showed higher injection pressure (86.552 ± 13.262) kPa in comparison to 25.128 ± 3.49 kPa for paraneural injection	5
Vuckovic et al. [52]	Rats & stillborn human fetuses	48	Median	• All perineural injections resulted in pressure ≤27.92 kPa, while the majority of intraneural injections had injection pressure ≥ 69.8 kPa	5
Rigaud et al. [42]	Dog	24	Sciatic	• Ink distribution patterns were not different between low and high stimulation threshold groups	5
				• One intraneural injection occurred in the high threshold group	
				• Average stimulation threshold in the hyperglycemic group was the same as in the low threshold normoglycemic group, but ink distribution patterns were all intraneural in the hyperglycemic animals	
Kroin et al. [34]	Rat	n/a	Sciatic	• All of the local anesthetic solutions produced a longer mean duration of sensory nerve block in diabetic rats versus nondiabetic rats	5
				• None of the sciatic nerves examined in the percutaneous injection study showed >3 % nerve fiber degeneration overall	
Belda et al. [20]	Piglet	12	Sciatic	• Cross-sectional area and relative echogenicity values were different immediately after the injections and returned to prepuncture values within 4 days	5
				• Injections did not exceed >20 psi or result in motor deficits	
				• Histology showed intact perineurium and signs of inflammation immediately and on days 1 and 2 postinjection	
Voelckel et al. [51]	Pig	20	Sciatic	• Motor response to currents >0.5 mA ensures extraneural injections while low current (<0.2 mA) is specific for intraneural injections	5
				• The mean ± SD current required to obtain a motor response was 0.4 ± 0.05 mA in the standard current group and 0.15 ± 0.04 mA in the low current group	
				• Standard current group showed no signs of inflammation. In 5/10 low current group animals, inflammation was found sub-, peri-, and intraneurally	
				• One sciatic nerve specimen of the low current group revealed disruption of perineurium and axons	
Steinfeldt et al. [46]	Pig	42	Sciatic	• Myelin damage following perineural hematoma was seen in 15 % of cases	5
				• Both blood and albumin around the nerve result in aseptic inflammation of the nerves and severe structural nerve injury/inflammation	
Steinfeldt et al. [47]	Pig	50	Brachial plexus	• Small (24 G) pencil-point needles do not seem to be superior to short-bevel needles of the same gauge with respect to damage from nerve perforation	5

Vassiliou et al. [50]	Pig	611	Brachial plexus, sciatic	• Dual guidance showed greater accuracy of needle tip placement in proximity to the nerve (98.5 %) and fewer intraneural needle placements (0.5 %)	5
				• Significant differences in close needle placement: US+NS (98.5 %); NS group (90.1 %), and US group (81.6 %)	
				• Fewer intraneural needle placements in the US+NS group (0.5 %) compared with the US group (4 %). Intraneural needle placement was 2.5 % in NS group	
				• Puncture-related hematomas more frequent with NS (10.8 %) compared with US (2.5 %) or dual guidance (1.5 %)	
Farber et al. [24]	Rat	16	Sciatic	• Animals that received intrafascicular injections showed increased severity of injury compared to control animals	5
				• A layering of severity of injury was found with most severely injured areas closest to and uninjured areas furthest from the injection site	
				• Bupivacaine caused more damage to large fibers than the other local anesthetics	
Hirasawa et al. [26]	Rabbit	50	Sciatic	• Least disturbance/damage from tapered needle	5
				• Followed in increasing order of damage by short bevel/parallel insertion, long bevel/parallel insertion, short bevel/perpendicular insertion, long bevel/perpendicular insertion	
Kalichman et al. [28]	Rat	20	Sciatic	• Streptozotocin-induced diabetic rats had lower motor nerve conduction velocity compared to normal rats	5
				• Extraneurally placed LA caused neural edema, which was more pronounced with lidocaine 4 % than saline or lidocaine 2 % in diabetic rats	
				• Nerve fiber injury scores were greater in diabetic rats compared to control groups	
Kalichman et al. [29]	Rat	?	Sciatic	• Procaine (10 %) but not saline, 80 % ethanol, or 80 % glycerol induced statistically significant decreases in nerve blood flow	5
				• Procaine and cocaine were associated with dose-dependent decreases in nerve blood flow, but cocaine was more potent	
				• At 48 h, injury scores were elevated significantly for 80 % ethanol and 10 % procaine; nerve injury from procaine and cocaine was dose dependent	
Kalichman et al. [30]	Rat	60	Sciatic	• Etidocaine, lidocaine, chloroprocaine, and procaine caused concentration-dependent nerve injury	5
				• The highest concentration of LA caused endoneurial edema, especially in larger fascicles	
Kalichman et al. [31]	Rat	83	Sciatic	• Nerve fiber injury and disturbances of endoneurial microenvironment occur after 48 h exposure to various LAs	5
				• Degree and extent of nerve injury varied among the LAs	
				• Edema and nerve injury were typically greatest subjacent to the site of LA injection; the most severe edema was not always found with the most severe nerve injury	
				• Nerve fiber injury, endoneurial edema, and lipid droplet formation were produced in dose-dependent fashion	
Kalichman et al. [32]	Rat	49	Sciatic	• Exposure to lidocaine, etidocaine, procaine, and chloroprocaine resulted in neuronal edema and lipid droplet scores greater than saline and water controls	5
				• Nerve injury was significantly different than with controls only at the highest concentrations of each drug	
				• Etidocaine was the least toxic LA	

(continued)

Table 5.2 (continued)

Study	Animal model	Number of blocks/ attempts	Block type	Key findings	LOE[a]
Myers et al. [38]	Rat	?	Sciatic	• Direct application of tetracaine 1 % and 2-chlorprocaine resulted consistently in subperineurial and endoneurial edema due to increased perineurial permeability	5
				• Between 24 h and 4 weeks, perineurial and endoneurial fibrotic changes were noted to varying degree as a result of increased perineurial permeability and endoneurial edema	
Selander et al. [43]	Rabbit	56	Sciatic	• Topical application of clinically recommended concentrations of bupivacaine around a nerve caused no detectable nerve injury; intrafascicular injection caused considerable axonal degeneration and damaged the blood–nerve barrier	5
				• Axonal degeneration was the same after injection of saline and bupivacaine 0.5 % but increased with increasing bupivacaine concentration and especially with addition of adrenalin	
				• Acute effects of intrafascicular injection changed little upon addition of adrenalin	
Williams et al. [56]	Rat	25/15	Sciatic	• Single injection or continuous infusion of bupivacaine or midazolam, combined with dexamethasone, clonidine, and buprenorphine, did not result in long-term neurologic deficits	5

[a]All studies using an animal model were assigned an LOE of 5, regardless of study design

Table 5.3 Assessment of human studies investigating neurological injury

Study	Type of study (Jadad score)	Guidance method	Block type	Key findings	LOE
Liu et al. [91]	Cohort study	US	Supraclavicular, interscalene	• Unintentional intraneural injection is common following supraclavicular or interscalene blocks (17 %)	2b
				• Incidence of temporary nerve injury was 0 % at both 1 and 4–6 week periods	
Hara et al. [78]	Cohort study	US + NS	Sciatic	• Unintentional intraneural injection is common following US-guided subgluteal sciatic nerve blocks (17 %) and may not necessarily result in neurological complications	2b
				• Intraneural injections have a fast block onset compared to extraneural injections, with no effect on block duration	
Ruiz et al. [98]	RCT (4)	US + NS	Femoral	• Needle–nerve contact and apparent intraneural injections can be more common with an out-of-plane approach (64 %) compared to in-plane approach (9 %) for femoral nerve block	1b
				• No differences between the groups regarding incidence of paresthesia or nerve injury	
Robards et al. [97]	Cohort study	US + NS	Sciatic	• Deliberate intraneural injection during popliteal sciatic nerve block with injection pressures <20 psi does not result in immediate neurological dysfunction	2b
				• Motor response was absent in 16.7 % with current up to 1.5 mA even when needle was intraneural on US	
Sala-Blanch et al. [99]	Cohort study	NS	Sciatic	• Intraneural (subepineurial) injection during nerve stimulation-guided popliteal sciatic nerve block may occur commonly (up to 66 %) without imminent neurological injury	2b
				• Intraneural injections may have a faster block onset	
Sala-Blanch et al. [100]	Lab study	Direct vision	Sciatic	• Intraneural needles likely traverse connective tissue rather than fascicular tissue	5
				• 30° bevel needles did not result in fascicular injury; incidence of fascicular injury after insertion of 15° bevel needles was ~3 %	
Sauter et al. [178]	Cohort study	US	Radial, ulnar	• High current thresholds [1.7 (0.4–4.5) mA radial and 1.0 (0.4–2.0) mA ulnar] and short nerve-to-needle distances were often needed to obtain motor responses	2b
Gadsden et al. [75]	Cohort study	US	Interscalene	• All extraneural injections had opening injection pressure <15 psi	2b
				• Limiting injection pressure to 15 psi prevented injection upon needle–nerve contact in all but one instance	
				• Monitoring of opening injection pressure may be helpful in detecting needle–nerve contact	
Bigeleisen et al. [63]	Cohort study	US	Supraclavicular	• Ultrasound was able to detect the location of the needle tip clearly in 69 % of cases	2b
				• Stimulation currents of ≤0.2 mA detect intraneural position of the needle reliably	
				• Stimulation thresholds >0.2 and ≤0.5 mA could not rule out intraneural needle tip placement	
				• 10 % of patients had temporary neurological symptoms mostly unrelated to nerve blocks	
				• Diabetic patients require higher stimulation thresholds both outside and inside the nerve to elicit a motor response	
Moayeri et al. [93]	Cohort study	US	Supraclavicular, sciatic	• Intraneural injection can be detected on US by injecting a small amount of injectate	2b
				• The ultrasonographic criterion 'increase in cross-sectional surface area together with change in echogenicity' identified intraneural injection with 94 % precision	
				• Cross-sectional surface area increased 8–9 % in both brachial plexus and sciatic nerve	

(continued)

Table 5.3 (continued)

Study	Type of study (Jadad score)	Guidance method	Block type	Key findings	LOE
Morau et al. [94]	Cohort study	NS	Sciatic	• Intraneural spread of local anesthetic was common following NS-guided popliteal sciatic block (39 % had a nerve surface area increase of 15 %)	2b
				• Patients with intraneural injections had faster block onset and better success rate	
Bigeleisen et al. [62]	Cohort study	US	Axillary	• Deliberate intraneural injection during axillary brachial plexus block did not result in long-term neurological dysfunction	2b
Moayeri et al. [115]	Cohort study	n/a	n/a	• The area of the connective tissue compartment surrounding the brachial plexus increased proximally to distally, while the neural component remained the same	2b
				• Ratio of connective to neural tissue increases progressively from proximal to distal part of brachial plexus	
Moayeri et al. [116]	Cohort study	n/a	Sciatic	• Ratio of neural to nonneural tissue in sciatic nerve changes significantly from 2:1 (midgluteal and subgluteal) to 1:1 (midfemoral and popliteal)	2b
Dufour et al. [73]	Cohort study	NS	Median	• NS-guided median nerve block has ~43 % incidence of intraneural injection	2b
				• In the absence of intraneural injection, presence of circumferential local anesthetic spread seemed predictive of successful sensory block in ~75 % of cases	
Krediet et al. [86]	Cohort study	US	Sciatic	• Random assessment of 500 video clips of injection of 0.5 mL injectate (211 intraneural, 268 extraneural, 21 undetermined), mean sensitivity of experts, and novices in detecting intraneural injections were 84 % and 65 %, respectively	2b
				• Assessments by both groups were highly specific (98 %) for intraneural injections	
				• Among novices, 20–50 % of all intraneural injections were missed	
Sala Blanch et al. [100]	Cohort study	NS	Sciatic	• None of the patients exhibited clinical or electrophysiological evidence of neurological injury after deliberate intraneural injection	2b
				• 16/17 (94 %) patients had US criteria of intraneural injection after deliberate NS-guided intraneural injection	
				• Average increase in postinjection nerve area was 45 %	
Orebaugh et al. [117]	Lab study (Cadaver)	US	Interscalene	• With US-guided needle tip placement in the interscalene region, frequency of intraepineurial injection was relatively high (50 %)	5
				• In cases with intraepineurial needle placement, there was no evidence of fascicular injection or axonal damage	
Sunderland and Ray [120]	Cohort study	n/a	Sciatic	• No exchange of bundles between the two popliteal divisions of the sciatic trunk	2b
				• Direct relationship found between number of fascicles and thickness of nerves (cross-sectional area)	
				• Branching of fascicles varied greatly among nerves at any given level	
Tran et al. [108]	RCT (3)	US	Sciatic	• A single subepineural injection resulted in better success rates, faster onset time, and fewer needle passes than targeted injections around tibial and common peroneal nerve	1b
				• None of the 45 patients followed up at 1 week showed sensory or motor deficit	
Theron et al. [107]	Cohort study	n/a	n/a	• Syringe feel cannot help anesthesiologists determine reliably whether needle tip is placed intraneurally irrespective of operator experience	5
				• 30 % of subjects correctly identified the nerve	
				• 30 % of self-identified experienced regional anesthesiologists correctly identified the nerve	

Tsui et al. [109]	Lab study	n/a	n/a	• When tested on nine different needle–syringe combinations, CAIT effectively maintained injection pressures below 1034 mmHg in an in vitro system	5
Claudio et al. [114]	Cohort study	n/a	n/a	• Anesthesiologists vary widely in perception of "normal" pressure and speed during simulated PNB injection	2b
				• Pressures varied as much as 20X among needles of the same gauge/length	
				• Pressure >20 psi was generated 70 % of the time; >25 psi, 50 % of the time; >30 psi, 10 % of the time	
Tsui et al. [121]	Cohort study	n/a	n/a	• No anesthesiologist generated pressures >1034 mmHg using CAIT	2b
				• 29/30 subjects generated pressures >1034 mmHg at some point when using 'syringe feel' method	
				• Mean pressure using CAIT was lower (636 ± 71 vs. 1378 ± 194 mmHg, $p = 0.03$); 'syringe feel' method resulted in higher peak pressures (1875 ± 206 vs. 715 ± 104 mmHg, $p < 0.001$)	
Sunderland [152]	Cohort study	n/a	Median, radial, ulnar	• Fascicular pattern changed along the entire length of each nerve	2b
				• The longest section of any nerve with a constant pattern was 15 mm	
				• Size and number of fascicles were inversely related at any one level	
				• There was no constant or characteristic fascicular pattern for any nerve. There was no constant or characteristic fascicular pattern for any nerve	
Choyce et al. [70]	Cohort study	Paresthesia	Axillary	• After paresthesia, 77 % of needle placements produced motor activity ≤0.5 mA (median 0.17 mA; range 0.03–3.3 mA)	2b
Kaiser et al. [83]	RCT (3)	NS	Sciatic	• Complete paralysis was achieved in all patients only with low current (0.1 mA)	1b
Keschner et al. [84]	Cohort study	NS	Infraclavicular	• Block success rate of 94 % with stimulating current <0.3 mA, with no neurological complications noted on first postoperative visit	2b
Seidel et al. [101]	RCT (3)	US vs. NS	Sciatic	• Success rate was significantly higher in the US group (94.9 % vs. 61.9 %, $p<0.001$). Paresthesia was more common in US group (51.7 %) vs. NS group (23.7 %)	1b
				• Paresthesias indicated an intraneural needle position with an odds ratio of 27.4 (specificity 98.8 %, sensitivity 45.9 %)	

Table 5.4 Incidence of neurological complications following peripheral nerve blocks

Study	Type of study[a]	Follow-up period	Number of PNB or claims (CC)	Incidence of temporary nerve injury (<6 months)	Incidence of long-term injury (>6 months)	Key findings	LOE
Barrington et al. [1]	P	6–10 days or 6 weeks for new onset neurological symptoms	8189	0.04 %	0 %	• Incidence attributable to nerve block is 0.04 % • 2/3 blocks with nerve injury related to PNB were done using NS alone; other used US+NS (not significant)	1b
Fredrickson et al. [3]	P	2nd to 4th weeks post-op	1010	8.2 %, 3.7 %, and 0.6 % at 10 days, 1 month, and 6 months, respectively	–	• Most common causes of postoperative neurological dysfunction are unrelated to PNB • Elicitation of paresthesia was associated with an increased odds ratio for development of new neurological symptoms	1b
Kroll et al. [87]	CC	N/A	1541	Most claims were for disabling injury	–	• GA (61 %) was more commonly associated with nerve damage claims compared to RA (36 %) • GA was involved in a majority of ulnar nerve injuries (85 %)	2b
Cheney et al. [69]	CC	N/A	4813	–	–	• RA was more frequently associated with nerve damage claims compared to GA • Ulnar nerve injury occurred predominantly in men (75 %) • Increase in spinal cord complications compared to previous analysis	2b
Lee et al. [88]	CC	N/A	189	–	–	• 51 % of claims were for nerve damage • 68 % of claims were for temporary or nondisabling injury • 32 % of claims were associated with permanent and/or disabling injuries • 6/8 spinal cord injury claims related to interscalene blocks with cervical spinal cord damage; 4 of these 6 blocks were performed under GA	2b
Lee et al. [89]	CC	N/A	1005	• 51 % of claims were for nerve damage • 68 % were for temporary or nondisabling injury • 32 % were associated with permanent and/or disabling injuries	6/8 spinal cord injury claims related to interscalene block and 4/6 blocks performed under GA	• Majority of claims (72 %) associated with temporary or nondisabling injuries • 1/4 of claims involved disabling injuries • Majority of claims were associated with outpatient procedures (66 %)	2b
Auroy et al. [2]	P (multicenter)	N/A	158,083	Incidence: • Popliteal (0.315 %) • Interscalene (0.029 %) • Femoral (0.029 %) • Sciatic (0.024 %) • Axillary (0.018 %) • Mid-humeral (0.014 %)	7/158,083	• Lidocaine spinals associated with more complications than bupivacaine spinals • Of 12 complications that occurred after PNB, 9 were done using NS	1b

Borgeat et al. [65]	P	days 1–5, 10; months 1, 3, 6, 9	520	14 %	0.4 %	• Up to 14 % and 7.9 % of patients have neurological symptoms not related to shoulder surgery at 10 days and 1 month, respectively • All symptoms appeared within 23 days after the block; 10 % developed symptoms between days 10 and 23, but most resolved spontaneously • Long-term neurological dysfunction due to interscalene block is rare (0.4 %); treatable causes (e.g., sulcus ulnaris syndrome) need to be identified early	1b
Jacob et al. [82]	R	N/A	3883	–	–	• Nerve injury following TKA was not associated with PNB (odds ratio 0.97) or type of anesthesia (odds ratio 1.1 [neuraxial vs. general]) but with prolonged tourniquet time • Patients with nerve injury who underwent PNB were less likely to have complete neurologic recovery	2b
Welch et al. [112]	R	N/A	6685	–	–	• 0.3 % incidence of iatrogenic injuries • Significant association of iatrogenic injuries with certain types of surgery, GA, and epidural anesthesia but a similar association was not found with PNB	2b
Jacob et al. [81]	R		2444	–	–	• Nerve injury following hip arthroplasty was not associated with type of anesthesia or PNB • The risk for nerve injury was associated with younger age, female gender, longer operations, and posterior surgical approach	2b
Candido et al. [144]	P	24 and 48 h, 2 and 4 weeks, and 3 months	693	3.3 %	0.1 %	• Incidence of neurologic sequelae in brachial plexus distribution after interscalene block was 3.3 % and 0.1 % at 1 and 3 months • Pain/paresthesia at the block site are independent predictors of neurological sequelae	1b
Sviggum et al. [104]	R	N/A	1138	–	–	• Use of interscalene block does not increase the risk of nerve injury in patients undergoing TSA • Use of interscalene block was associated with significantly lower odds for nerve injury (0.44; 95 % CI = 0.22–0.86) • Incidence of nerve injury after elective TSA was ~2.2 %	2b
Hebl et al. [79]	R	2, 3, and 6 weeks post-op	100	6/100 receiving axillary block and 4/100 receiving GA at 2–3 weeks. follow-up	–	• RA does not seem to worsen neurologic outcome in patients with preexisting ulnar neuropathy who undergo ulnar nerve transposition	2b
Borgeat et al. [66]	P	Days 1–5 and 10 post-op; 1, 3, and 6 months	700	8 % on day 10; 2.4 % at 1 month	0 %	• Minor neurologic complications of 2.4 %, 0.3 %, and 0 % at 1, 3, and 6 months, respectively, using lateral modified approach for interscalene block • Two patients had a severe and prolonged sensory-motor deficit involving the middle and lower trunks; these patients needed 19 and 28 weeks to recover, respectively	1b

(continued)

Table 5.4 (continued)

Study	Type of study[a]	Follow-up period	Number of PNB or claims (CC)	Incidence of temporary nerve injury (<6 months)	Incidence of long-term injury (>6 months)	Key findings	LOE
Capdevila et al. [68]	P (multicenter)	Post-op period, 2 weeks, 6 weeks, and 3 months	1416	0.21 %	0 %	• Incidence of short-term neurological dysfunction following continuous PNB is ~0.21 % for femoral nerve block • Minor symptoms such as dysesthesia range between 1.5 and 3 % • High risk for neurological dysfunction include intensive care unit stay, patient age <40 years, and bupivacaine infusion	1b
Brull et al. [67]	Systematic review of P and R studies	N/A	50,117	1.8 %	0.004 %	• Transient postblock neuropathy has an overall incidence of 1.8 % with the highest risk being with interscalene and axillary blocks followed by proximal sciatic, femoral, and popliteal blocks	2a
Orebaugh et al. [4]	R	24 h or until the block resolved	5436	N/A	0.09 %	• 3 EMG-confirmed cases of nerve injury with landmark-NS technique vs. no long-term injury with US technique • No statistically significant difference between the two groups in frequency of neurologic injury	2b
Ecoffey et al. [74]	P (multicenter)	10 days	27,031	0.37 per 10,000 (none attributed to regional anesthesia)	N/A	• After US-guided axillary block, overall incidence of postoperative neurologic symptoms was 0.37/10,000 • Most were mild in nature and unrelated to the block	1b
Sites et al. [6]	R	5 days–6 months	12,668	• Femoral 0.09 % [95 % CI = 0.02–0.23]	• Femoral 0.02 % [95 % CI = 0–1.2]	• Overall incidence of short-term (lasting up to 5 days) symptoms following PNB was 0.18 %	2b
				• Interscalene 0.35 % [95 % CI = 0.14–0.73]	• Interscalene 0.25 % [95 % CI = 0.08–0.58]		
				• Supraclavicular 0.20 % [95 % CI = 0.04–0.58]	• Supraclavicular 0 % [95 % CI = 0–0.24]		
				• Popliteal 0.40 % [95 % CI = 0.11–1.04]	• Popliteal 0.31 % [95 % CI = 0.06–0.89]	• Symptoms lasting >6 months was 0.09 %	
				• Femoral (continuous) 0.1 % [95 % CI = 0.11–1.04]	• Femoral (continuous) 0.1 % [95 % CI = 0.11–1.04]		
				• Interscalene (continuous) 1.2 % [95 % CI = 0.27–3.76]	• Interscalene (continuous) 0.87 % [95 % CI = 0.10–3.11]		
				• Axillary 2.3 [95 % CI =0.06–12.57]	• Axillary 0 % [95 % CI = 0–8.4]		
Orebaugh et al. [5]	R	1 year	9069	4/9069 at 6–12 months	1/9069 at >12 months	• Nerve injuries lasting 6–12 months were more frequent with NS-guided blocks compared to US-guided blocks • Long-term nerve injuries (>12 months) were no different between NS- or US-guided blocks	2b
Szypula et al. [106]	CC	N/A	366			• Claims related to PNB constituted 3 % of the total closed claims and 13 % of all regional anesthesia claims • Epidural (72 %), spinal (15 %) and combined spinal/epidural (2 %) constituted most of the claims and were mostly related to obstetrics • Nonobstetric claims had worse outcomes compared to obstetric claims	2b

Auroy et al. [60]	P	N/A	21,278	Spinals (70.58 %) Epidurals (17.64 %) PNB (11.76 %)		• 4 neurological injuries total; incidence of 1.9/10,000 blocks	1b
Bogdanov et al. [64]	R	4–8 weeks	548	None	None	• Modification of Winnie's technique allows interscalene block to be performed safely on anesthetized patients	2b
Klein et al. [85]	P	day 7 and further work-up	2382	0.17 %	–	• Neurological injury occurs infrequently with the use of long-acting LA	1b
Lenters et al. [90]	RNeurologic complications, PNB:retrospective review	N/A	3172	27/3172; 11 of which had recovery of normal function at a mean of 202 days (range, 10–760 days)	Persistent deficits present in 14/3172 at a mean of 176 days (range, 17–416 days)	• ISB is associated with a 0.73 % incidence of neurological dysfunction and 0.16 % incidence of chronic neuropathy	2b
Weigel et al. [113]	R	Third month post-op	1398	12 (0.9 %) had transient neurological deficits	One permanent neurological injury noted after femoral nerve block	• Major complications after CPNB are rare, but minor transient adverse effects are not uncommon after CPNB	2b
Watts et al. [110]	P	Day 10–12 post-op	1065	13/1065 (1.22 %)	2/1065 (0.22 %) had long-term injury (>6 months)	• 30 % blocks performed on awake patients; 25.6 % under sedation, and 44.4 % under GA • Catheters used in 7/13 blocks associated with neurological dysfunction	1b
Weber et al. [111]	R	N/A	218	2/218 (0.91 %)	–	• Two patients had temporary neurologic injuries that persisted at 6 weeks • One patient had long-term nerve damage (>1 year)	2b
Cuvillon et al. [72]	P	N/A	211	–	0.4 %	• 0.48 % incidence following 48 h infusion through femoral catheter	1b
Hajek et al. [77]	R	N/A	157	–	1.26 %	• Higher prevalence of neurological dysfunction and long-term neuropathy compared to other studies with 72-h CPNB	2b
Compere et al. [71]	P	3, 6 and 12 months	400	–	2/400 (0.05 %)	• One complication resolved at 18 months, and the other persisted; paresthesia was noted during block placement in the latter patient	1b
Neuberger et al. [95]	P	N/A	3491	0.3 % at <6 weeks; 6 patients (0.2 %) had symptoms lasting >6 weeks	–	• Neurological complications following PNB catheters are rare	1b
Nye et al. [96]	R	surgery clinic follow-up	213	6.6 %	1.9 %	• High incidence of temporary (6.6 %) neurological dysfunction following 72-h lumbar plexus catheters	2b
Selander et al. [102]	Cohort study	N/A	533	1.9 % (8 in paresthesia-guidance group and 2 in artery-guidance group)	3/533 (0.56 %) (1.03 % in paresthesia group) had symptoms lasting >1 year	• Difficult to avoid paresthesia in the artery group • All 10 patients with complications reported painful paresthesia during block procedure	2b
Sharma et al. [103]	R	2, 6, 12 weeks and 1 year	709	0.66 %	0.13 %	• Overall rate of femoral neuropathy/neuritis was 0.59 % • In all but one patient, neurologic deficits resolved within 1 year of TKA	2b
Swenson et al. [105]	R	N/A	620	2/620 (0.3 %)	–	• In both patients reporting neurological dysfunction, complications resolved within 6 weeks	2b

a*P* prospective study, *R* retrospective review, *CC* closed claims analysis

Table 5.5 Case reports of neurological dysfunction following peripheral nerve blocks

Author	Block type	Age/Sex	Intraneural injection detected?	Risk factors	Single shot/ catheter	Guidance method	Procedural problems	EMG findings	Presentation	Time of resolution	Pearson score
Al-Nasser and Palacios [122]	Psoas compartment	60/F	N/A	None	Catheter	NS	Intrathecal placement on first attempt	Severe femoral nerve injury at 24 h	Dense motor and sensory block despite low LA concentration	12 months (6 months partial recovery)	6
Atchabahian and Brown [124]	Fascia iliaca	78/F	N/A	None	Single shot	Landmark	None	N/A	Complete anesthesia over anterior thigh and motor weakness	POD 8	4
Barrington et al. [125]	Infraclavicular	60/M	No	C8 radiculopathy, smoking, alcohol abuse	Catheter	US	None	Recent onset brachial plexopathy at 3 weeks	Sensory deficits in radial and medial antebrachial nerve; persisting paresthesia and allodynia	Did not resolve	9
Barutell et al. [126]	Interscalene	49/F	Possibly	Obesity	Single shot	Landmark	Paresthesia, loss of consciousness, respiratory failure	Total denervation in C8/T1 supply; partial denervation in C7 supply on POD 1	Paralysis of extensor muscles of hand	Did not resolve	7
Ben-David and Stahl [127]	Axillary	38/M	N/A	None	Single shot	Landmark	None	Neurapraxia at 4 weeks	Sensory and motor changes in radial territory with pain	6 months	3
Blumenthal et al. [128]	Femoral nerve	72/M	N/A	Subclinical polyneuropathy	Catheter	NS	None	Low-voltage denervation activities on POD 4	Persistent quadriceps weakness and hypesthesia	Did not resolve	7
Bonner and Pridie [129]	Sciatic nerve	59/F	N/A	Peripheral vascular disease	Single shot	NS	None	Absent conduction in common peroneal and posterior tibial nerves at 2 weeks	Persistent weakness in sciatic distribution	12 months (6 months partial recovery)	4
Cohen and Gray [130]	Interscalene	36/M	Yes	None	Single shot	US	None	N/A	Persistent weakness below elbow	6 weeks	2
Funk et al. [131]	Interscalene	35/M	N/A	None	Single shot	NS	High injection resistance, twitches at 0.1 mA	No electrical activity in triceps on POD 10	Weakness and hypesthesia in dorsum of hand	18 months	3
Giabicani et al. [132]	Popliteal sciatic nerve	54/F	N/A	Subclinical poly-neuropathy	Single shot	US	None	Decreased bilateral amplitudes of potentially prolonged distal latencies and slowing conduction velocities on POD 40	Persistent sensory and motor block	2 years	3
Gungor et al. [133]	Psoas compartment	44/M	N/A	None	Single shot	NS	None	Partial lesion of proximal femoral nerve (? POD)	Weakness in knee extensors	6 months	4
Imran et al. [134]	Axillary	44/M	N/A	None	Single shot	Landmark	None	Significant denervation of axillary nerve at 6 weeks	N/A	Did not resolve	2
Jung et al. [135]	Axillary	62/F	N/A	None	Single shot	US	None	Medial antebrachial nerve injury (? POD)	Pain and numbness	Did not resolve	8
	Axillary	30/F	N/A	None	Single shot	US	None	Medial antebrachial nerve injury (? POD)	Pain and numbness	Did not resolve	
Kim et al. [136]	Brachial plexus	54/F	N/A	None	Single shot	?	Radiating pain in median nerve territory upon injection	Median nerve injury at 1 month	Pain and numbness	?	2
Koff et al. [143]	Interscalene	65/M	No	Multiple sclerosis	Single shot	US+NS	No	Denervation of median and ulnar nerves (POD 4; 3 weeks, 3 months)	Weakness	Did not resolve	4

Lim and Pereira [137]	Supraclavicular	34/F	N/A	None	Single shot	Paresthesia	Paresthesia	Focal demyelination at level of cords at 1 week	Paralysis of hand and paresthesia	Lost to follow-up (resolving neuropathy at 8 weeks)	4
Shah et al. [139]	Anterior sciatic nerve	51/F	? (high injection pressure noted)	None	Single shot	NS	High injection pressure	Peroneal component of sciatic nerve injured at level of thigh at 4 weeks	Weakness and hypesthesia	Did not resolve	5
Stark [140]	Axillary	51/M	? (disruption of fascicular anatomy on exploration)	None	Single shot	NS	N/A	Median nerve damage at 6 weeks	Median nerve paralysis	Did not resolve	2
	Axillary	69/F	N/A	None	Single shot	NS	N/A	Ulnar nerve demyelination at 6 weeks	Ulnar nerve paralysis	Did not resolve	
	Axillary	55/M	N/A	Scleroderma	Catheter	NS	N/A	Ulnar nerve demyelination at 8 weeks	Ulnar nerve paralysis	Did not resolve	
Uppal et al. [141]	Sciatic nerve	46/M	N/A	None	Single shot	NS	Distended sciatic nerve noted during surgery	Severe axonal loss in sciatic nerve (? POD)	Sciatic nerve weakness/ foot drop	Did not resolve	2
Walton et al. [142]	Interscalene	36/M	No	None	Single shot	NS	None	Complete denervation of multiple nerves at 5 weeks	Paresis and numbness	26 weeks	3

Table 5.6 Summary of evaluated outcomes with statements of evidence and grades of recommendation

Evaluated outcomes	Level of evidence	Grade of recommendation	References
Host factors			
Anatomical factors			
• Intraneural fascicular topography has wide variability with no consistent pattern of branching or anastomosis at any given site	2b	B	[115, 116, 120]
• The connective tissue content of a peripheral nerve varies depending on the number of fascicles at a given site	2b	B	[120, 152]
• Neural connective tissue and number of fascicles increase from proximal part of the nerve distally	2b	B	[115, 116]
Surgical factors			
• Certain types of surgery are associated with a higher risk of postoperative nerve injury	2b	B	[112]
Peripheral nerve blocks do not increase the risk of postoperative neurological dysfunction	2b	B	[66, 104, 112, 144]
Neuropathy			
• Preexisting neuropathy is thought to increase the risk of postoperative neurological dysfunction following PNB	5	D	[11, 125, 128, 129, 132, 140, 143, 162]
• Neuropathic nerves are more prone to the prolonged effects of local anesthetics	5	D	[29, 35]
Causative agents			
Mechanical agent: *needle trauma*			
• Nerve trunks usually slide under an advancing short-bevel needle compared to long-bevel needles	5	D	[17, 38, 119]
• Long-bevel needles cause more functional or histological damage compared to short-bevel, pencil-tip, or Tuohy needles but the superiority among the latter three needle types is currently unknown	5	D	[37, 38, 45, 46, 119]
• Needle gauge may in itself influence the degree of damage irrespective of needle type	5	D	[45]
• When short-bevel needles do penetrate perineurium, the resulting nerve damage is greater than that of long-bevel needles	5	D	[42]
• The amount of damage is smaller when the needle bevel is parallel than when it is perpendicular to the nerve fibers	5	D	[17, 27, 37]
Mechanical agent: *pressure injury*			
• Perineural injections require the least injection pressure followed by extrafascicular injection, while intrafascicular injections generate high injection pressure	5	D	[53, 54, 167]
• While high injection pressures result in functional and histological nerve damage , intraneural injection with low injection pressures may not necessarily result in nerve damage	2b	C	[9, 21, 34, 97]
Chemical agent: *neurotoxicity*			
• Both extra- and intrafascicular injection of local anesthetic can result in histological damage, but is far greater following intrafascicular injection leading to functional injury as well	5	D	[22, 23, 25, 26, 28–33, 35, 36, 39, 40, 44, 50, 57]
• All local anesthetics are neurotoxic in increasing concentrations and individual local anesthetics differ in their neurotoxic potential	5	D	[25, 26, 44, 55, 58, 59]
• Both epinephrine and local anesthetics decrease neural blood flow, and their combination has synergistic effects	5	D	[22, 23, 25, 26, 39]

Chemical agent: adjuvants			
• Local anesthetics are more neurotoxic than their adjuvants, but while some adjuvants may have neurotoxic potential, others may be neuroprotective	5	D	[50, 57, 58, 173]
Environmental influences			
Nerve stimulation			
• Nerve stimulation has low sensitivity but high specificity for proximity of the needle tip to the target nerve when stimulation is present at low currents	2b	B	[52, 70, 97]
• Nerve stimulation cannot differentiate between intraneural needle placement and needle–nerve contact	5	D	[56]
• Diabetic nerves require higher stimulating currents for both intra- and extraneural needle placement	2b	C	[43, 63]
Injection pressure monitoring			
• High injection pressures are often reached unknowingly by experienced and nonexperienced practitioners	2b	B	[109, 114]
• Syringe feel is inaccurate in differentiating tissues, and higher pressures are generated by performers unknowingly	2b	B	[107]
• Injection pressure can be kept within safe limits reliably by using CAIT or pressure measurement devices	2b	C	[109, 121]
• Opening pressure can detect needle nerve contact reliably	2b	C	[75]
Ultrasound			
• Ultrasound guidance can detect intraneural injection but is dependent on the operator experience	2b	B	[63, 78, 86, 91, 98, 117]
• Use of ultrasonography does not prevent intraneural injection	2b	B	[63, 78, 91, 98]
• Neurological complications following PNB have not declined as a result of US guidance	2b	B	[4, 5, 92]
Neurological injury and regional anesthesia			
Incidence of intraneural injection			
• Unintentional intraneural injections happen more often than previously expected	2b	B	[63, 78, 91, 94, 98, 99]
• Intraneural injections may not necessarily result in neurological dysfunction	2b	B	[62, 63, 78, 91, 94, 97–100, 108]
• Intraneural injections have a fast onset	2b	B	[78, 94, 99]
Incidence of neurological complications following PNB			
• Transient neurological dysfunction following peripheral nerve blocks are more common than long-term dysfunction and usually resolves with time	1b	A	[2, 3, 65–68, 144, 145]
• Procedure-induced paresthesia may increase the risk of postoperative neurological dysfunction	1b	A	[3, 102, 144]
• The safety of performing PNB under general anesthesia and its impact on neurological outcomes is currently unknown	2b	C	[64, 110]

between 8.2 and 15 % [3, 145]. Transient neurologic symptoms are known to resolve by 6 months to 1 year [3, 66]. Neither ultrasound nor nerve stimulation guidance affected the incidence of short- or long-term neurologic dysfunction following PNB in one retrospective review [5], although a recent update of the same database showed a lower incidence of short-term neurologic dysfunction with the use of ultrasound guidance [4]. A retrospective database review of ultrasound-guided blocks showed an incidence of long-term neurologic dysfunction of 0.9/1000 [6], which is about 22 times higher than those reported by others [1–3, 67]. Various definitions of long-term neurologic dysfunction (e.g., >6 vs. >12 months) may have accounted for the difference in incidence between these studies.

Procedure-induced paresthesia may increase the likelihood of transient neurologic symptoms following PNB as reported in three prospective cohort studies [3, 102, 144]. Certain peripheral nerve blocks have a predilection for neurologic complications than others. In a retrospective review of 12,668 patients undergoing ultrasound-guided nerve blocks, Sites et al. [6] reported short-term neurologic dysfunction being highest with axillary nerve block (2.3 %), followed by interscalene catheter (1.2 %), popliteal sciatic block (0.4 %), single-injection interscalene block (0.35 %), supraclavicular block (0.2 %), and femoral nerve block (0.1 %). Long-term dysfunction was again common with interscalene catheters (0.87 %), popliteal sciatic block (0.31 %), and single-injection interscalene block (0.25 %). In contrast, supraclavicular, axillary, and femoral nerve blocks rarely caused long-term problems. In an internet-based survey of 36 centers (27,031 patients), Ecoffey et al. [74] reported an overall incidence of postoperative neurologic symptoms of around 0.37 per 10,000 following ultrasound-guided axillary brachial plexus block, most of which were thought to be unrelated to the block. Although the reported incidence indicates a decrease in block-related neurologic symptoms compared to other studies [6], whether or not the observed results are due to ultrasound guidance cannot be extrapolated.

Neurologic complications must increase following prolonged exposure to nerves according to lab studies but there has been conflicting evidence regarding this. While some studies have noted a higher than normal incidence of neurologic complications with the use of catheter in psoas compartment blocks, popliteal sciatic nerve blocks [77, 96], other studies note a very low complication rate [68, 71, 72, 95, 105, 113]. This may be related to the method of data collection and the definition of neuropathy. Future prospective data collection methods are needed to address this issue.

Although there are articles reporting low incidence of neurologic complications following PNB performed under general anesthesia [64, 110], there is limited information on whether blocks performed under general anesthesia increase the risk of postoperative neurologic dysfunction. A retrospective review by Bogdanov et al. [64] did not report neurologic complications following interscalene blocks performed under general anesthesia but two patients in the study by Watts et al. [110] reported long-term neurologic dysfunction. The details of whether these blocks were performed under sedation or general anesthesia are not known from the study. To date, there is no known pathological reason why general anesthesia would directly increase the patient's susceptibly (host factor) in neurologic injury when receiving regional anesthesia. However, one would expect that general anesthesia would compromise the patient's (environmental influences) ability to communicate and provide feedback of either early symptoms of LAST or paresthesia from needle–nerve contact. In a recent report, threshold currents that are needed to generate a motor response were higher in an anesthetized patient than those in awake patients. This observation may suggest that there is a possibility of potential error which can be made when using nerve stimulation to locate the nerve when a patient is under general anesthesia [146].

Nevertheless, the current ASRA advisory panel suggested that a conscious patient is preferred while performing PNBs unless in selected patient populations (e.g., dementia and developmental delay) where the risk-to-benefit ratio of performing regional anesthesia under general anesthesia may improve [147].

Lessons from Case Reports

Case reports identify the patient and performance characteristics, neurologic presentation, and subsequent outcomes. A total of 21 case reports/series reported on the occurrence of neurologic complication in 24 patients following PNB (Table 5.5). The majority was middle aged (Median age 50.5 years) and consisted of 12 males and 12 females. Only four of the 24 cases had some signs of intraneural injections while the rest of the cases did not mention the possibility. It is not only those with some form of subclinical or overt neuropathy ($n = 5/24$ patients) who are susceptible, but quite often it is an otherwise healthy patient who suffers this unfortunate complications. The presence of risk factors may be a bad prognostic sign since only two of these 5 patients had recovery of some nerve function after a prolonged period of time. The most common presentation was persistent weakness (16 cases) followed by pain and paresthesia (three cases) and a combination of both in the remaining. Only 4 patients had catheters placed while the rest had single shot blocks. A total of 12 patients did not have recovery of nerve function back to normal while the rest of the patients had recovery ranging anywhere from 1 week to 2 years. Five blocks were performed under US guidance while 11 cases utilized neurostimulation, 1 case

used the combined US+NS technique, 1 case did not document the guidance method used, and 5 cases used the landmark/paresthesia technique.

Benumof [148] reported a case of spinal cord injury following an interscalene block performed under general anesthesia. This case report is an invaluable reminder of the risks associated with RA but is not strictly speaking PN injuries.

Analyzing Neurologic Injury from the Perspective of Disease Causation

Given their complexity, neurologic complications can best be evaluated by the same epidemiological principles of event causation (Fig. 5.1). The epidemiological triangle is a common injury model used to describe the relationship between an agent, a host, and the environment [14, 15]. A neuronal injury is more likely to occur when there is interaction between a susceptible host (inadequately protected nerve), an injurious agent (local anesthetic, needle, or injection pressure), and a hazardous working environment (poor supervision/guidance for locating needle, unsafe practices, unintended exposure). Elimination of one of the triangle's components should, in theory, prevent the occurrence of the event. Hence, the safest approach appears to be identification of potential risk factors and prevention of their interaction.

Epidemiological Triangle

Host/Biological Factors

The history of neurologic complications is as old as the field of regional anesthesia itself. Early performers of regional anesthesia acknowledged both the possibility of neurologic complications following PNB [149, 150] and the lack of complications following deliberate needle–nerve contact [151]. Various anatomical, surgical, and patient factors may affect the incidence of postoperative nerve injury and include the type of surgery, associated comorbidities, the presence of preexisting neuropathy, and whether temporary or permanent injury is being considered.

Anatomy and Physiology

Not all nerves or nerve blocks are the same since intraneural fascicular topography shows wide variability (*LOE 2b*; *Grade B*). *The connective tissue content of a peripheral nerve varies depending on the number of fascicles at a given site* (*LOE 2b*; *Grade B*). *Neural connective tissue and number of fascicles increase from proximal part of the nerve distally* (*LOE 2b*; *Grade B*).

A total of three studies looked into the neural anatomy with relevance to PNB [115, 116, 120]. In most cases, a peripheral nerve is a mixed entity consisting of both sensory and motor components and has both myelinated and unmyelinated axons. Connective tissue covering the axons is present in different layers, providing support and nutrition to the nerves and acting as a protective barrier to the axon (Fig. 5.2). The three protective covers are the epineurium which covers the nerve overall and separates the fascicles, perineurium which lines the fascicles, and the endoneurium which lies inside the fascicles and surrounds the axons. The epineurium—the outer covering of the nerve—encases the fascicular bundles within a connective tissue network known as interfascicular epineurium. The adipose tissue in the interfascicular epineurium acts as a cushion for the fascicles and causes them to slide under or over a slowly advancing needle, protecting the fascicles from needle trauma. The fascicular bundle is in turn encased by multiple layers of cells, known as the perineurium, which act as a functional barrier for the axons and protects against physical and chemical

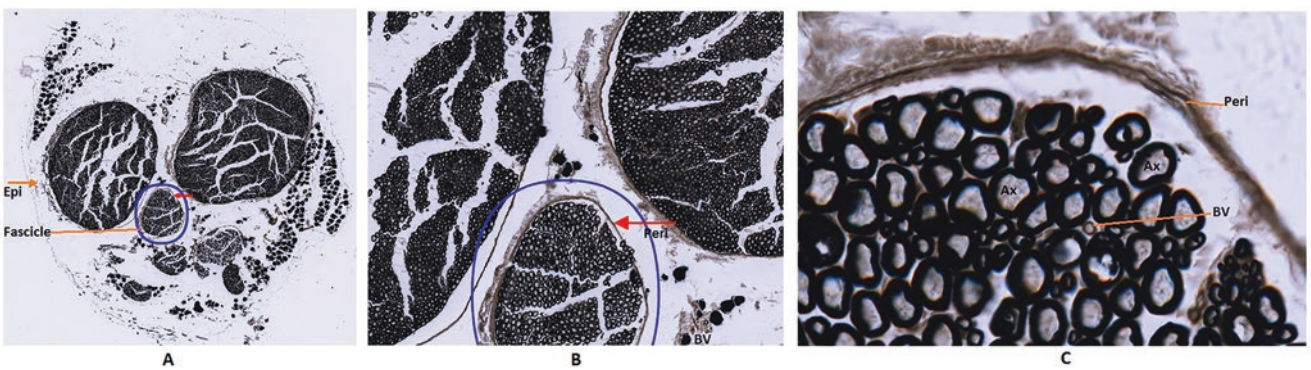

Fig. 5.2 Electron micrograph of a peripheral nerve stained with osmic acid. (a) The entire nerve is encased in a connective tissue layer, the epineurium (Epi), and the nerve fibers are arranged in fascicles. (b) Each fascicle is surrounded by a cellular layer, the perineurium (*red arrow*). Blood vessels (BV) can be seen collapsed in the interfascicular epineurium. (c) Axons (Ax) within the fascicle are in an endoneurial network, interspersed with nonfenestrated blood vessels (BV). (Reproduced with permission from the Department of Anatomy and Cell Biology, Schulich School of Medicine and Dentistry, Western University, London, ON, Canada. http://slides.uwo.ca/spinal_cord.html)

insults. The perineurium bathes the axons in an interstitial fluid which is similar to CSF in composition and is continuous with the neuraxis [152, 153]. Inside the fascicle, myelinated or unmyelinated axons are supported by a network of connective tissue known as endoneurium which also contains the nonfenestrated capillaries that provide nutrition to these tissues. The endoneurium serves a vital role in nerve regeneration by aligning the regrowing axons toward its target. The perineurium maintains an intrafascicular pressure which is reflected in the intracellular pressure of the axons [154, 155]; thus, injection deep to the perineurium generally requires greater injection pressure compared to injection within the epineurium.

Nerve composition varies among different nerve types and also within a given nerve. Sunderland [152] noted that, in the upper limb, the fascicular topography of the radial, median, and ulnar nerves varied every 0.25–0.5 mm segment, and the branching pattern was not constant for a given nerve at a given site. While the sizes of individual fascicles are inversely related to their number at a given location along the nerve [152], the connective tissue content and cross-sectional area of a nerve are directly proportional [120]. This suggests that the amount of injury following intraneural injection depends not only on the characteristics of the insult but also on how protected a nerve is at the site of injection. Nerves are thought to be oligofascicular at the level of nerve roots and polyfascicular in areas prone to physical stress, such as the joints. Hence it is common to see hypoechoic (mono/oligofascicular) nerves at the level of roots (interscalene block) whereas they are hyperechoic (multifascicular) near a joint (popliteal nerve block). Moayeri et al. noted a proximal oligofascicular pattern progressing to a polyfascicular pattern in the brachial plexus [115] and sciatic nerve [116]; Sunderland and Ray [120] noted a wide variation in the fascicular pattern of the sciatic and forearm nerves with no consistent pattern in any part of the nerve. Whether neurologic complications are related to the fascicular morphology is currently unknown [97, 99] since proximal blocks (ISB, subgluteal sciatic nerve block) are known to have similar complications as distal blocks (popliteal sciatic, axillary brachial plexus block). Although the connective tissue content increases with age due to endothelial proliferation as a reaction to decreased vascularity of the nerves [156]. This may influence block onset and recovery, but its implications for neurologic injury are currently unknown. Since we did not anticipate any differences between cadaver and live tissue in terms of nerve composition, cadaver studies provided good evidence to support the earlier statements even in the absence of studies of live human tissue.

Surgical Factors

Certain types of surgery are associated with a higher risk of postoperative nerve injury (*LOE 2b*; *Grade B*). *Peripheral nerve blocks do not increase the risk of postoperative neurologic dysfunction*. (*LOE 2b*; *Grade D*).

Some surgeries are more prone to nerve injuries than others, especially those involving excessive neural stretch [157], trauma [158], inflammation [80], or ischemia [127] including a prolonged tourniquet time [82, 159]. In a retrospective review of 380,680 anesthetics during a 10-year period, Welch et al. [112] found a 0.3 % incidence of iatrogenic injuries. There was a significant association of iatrogenic injuries with certain types of surgeries, general anesthesia, and epidural anesthesia but a similar association was not found with peripheral nerve blocks. The lack of association between regional anesthetic nerve blocks and iatrogenic injuries is also confirmed by other studies in shoulder [65, 66, 144], knee [82], and hip surgeries [81]. Shoulder surgeries have a predilection for iatrogenic nerve injuries [13, 160] and the incidence can be as high as 8.2 % following anterior stabilization, around 1–4 % following shoulder arthroplasty or 1–2 % following rotator cuff repairs [161]. While Borgeat et al. [66] and Candido et al. [144] noted different incidences of persistent neurologic sequelae unrelated to surgery 1 month after ISB (7.9 % vs. 3.3 %), most of these complications were unrelated to ISB. Further, a retrospective review of 1569 patients undergoing total shoulder arthroplasty by Sviggum et al. also noted no such relationship between interscalene block and nerve injury [104]. While some studies indicate that the likelihood of complete recovery from peripheral nerve injury is lower when the patient had a PNB [82], other studies have not shown a similar association [82].

Neuropathy

Preexisting neuropathy is thought to increase the risk of postoperative neurologic dysfunction following PNB (*LOE 5*; *Grade D*). *Neuropathic nerves are more prone to the prolonged effects of local anesthetics* (*LOE 5*; *Grade D*).

Currently, there is no high-quality evidence regarding cause and effect of neurologic sequelae following nerve blocks but most anesthesiologists have a tendency to avoid PNB in patients with neuropathy. Although a retrospective cohort study [79] did not demonstrate worsening of neurologic outcomes following PNB in patients with preexisting neuropathy, a number of case reports [125, 128, 129, 132, 140, 143] indicate that either subclinical or overt preexisting neuropathy may make them susceptible to long-term nerve damage. Hence, the expert opinion regarding regional anesthesia in patients with neurologic disease tends to err toward caution [11, 162]. The degree of neural dysfunction in a chronically compromised nerve may be clinical or subclinical, and any secondary insults such as hypoxia or ischemia, local anesthetic neurotoxicity, or direct mechanical trauma following nerve blockade is thought to exacerbate it [162]. Importantly, the secondary insult need not be at the site of the neural compromise itself, a phenomenon known as "double-crush syndrome" [163]. In fact, a double-crush injury in the form of two distinct low-grade insults has been shown to be more damaging to the nerve compared to an

insult at a single site [164]. Thus, when suspecting underlying chronic neuropathy such as in patients with peripheral vascular disease, mechanical compression, metabolic derangements (diabetes mellitus) or postchemotherapy (cisplatin neurotoxicity), the decision to perform a PNB should be made on a case-by-case basis after thorough physical examination and discussion with the patient and the surgical team [162, 165]. It is generally thought that any evolving lesions or active inflammation of the nerves is a contraindication for PNB [162].

Two animal models of diabetic neuropathy have been tested for local anesthetic neurotoxicity [29, 35]. In the study by Kroin et al., local anesthetics produced a longer mean duration of sensory nerve block in diabetic rats versus nondiabetic rats [35]. Doses of lidocaine (with or without adjuvants) or ropivacaine that did not cause noteworthy nerve fiber damage in nondiabetic rats also failed to produce major pathology in nerves of rats with streptozotocin-induced diabetic neuropathy. The study by Kalichman [29] not only showed a lower conduction velocity in diabetic nerves, but also it had neuronal edema subsequent to extraneurally placed LA in a concentration-dependent fashion. This study along with others indicating that local anesthetic neurotoxicity is directly proportional to the dose and duration of local anesthetic exposure [59, 166], higher LA concentrations should be strongly discouraged for neuropathic patients and deliberate intraneural injections should be avoided based on conventional wisdom.

Causative Agent Factors

The insulting injury to a nerve can be as a result of direct needle trauma, pressure injury, or local anesthetic neurotoxicity. A majority of these factors have been evaluated in animal studies since human studies are not feasible due to obvious ethical concerns and hence most of the evidence is extrapolated to humans. It is difficult to judge as to which factor is the most damaging since most of the evidence originated from different animal models and more than one injurious agent may be evaluated in these studies.

Mechanical Agents

Needle Trauma

Nerve trunks usually slide under an advancing short-bevel needle compared to long-bevel needles (*LOE 5*; *Grade D*). *Long-bevel needles cause more functional or histological damage compared to short-bevel*, *pencil-tip*, *or Tuohy needles but the superiority among the latter three needle types is currently unknown* (*LOE 5*; *Grade D*). *Needle gauge may in itself influence the degree of damage irrespective of needle type* (*LOE 5*; *Grade D*). *When short-bevel needles do penetrate the perineurium*, *the resultant nerve damage is greater than that of long-bevel needles* (*LOE 5*; *Grade D*). *The amount of damage is greater when the needle bevel is perpendicular to nerve fibers than when it is parallel* (*LOE 5*; *Grade D*).

Eight animal studies and one cadaveric study evaluated the impact of needle design on nerve injury. The degree of nerve damage from needle trauma depends on the bevel type, the angle of needle insertion, and the needle size (gauge). Long-bevel (14° angle) needles penetrate fascicular bundles through the perineurium, while these fascicles slide under or away from short-bevel (45° angle) needles [17]. Animal [38] and human cadaver [119] studies demonstrate that injection with a long-bevel needle has a greater chance of being intrafascicular and resulting in nerve injury. One animal study showed that even in the absence of direct neural trauma, the presence of perineural hematoma might in itself result in inflammation and structural injury to the nearby nerves [48] and this has been implicated as a possible cause of injury in a case report [127]. Using cadaveric tissue, Sala-Blanch et al. [119] showed that, although fascicular contact is fairly common with intraneural injections, injury to these fascicles rarely occurs. Of the 134 fascicles contacted by the needle, only four were damaged, all from long-bevel needles. In animal studies, needles with a tapered end, such as Whitacre and Sprotte needles, are comparable to each other [37] and to Tuohy needles with respect to neural damage [37, 45, 46]. While two studies show superiority of tapered-tip needles over short-bevel needles in terms of neural damage caused [27, 37], and its effect on nerve conduction [27] another study reported similar neural perforations with tapered-tip and short-bevel needles of the same gauge [46].

The amount of nerve damage following intraneural needle placement is also higher when the bevel is inserted transversely to the nerve fiber compared to insertion along the long axis of the nerve [17, 27, 37]. Regardless of the type, needle gauge is directly proportional to the extent of nerve damage, as demonstrated by the stark difference in the extent of fascicular damage from 22G needles (3 %) and 17/18G needles (40 %) [45]. In general, short-bevel needles are preferred for PNB since they have difficulty penetrating perineurium; however, when short-bevel needles do penetrate the perineurium, the amount of mechanical trauma far exceeds that done by a long-bevel needle [42].

It is important to point out that basic science research using animals or cadaver tissue as a study model, such as the ones described earlier, were considered to be level 5 evidence and given a grade D recommendation irrespective of study design. This is because these studies arguably do not provide direct research evidence in live human subjects, although ethical issues and other difficulties obviously preclude doing these studies in live subjects. Nevertheless, the available evidence is quite convincing despite having a lower grade.

Pressure Injury

Perineural injections require the least injection pressure followed by extrafascicular injection, while intrafascicular injections generate high injection pressure (*LOE 5*; *Grade D*). *While high injection pressures result in functional and histological nerve damage, intraneural injection with low injection pressures may not necessarily result in nerve damage* (*LOE 2b*; *Grade C*).

The axons inside the fascicles are under pressure created by the perineurium and hence any injection into the perineurium will probably require higher injection pressure subsequently resulting in pressure injury. The evidence for pressure injury is purely based on animal models [9, 17, 21, 34, 53, 54, 167] and the human evidence is limited to studies looking at pressure monitoring during PNB [75]. In animal studies, low injection pressures (<25.1–27.9 kPa) are noted for injection performed around the nerve without penetration of the outer epineurium, while injection pressures increase slightly (69.8–86.5 kPa) upon entering the epineurium [53, 54]. Selander et al. [167], in a study of intraneural injection at different locations within the rabbit sciatic nerve, showed that a relatively low injection pressure (25–60 mmHg [3.3–7.9 kPa]) was required for subepineurial (extrafascicular) injections and resulted in limited spread of injectate, whereas intrafascicular injections required higher pressures (300–750 mmHg [39.9–99.7 kPa]) and resulted in rapid spread of injectate over long distances within the fascicle. To study the clinical consequence of such injections, Hadzic et al. [9] performed intraneural injections with 4 mL lidocaine in the canine sciatic nerve. Low-pressure (<4 psi) injections (3/7) were extrafascicular while high pressure injection (25–45 psi) (4/7) were intrafascicular in location which was similar to that noted by Selander et al. [167]. In a similar study design, Kapur et al. [34] showed that all intrafascicular injections resulted in clinical deficits in the form of paresis or disability while none of the extrafascicular injections resulted in any neural dysfunction. A study of ultrasound-guided deliberate intraneural injections in piglets with injection pressures <20 psi (~138 kPa) also showed that none of the injected nerves had a breach in the perineurium. Although the nerves showed signs of inflammation for up to 2 days postinjection and changes in nerve architecture under ultrasound for up to 4 days, none of the animals developed any functional deficits [21]. A similar evidence from a human study also showed that a low injection pressure during deliberate intraneural popliteal sciatic nerve block does not necessarily lead to early postoperative neurologic dysfunction [97] but further studies on injection pressure in clinical practice are needed. The pressure measurements following subepineurial injections are similar between those obtained by Vuckovic et al. [53, 54] and Hadzic et al. [9] but are higher than those reported by Selander et al. [167]. This could be related to differences in animal models, syringe, and injectate volumes used in the two studies. Although injection pressures <15 psi is recommended safe in clinical practice, this needs to be further validated.

The generation of high injection pressures during intrafascicular injection can be explained by the high intrafascicular pressure created by the perineurium and may also lead to pressure injury. The low injection pressures needed for perineural injection compared to subepineurial and intrafascicular injections show the potential utility of continuous monitoring of injection pressures during PNB. There is a need for further evidence regarding the short- and long-term safety of low-pressure intraneural injections.

Similar to studies related to needle design (see earlier), it would be difficult and unethical to perform studies in live humans to evaluate injury from high pressure injection. Thus, the published evidence is limited to basic science research using animals and cadaver tissue as study models. However, as with studies of needle design, the available evidence is fairly persuasive despite being assigned a lower grade.

Chemical Agents

Neurotoxicity

All local anesthetics are neurotoxic in increasing concentrations and individual local anesthetics differ in their neurotoxic potential (*LOE 5*; *Grade D*). *Both extra- and intrafascicular injection of local anesthetic can result in histological damage, but is far greater following intrafascicular injection leading to functional injury as well* (*LOE 5*; *Grade D*). *Both epinephrine and local anesthetics decrease neural blood flow, and their combination has synergistic effects* (*LOE 5*; *Grade D*).

A total of 21 studies evaluated the neurotoxicity of LA in different animal models. Broadly, the studies looked at comparative neurotoxicity of different LA solutions with or without adjuvants [25, 26, 44, 55, 58, 59], the impact of topical application of LA [22, 23, 29–33, 39, 40, 50, 57], or their intraneural injection [25, 26, 28, 35, 36, 44]. Intraneurally injected LA may often result in histological changes without any functional neuropathy [28, 35, 36]. While there is a general agreement over the increased amount of nerve damage following intrafascicular injection of LA as compared to topical application [44], whether or not LA solutions are more toxic than saline intrafascicularly is currently debated. While Farber et al. [25] in a study of Lewis rats noted intrafascicular injection of LA was more damaging than saline [25], a study by Selander et al. [44] on rabbits showed both saline and 0.5 % bupivacaine to cause equal amount of axonal damage. Although the amount of damage was greater with increasing concentrations of LA indicating that the

pressure injury is far more damaging than LA neurotoxicity. The damage following intrafascicular injections is a result of a breach in the blood–nerve barrier and the loss of internal hypertonic milieu [25] compounded by pressure injury, interstitial edema, and direct neurotoxicity, resulting in clinical nerve damage.

At therapeutic doses, all local anesthetic agents exhibit neurotoxic potential [168] and, although debatable, some drugs may be more neurotoxic than others. The direct neurotoxicity of local anesthetics is thought to be related to prolonged increases in cytosolic Ca^{2+} leading to depletion of adenosine triphosphate, mitochondrial injury, membrane dysfunction, and, ultimately, cell death [169, 170]. Transient neurologic symptoms following spinal anesthesia are thought to represent a mild consequence of local anesthetic neurotoxicity [171], and transient neurologic symptoms following PNB may represent a similar event, with small-diameter axons (pain and temperature) being more affected than large-diameter axons (motor and proprioception) [172].

The neurotoxic effect of local anesthetics is time and concentration dependent in an animal study and in vitro models of cell cultures [59] but whether this holds true in human subjects is not known. While long-acting LA [85] and continuous catheters [6, 68, 72] have been employed safely with a low incidence of long-term nerve damage, some catheter studies [3, 77, 95, 96] and case reports [122, 125, 128, 140] do point toward a fairly high incidence of nerve dysfunction. While Capdevilla et al. [68] in a study of continuous catheters noted a low incidence of long-term neuropathy, bupivacaine infusion was one of the risk factors for the same along with ICU stay and age <40 years. Further prospective studies are needed to know whether prolonged exposure of nerves to different concentrations of LA is safe or neurotoxic.

The local anesthetic neurotoxic potential of individual agents differs depending on the animal model and study methodology but in general, most local anesthetics have vasoconstrictive properties and that includes the common agents such as lidocaine [39], levobupivacaine, and ropivacaine [23], hence making them both directly neurotoxic and have neuronal ischemic effects. Although bupivacaine has a vasodilatory effect on intraneural blood flow [22] and is thought to be less neurotoxic following intraneural injection according to one study [26], another study found it to be more neurotoxic than lidocaine or ropivacaine when injected into the fascicle [25]. Given that local anesthetic neurotoxicity is well documented, deliberate intraneural injection of local anesthetic is still strongly discouraged, despite the fact that most of the evidence comes from animal studies.

Adjuvants

Local anesthetics are more neurotoxic than adjuvants and, while some adjuvants may have neurotoxic potential, others may be neuroprotective (*LOE 5*; *Grade D*).

The neurotoxic potential of local anesthetics far exceeds that of any adjuvants used in regional anesthesia [57, 58], and effects on nerve tissue depend on the individual agent. While adjuvants, including opioids, clonidine, dexamethasone, and neostigmine, do not influence the neurotoxic potential of local anesthetics in vitro, drugs such as ketamine and midazolam may themselves be neurotoxic at higher doses [173]. On the other hand, dexmedetomidine was shown to be neuroprotective in rats following intraneural sciatic nerve injection [50]. It was postulated that dexmedetomidine decreased the neurotoxic potential of bupivacaine by decreasing mast cell degranulation at the site of injury. Nevertheless, the current evidence is limited to studies in animal models.

Intraneural Injections

Unintentional intraneural injections occur more often than previously expected (*LOE 2b*; *Grade B*), *but they may not necessarily result in neurologic dysfunction* (*LOE 2b*; *Grade B*). *Intraneural injections have a rapid block onset* (*LOE 2b*, *Grade B*).

Six trials studied the incidence of unintentional intraneural injection [73, 78, 91, 94, 98, 99]. Three were performed with the aid of nerve stimulation alone, one was done with ultrasound guidance alone, and two used dual guidance. The results showed that unintentional intraneural injection occurs frequently in both upper and lower limb blocks, with the incidence varying from ~17 % to as high as 66 % [73, 78, 91, 94, 98, 99]. Intraneural injections were also shown to hasten block onset [78, 94, 99], improve block success [108], and have also been shown to prolong block duration in animal models [34]. The incidence of needle nerve contact could possibly be higher with an out-of-plane (OOP) approach (64 % for femoral nerve block) [98] but whether or not this results in an increased incidence of intraneural injections is currently unknown. OOP approaches although have not been shown to increase the incidence of neurologic complications [3].

Irrespective of unintentional or targeted intraneural injections using either low current neurostimulation or US guidance, none of the trials reported long-term postoperative neurologic dysfunction related to PNB [62, 63, 78, 94, 97–100, 108]. However, the follow-up period in some of these studies was not long enough to allow symptoms to develop, and none of the studies were sufficiently powered to assess the incidence of neurologic dysfunction or nerve injury. Hence, it cannot be recommended as safe practice to perform deliberate intraneural injections until data from larger studies are available.

Five studies investigated deliberate intraneural injection [62, 97, 100, 108]. In each one, ultrasound was used to identify intraneural injection, and one study used nerve stimulation in addition to ultrasound [97]. A 10 % incidence of transient neurologic deficit was observed in one of

the studies [63], and another study evaluating the deliberate intraneural injections performed under ultrasound versus neurostimulation showed an increased success rate with US but resulted in a higher incidence of paresthesia [101]. None of the studies revealed any increase in neurologic complications during follow-up (1–4 weeks after the procedure). A cadaveric study of interscalene blocks reported a 50 % incidence of subepineural injection when the needle tip was placed adjacent to the brachial plexus trunks [117]. While the results of these studies do not imply that intraneural injection is a safe procedure, they do show that it is a fairly common occurrence and does not always lead to neurologic complications.

The take-home message is not to think that deliberate intraneural injections are safe to perform but to think that it is fairly common in clinical practice to note intraneural injections and it does not necessarily result in neurologic complications. The occurrence of neurologic complications may increase following intrafascicular (subperineural) injections but currently most of the evidence for this is based on animal studies and case reports.

Environmental Influences

The time-honored statement that "an ounce of prevention is worth a pound of cure" is essential when considering the ways to minimize adverse outcomes following intraneural injection. To help reduce or prevent the possibility of intraneural injection, an effective method of detecting and monitoring the presence and extent of intraneural injection is critical, as is the skill and willingness to use it in regional anesthesia practice.

Nerve Stimulation

When used at low currents, *nerve stimulation has low sensitivity but high specificity for detecting proximity of the needle tip to the target nerve* (*LOE 2b*; *Grade B*). *Nerve stimulation cannot differentiate between intraneural needle placement and needle–nerve contact* (*LOE 5*; *Grade D*). *Higher stimulating currents are required in diabetic patients for detecting intra- and extraneural needle placement* (*LOE 2b*; *Grade C*).

For electrical nerve stimulation, the minimal stimulating current intensity is proportional to the square root of the distance between the needle tip and the nerve, provided there is a constant magnitude of charge between the two points. In animal studies, a low stimulating current requirement (<0.2 mA) was originally shown to correlate with histological evidence of nerve injury in 50 % of the study animals, while current intensity >0.5 mA implied extraneural placement [52]. A similar study in humans employing noninsulated needles showed that the median (Range) stimulating current noted when a deliberate paresthesia is obtained was 0.17 (0.03–3.3 mA) [70]. This led to the popular practice of eliciting motor response at stimulating currents between 0.2 and 0.5 mA and deliberately withdrawing the needle when stimulation is obtained at currents <0.2 mA. A number of studies later showed the inaccuracies of neurostimulation both at low and high current stimulation. Even the studies which established the notion that an MSC of <0.2 mA was specific but not sensitive indicator of intraneural needle placement possibly had extraneural needle placements as evidenced by an extraneural injection in 50 % of injections in the animal study [52] and the wide range of MSC noted with the human study [70]. Animal studies have shown that higher stimulating currents are sometimes needed to elicit a motor response following intraneural needle placement [20, 24, 174]. The same phenomenon was observed in 16.7 % of patients receiving deliberate low-pressure intraneural injections during popliteal sciatic nerve block [97]. On the contrary, low stimulation currents have been employed for performing sciatic nerve block [83] and infraclavicular block [84] without evidence of nerve damage.

Recently, Weismann et al. [56] showed that a low stimulating current may indicate either needle–nerve contact or intraneural placement. Hence, a low stimulating current, if present, may only indicate that the needle tip is too close to or within the nerve, rather than differentiating between the two. The noncorrelation of needle tip location and nerve stimulation is due to a variety of factors influencing motor response following stimulation. The stimulating current is influenced by pulse width, interaction of the needle tip with the fascicles, and the degree to which a depolarization or hyperpolarization occurs as a result of the stimulating current [175–177]. Since the minimal stimulating current for each nerve is different [178], a single value cannot be extrapolated for all nerves.

Evidence regarding whether or not diabetic individuals require a higher stimulation threshold is evolving. In animal models of hyperglycemia, when a low stimulation threshold was used to guide the needle, all injections were intraneural, while none of the low current stimulation injections in normoglycemic animals had the same pattern of injectate dispersion [43]. A significant number of diabetic patients undergoing supraclavicular brachial plexus block required a higher stimulation threshold when the needle was placed perineurally (57 % required currents >1.0 mA vs. 9 % nondiabetic) or intraneurally (29 % required currents of 0.5–1.0 mA vs. 2 % nondiabetic) [63]. It has been reported and is worth pointing out that it also has been that the threshold currents used for motor response from nerve stimulation under general anesthesia might be higher than those in awake patients [146]. Thus, their result also suggested that using nerve stimulation as a technique to warn for intraneural placement in patients under general anesthesia may require different parameters compared with patients who are not under general anesthesia.

Injection Pressure Monitoring

High injection pressures are often reached unknowingly by experienced and nonexperienced practitioners (*LOE 2b*; *Grade B*). *Syringe feel is inaccurate for differentiating tissues*, *and higher pressures are generated unknowingly* (*LOE 5*; *Grade D*). *Injection pressure can be kept within safe limits reliably by using compressed air injection technique* (*CAIT*) *or pressure measurement devices* (*LOE 2b*; *Grade C*). *Opening pressure can detect needle nerve contact reliably in interscalene block* (*LOE 2b*; *Grade C*).

While intrafascicular injections require higher injection pressures, a low injection pressure has a good negative predictive value for neurologic dysfunction [21, 97]. Two important pressures to monitor when performing a PNB are the opening pressure (OP) and injection pressure (IP). The OP is the pressure in the needle–tubing–syringe assembly before the injectate begins to flow through the needle. A high OP (>20 psi) has been shown to correlate with nerve damage [75]. Once flow has begun, IP at the needle tip depends on various factors, including needle size, length of tubing, and syringe volume. Avoiding high IP is as important as OP in preventing further damage from injectate flow into the perineurium. Simple "syringe feel" is inaccurate in determining what tissues the performer is injecting into, irrespective of operator experience as shown in an animal model where only 12 of 40 anesthesiologists (30 %) correctly identified intraneural injection using "syringe feel" [107]. Anesthesiologists also vary widely in their perception of injection pressure and the speed of injection. In a study of 30 anesthesiologists performing simulated injections in a lab model, a 20-fold variability in baseline injection pressure and speed of injection was noted. When resistance was increased gradually in a blinded fashion during injection, 70 % of anesthesiologists exceeded the recommended injection pressure of 20 psi [109, 114].

The inaccuracy of "syringe feel" and a wide variability in baseline perception of the performer has led to the use of objective methods and devices to monitor injection pressure during PNB performance. These include the compressed air injection technique (CAIT) [109, 121] and B.Braun's BSmart™ injection pressure monitor. When using CAIT, a set volume of air is drawn into the syringe containing the injectate, and the air is compressed to a certain percentage of its initial volume when injecting. In vitro evaluation of this technique has been shown to ensure injection pressures substantially below the threshold considered significant for nerve injury, irrespective of the needle or syringe type when the air compression was ≤50 % of the original volume. Currently, no animal or clinical studies have evaluated the technique, so its impact on clinical outcomes is unknown. Recently, the use of the BSmart™ device in patients ($n = 16$) undergoing ultrasound-guided interscalene brachial plexus block consistently (97 %) revealed an opening pressure of ≥15 psi at the time of needle–nerve contact [75]. Nevertheless, the specificity of using injection pressure monitoring to avoid intraneural needle placement is still suspect. High injection pressures can be caused by contact with fascia, tendon, or bones. Moreover, needle tip pressure may be dependent on the needle–syringe combination [179].

Ultrasound

Ultrasound guidance can detect intraneural injection and is dependent on operator experience (*LOE 2*; *Grade B*). *Use of ultrasonography does not prevent intraneural injection* (*LOE 2*; *Grade B*). *Long-term neurologic complications following PNB have not declined as a result* (*LOE 2b*; *Grade B*).

Ultrasound can be a useful tool for avoiding and detecting intraneural needle placement and injection but is not foolproof in preventing intraneural injection. Currently available ultrasound technology cannot differentiate between the different layers of the nerve and therefore cannot distinguish between inter- and intrafascicular injection. Possible ultrasonographic indicators of intraneural injections include visualization of the needle tip within the nerve, increase in the nerve cross-sectional area by at least 15 %, spread of local anesthetic within the epineurium upon proximal-to-distal scanning, and real-time visualization of fascicle separation on injection. It is important to note that, if any of these signs is observed on ultrasound, intraneural injection has already occurred.

When performing PNB, the needle tip is often not visualized on ultrasound, and needle advancement without proper needle tip visualization is a common error that persists even after adequate experience. Surrogate markers, such as increase in cross-sectional surface area or local anesthetic solution found between the fascicles, are therefore used to monitor for intraneural injection. The occurrence of unintentional intraneural injections during ultrasound-guided PNB has been noted frequently in cadaveric studies [117] and the clinical setting [63, 78, 91, 98] and is most likely due to dependence on the practitioner's expertise in detecting intraneural needle placement or injection. In a study of assessment of intraneural injection by novices and experts, the sensitivity of detecting a low volume (0.5 mL) intraneural injection was 65 % in novices and 84 % in experts, but the specificity of assessment was 98 % irrespective of the level of expertise [86]. Although Bigeliesen et al. [63] showed that intraneural needle tip placement was detected reliably in only 69 % of cases, surrogate markers of intraneural injection (e.g., increase in cross-sectional area of nerve) can detect intraneural injections reliably (94 %) [93, 100]. Ruiz et al. [98] evaluated whether an in-plane (IP) approach to femoral nerve block was better than an out-of-plane (OOP) approach for avoiding needle–nerve contact and intraneural injection. Although they noted a higher incidence of intraneural injec-

tions with an OOP approach (64 % vs. 9 % IP), their definition of intraneural injection was the presence of local anesthetic below the nerve, rather than visualization of intraneural needle tip or injectate placement on ultrasound. This, combined with the lack of evidence from other types of PNBs, suggests that further study is needed to conclude with certainty that OOP approaches increase the chances of needle–nerve contact and intraneural injection.

Orebaugh et al. [4, 5] investigated whether the use of ultrasound has led to a decrease in neurologic complications. In both retrospective reviews, no differences in long-term neurologic complications were found between blocks performed under nerve stimulation or ultrasound guidance. Electromyography detected nerve injury following nerve stimulation-guided block in 3/3290 cases, but no long-term neurologic injuries were detected following ultrasound-guided blocks (0/2146). An update in 2012 showed the incidence of nerve injury lasting 6–12 months was significantly higher with nerve stimulation alone (4/5436) compared to ultrasound guidance (1/9069), but no significant difference in the incidence of long-term injuries (>1 year) was observed between the two groups (3/5436 nerve stimulation vs. 0/9069 ultrasound). This has also been supported by a prospective study by Liu et al. [92]. Although the underlying reason(s) for not seeing a reduction in complications despite the increasing use of ultrasound in regional anesthesia practice is unclear, it may explained in part by the old adage, "A tool is only as good as the person using it," which is highly applicable when it comes to using imaging technologies such as ultrasound.

Monitoring neurologic outcomes following regional anesthesia.

To monitor and manage patients effectively with possible peripheral nerve injury following regional anesthesia, it is important to have a basic understanding about classification and the pathophysiology of neurologic injuries.

Pathophysiology

The overall clinical course of pathophysiology of peripheral nerve injury usually takes 2–4 weeks to manifest and progress [180, 181] for most nerves. However, there is a primary histological change involving physical fragmentation of both axons and myelin, a process that begins within hours of injury (Wallerian degeneration) occurring at the axon distal to the site of injury [181]. For the portion of the nerve proximal to the injury, it also undergoes a retrograde degeneration. Eventually, the axons in the endoneurial network undergo chromatolysis and are replaced by Schwann cells. The process of recovery begins after 4–6 weeks, and the integrity of endoneurial network is crucial at this recovery phase and correlates with clinical recovery (see the section on practical aspects below). If the endoneurium is intact, the regenerating axons grow into them and are subsequently myelinized by the Schwann cells. If there is a disruption of endoneurial network, the regenerating axons grow aimlessly in all directions, resulting in a neuroma. The classification of nerve injury and its subsequent course is described in Table 5.7. For practical purposes, Sunderland's classification is used to classify and predict outcomes.

As presented in Table 5.7, nerve injury is not necessarily synonymous with clinical complications and at times may not lead to any detectable clinical symptoms or signs. In other words, the injury may lead to subclinical complications with no overt clinical manifestations. Individuals who present with neurologic symptoms and sequelae may therefore only represent the tip of the iceberg (Fig. 5.3). Thus, it is important to consider and interpret carefully the evidence regarding the incidence of clinical neurologic complications.

Practical Points in Mechanism of Nerve Injury

A neuronal injury is more likely to arise when a negative interaction between a susceptible host (inadequately protected nerve), an injurious agent (local anesthetic, needle, or injection pressure), and a hazardous working environment (poor supervision/guidance for locating needle, unsafe practices, unintended exposure) occurs. Risk stratification by minimizing one of the triangle's components should, in theory, preclude the manifestation of the event. Hence it is vital to choose a technique tailored to each patient's existing physiology (nonmodifiable risks) as delineated earlier. The clinician should attempt to minimize all modifiable risks

Table 5.7 Classification of nerve injury

Sunderland	Seddon	Description of injury	Recovery
First degree	Neuropraxia	Nerve is intact. Conduction block and demyelination noted	Complete recovery within days–weeks
Second degree	Axonotmesis	Wallerian degeneration noted from this stage onward. Nerve structure is intact but with axonal disruption	Recovery within weeks to months following axonal regeneration
Third degree	Axonotmesis	Disruption of endoneurium	Partial recovery may occur but not complete recovery
Fourth degree	Axonotmesis	Disruption of perineurium. Cell body loss from this stage onward	Permanent deficits. Recovery unlikely
Fifth degree	Neurotmesis	Disruption of epineurium	Permanent deficits. Recovery unlikely even with surgery

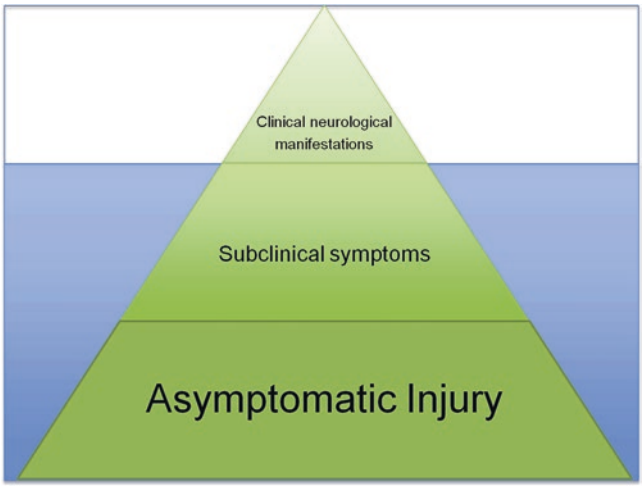

Fig. 5.3 Schematic diagram of relationship of injury and clinical symptoms

such as needle trauma, pressure injury, and LA neurotoxicity using appropriate monitoring techniques and safe practices. A clear understanding of the procedure by the patient and good communication between the clinician and the patient is vital to detect iatrogenic injury either during performance of the block or in the recovery period. Hence we recommend the following practice points which may help in early identification of neurologic outcomes:

- Preoperative assessment and documentation of neurologic function (Identify at-risk patient)
- Clear communication with the patient regarding the block procedures and postoperative recovery of sensory and motor function
- Minimal sedation during the performance of PNB to permit patient–clinician communication.
- Use of all available monitoring technique during the performance of PNB. We routinely use US + NS guidance (0.2 mA) for needle placement and employ CAIT for injection pressure monitoring.
- Close monitoring and adequate follow-up in the event of procedural paresthesia/signs of intraneural injection to ensure recovery of neurologic function
- Use dilute LA solutions in high risk patients (i.e., preexisting neuropathy and presence of surgical risk for compartment syndrome).
- Early neurology referral in those patients with red flags for iatrogenic nerve injury.

Classifying and managing patients with neurologic injury can be challenging given that a widely accepted algorithm is lacking for monitoring neurologic recovery following PNB. We present a simplified algorithmic approach for follow-up of peripheral nerve blocks (Fig. 5.4). Most common symptoms following neurologic injury are sensory changes such as persistent numbness, pain, or persistent paresthesia/dysesthesia in the distribution of the nerve block. The presence of motor weakness out of proportion to that from PNB or after the discontinuation of the block should prompt early referral after ruling out mechanical causes such as tight surgical dressing/tourniquet injury. Evolving sensory/motor lesions also mandate early referral since neurologic deficits arising within the first 24 postoperative hours likely represent acute injury. The routine practice in the majority of institutions includes a follow-up visit or phone call on POD-1 to ensure the resolution of block following discontinuation but, many of the sensory-motor disturbances arise several days to a couple of weeks following PNB and such cases need to be referred to neurology for evaluation if it does not resolve within 4–6 postoperative weeks. Neurologists commonly perform nerve conduction studies, evoked potentials, and electromyography which identifies the site of lesion and the timing of injury thereby helping in the diagnosis and prognosis of injury. These tests are invasive procedures and are not without limitations. Nerve conduction studies are useful in evaluating large sensory-motor nerve fibers while unmyelinated fibers may be missed. EMG requires several weeks of denervation before changes can be detected. Hence cases wherein an evolving/nonresolving lesion is suspected or motor weakness is present are referred to neurology and the majority of cases with mild sensory disturbances are managed conservatively with follow-up.

Conclusion

In summary, long term neurologic complications following regional anesthesia are rare and are usually a result of an interplay between the host (patient) factors, causative agents (mechanical and chemical), and environment (regional anesthesia tools and methods). Many of the factors responsible for the neurologic complications are nonmodifiable and hence screening for at-risk patients is necessary. Unintentional intraneural injections are thought to occur frequently during PNB and intraneural injections may not necessarily result in neurologic complications as long as they are extrafascicular. Most of the evidence for neurologic injury following PNB such as needle design, pressure monitoring, and local anesthetic neurotoxicity arises from animal models and their findings are being extrapolated to clinical practice. Evidence from animal experiments indicates that intrafascicular injections used with higher injection pressures are more likely to result in nerve injury. While technological improvements in regional anesthesia practice continue to improve our ability to detect and prevent nerve damage, preparation, vigilance, and careful observation remain a regional anesthesiologist's most important tools in ensuring patient safety.

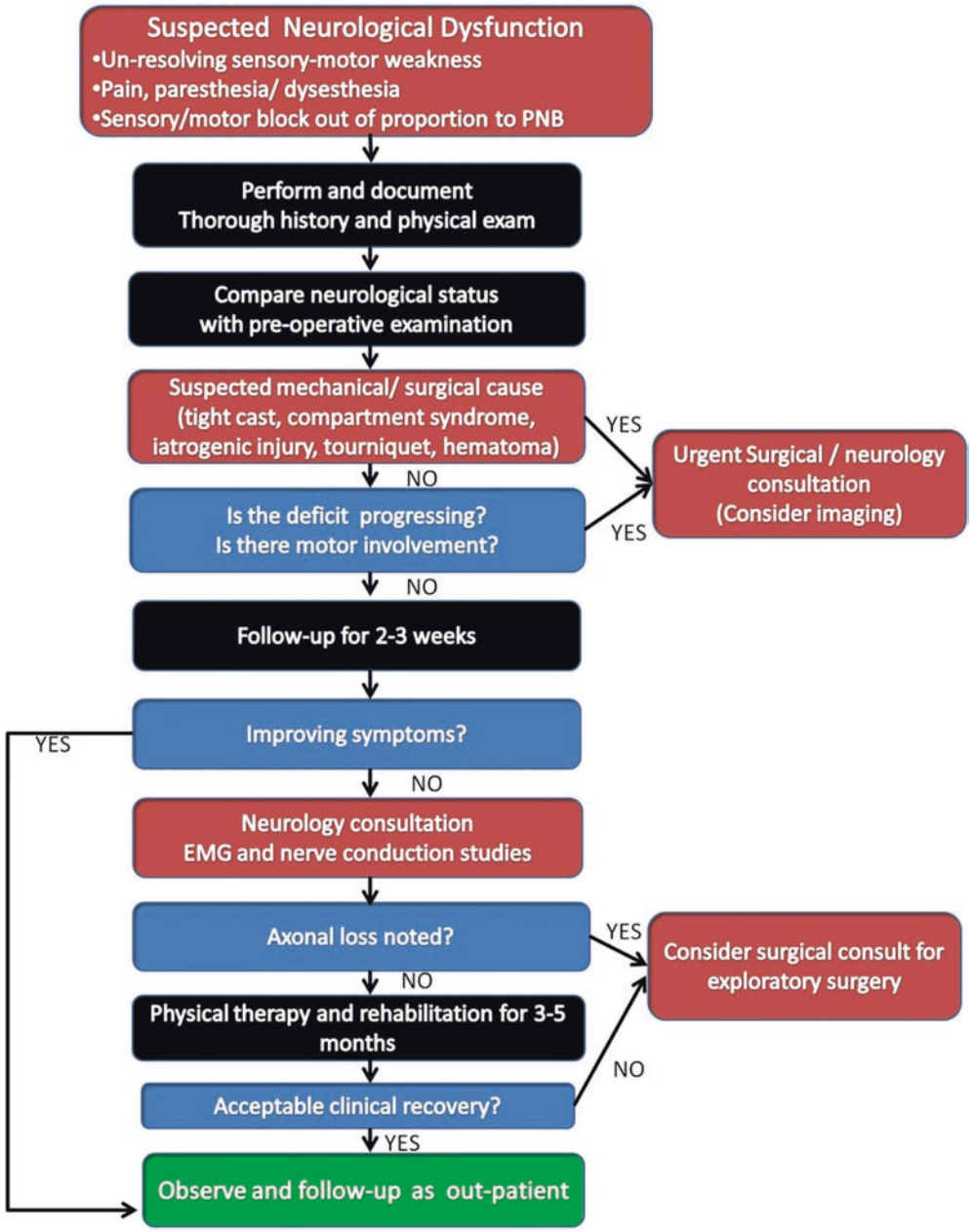

Fig. 5.4 Pathway to classify and manage neurological injury following peripheral nerve blocks

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Regional Anesthesia in the Presence of Neurologic Disease

6

John Shepler, Andrea Kattula, and George Arndt

Key Points

- Most anesthesiologists are very cautious about the use of regional anesthesia in patients with neurologic disease, mainly because of the medical legal risk. Lawyers seem to have more success linking the exacerbation of neurologic disease following regional anesthesia, than that following general. In truth we really do not have sufficient data to determine which technique is more likely to cause an exacerbation of neurologic disease. Therefore the choice of anesthetic technique should be based primarily on the preoperative assessment of the patient. As always, a thorough consideration of the risks and benefits should be performed for each patient.
- A number of reports describe successful regional anesthesia in individuals suffering from multiple sclerosis, including obstetric patients. However, practitioners should be aware of other cases in which exacerbation of symptoms or relapse has occurred following anesthesia administration.
- Regional anesthesia can be used for individuals with spinal cord injuries, but this can be challenging and may require use of adjunct technologies such as nerve stimulation or ultrasound. Similarly, regional blocks have been performed successfully in patients with peripheral neuropathy, but unique risks, such as hemodynamic instability in diabetic individuals, must be considered.
- A complete neurologic exam is required for all patients with preexisting neurologic disease regardless of the choice of anesthetic technique and this information must be carefully recorded in the patient's medical record.

J. Shepler, MD (✉) • G. Arndt, MD
Department of Anesthesia, University of Wisconsin Madison, Madison, WI, USA
e-mail: jashepler@wisc.edu; gaarndt@facstaff.wisc.edu

A. Kattula, MBBS, FANZCA
Department of Intensive Care, The Austin Hospital, Heidelberg, VIC, Australia

Department of Surgery, The Austin Hospital, Heidelberg, VIC, Australia

Introduction

Performing regional anesthesia in patients with preexisting neurologic or neuromuscular disease remains controversial and presents a special challenge to anesthesiologists. Historically, regional anesthesia has been relatively contraindicated in these patients for fear of worsening neurologic outcomes [1]. In addition, many practitioners may be reluctant to provide regional anesthesia to these patients due to medicolegal concerns. Factors contributing to this belief include local anesthetic toxicity to neurons, ischemia secondary to additives such as epinephrine, and injury to nerves from direct needle trauma. Upton and McComas described the "double crush" phenomenon which suggested that patients with nerve injury are more susceptible to nerve damage at another site [2]. Other studies appear to not only support the double crush phenomenon but suggest that the cumulative or dual injury to the nerve is greater than the expected additive damage that one might expect [3]. Thus, placing nerve blocks in patients with preexisting nerve injury may theoretically increase their risk of further injury. In addition, local anesthetic and additives in blocks may cause a subsequent injury to nerves based on their neurotoxic properties. In fact, studies evaluating the toxicity of local anesthetic and additives that have been conducted in animal models suggest that nerve injury is possible [4–6]. Therefore it may be prudent to minimize the dose or avoid local anesthetics in some patients.

Numerous studies or case reports describe the successful use of regional anesthetic techniques in a variety of neuromuscular disorders including multiple sclerosis, post-polio syndrome, amyotrophic lateral sclerosis (ALS), muscular dystrophies, myotonias, and others [7, 8]. These large studies

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_6

are retrospective in nature and provide some evidence of the safety of regional anesthetic techniques in such patients. However, prospective randomized studies are not likely to be conducted due to the relative infrequency of patients with these disorders presenting for surgery. Specific guidelines regarding the use of regional techniques in the setting of neurologic disease are difficult to define because of these limitations. Therefore, the goal of this chapter is to review several of the more common neurologic disorders that an anesthesiologist may encounter and outline what information currently exists to help guide the use of regional anesthesia. The use of a regional anesthetic technique along with careful use of local anesthetics in terms of concentration and dose should be made in all patients but especially in patients with preexisting neurologic disorders [9].

General Considerations

Evaluation of the patient with neuromuscular disease must consider not only the neuromuscular derangements, but also the secondary effects the disease may have had on other organ systems, particularly respiratory and cardiovascular. These secondary effects may have a significant impact on the administration and course of both general and regional anesthesia in these patients. In many cases, it may be advantageous to utilize a regional anesthetic technique. Evaluation and careful documentation of preexisting neurologic deficits is a vital part of the preoperative anesthesia workup for any patient with an underlying neurologic disorder. This is imperative whether regional or general anesthesia is planned. Changes in neurologic status are frequently seen in the perioperative period in these patients, and the documentation of preexisting deficits facilitates the interpretation of any changes seen postoperatively.

The patient with neuromuscular disease may be at risk for respiratory compromise in the perioperative period. In particular, impaired ventilatory reserve with reduced ability to respond to hypercapnia and hypoxia may result in an increased risk of respiratory failure [10, 11]. The site of surgical incision affects the risk of respiratory complications, with a higher incidence in patients undergoing upper abdominal and thoracic procedures. The method of perioperative analgesia may have a significant influence on this risk of respiratory compromise, providing the anesthesiologist with an opportunity to positively influence the patient's course.

In addition to hypoventilation, dysfunction of the pharyngeal muscles and the potential of aspiration add to the possibility of pneumonia postoperatively. Maintenance of an awake patient using a regional technique can only aid in the prevention of aspiration. In contrast, an endotracheal tube can be protective at the expense of further loss of muscle tone of both the respiratory and pharyngeal muscles. Finally, patients with severe neurologic disorders may have a component of restrictive lung disease which places them at higher risk for pulmonary complications during mechanical ventilation [12]. Preoperative assessment of respiratory function is an essential component of the preoperative evaluation.

Similarly, the cardiovascular effects of neuromuscular disorders must also be considered in the preoperative evaluation. Autonomic dysfunction occurs with many neurologic disorders and constitutes the major contributor to complications related to this organ system. ALS, Guillain–Barré syndrome, multiple sclerosis, and spinal cord lesions above the level of T6 can all have alteration of the autonomic nervous system. Several findings in the preoperative evaluation may guide the clinician to an increased suspicion for the presence of autonomic dysfunction. The absence of beat-to-beat heart rate variability with deep breathing is one of the most sensitive signs of autonomic dysfunction. Additional characteristic signs include resting tachycardia, orthostatic hypotension, cardiac dysrhythmias, and impotence. Because of the presence of autonomic dysfunction, these patients are at risk for cardiac conduction abnormalities and wide fluctuations in blood pressure. Required avoidance of oral intake makes the presence of relative hypovolemia common. A sympathectomy from neuraxial blockade, but potentially a variable amount from narcotics and inhalational anesthetics as well, can result in exaggerated hypotension in this setting. Finally, unexpected intraoperative cardiorespiratory arrests have been reported in patients with autonomic dysfunction which is second in frequency only to respiratory failure [8, 9].

Myocardial dysfunction and arrhythmias caused by changes in the cardiac muscle and conduction pathways are associated with numerous myopathic diseases including the muscular dystrophies, Guillain–Barré syndrome, and polio. A high index of suspicion must be maintained in the preoperative evaluation of these patients, as exercise tolerance is likely to be very limited by underlying neuromuscular disease.

Regional Anesthesia and Multiple Sclerosis

Multiple sclerosis is an acquired central nervous system disease characterized by multiple sites of demyelination primarily in the brain and spinal cord. Multiple sclerosis was once thought to spare the peripheral nervous system; however, emerging evidence suggests that peripheral neuropathy can result as well [13, 14]. Demyelination of axons results in a slowing of sensory and motor conduction which leads to widely variable clinical signs and symptoms specific to the sites of demyelination. MS typically begins in early adulthood and affects women more than men. It has a variable prognosis and up to 50 % of patients may require assistance

with ambulation within 15 years of diagnosis [15]. Symptoms most commonly include fatigue, visual disturbances, gait disturbances and incoordination, numbness and tingling, weakness, depression, and bowel/bladder incontinence [16].

The diagnosis of multiple sclerosis is made on clinical criteria with support from laboratory data such as cerebral spinal fluid analysis showing oligoclonal bands and repeated magnetic resonance images with findings of multifocal lesions of differing ages. Supportive information may be gained from evoked potential studies with visual, brainstem, and somatosensory potentials revealing slowed conduction [15].

The clinical course of multiple sclerosis is variable in nature and can include several forms with different phenotypes. The two main types of MS include relapsing-remitting disease or progressive disease. Eventually residual symptoms begin to persist between relapses. Extreme variability is seen among individuals, and the waxing and waning course makes it difficult to evaluate the effects of therapeutic interventions. Treatment with corticosteroids is often used to treat relapses. Other treatments include Interferon β, glatiramer acetate, immune globulin, mitoxantrone hydrochloride and plasma exchange but these may not change the long-term course of the disease.

The exacerbating factors of stress, fatigue, changes in temperature, and infection are associated with the perioperative period for more than one reason [17]. Delineating the natural course of the disease from the exacerbations due to surgery and anesthesia can be difficult. The purported effects of anesthesia on the course of multiple sclerosis continue to be controversial. However, it is the one neurologic disease that has the most information about the effects of regional anesthesia particularly in the obstetric population. Because of a continuing lack, or perceived lack of evidence, there is reluctance to utilize a regional technique in patients with multiple sclerosis, especially when considering epidural or spinal anesthesia.

Many of the studies and case reports available involve obstetric patients with multiple sclerosis, which constitutes a subset of patients likely to be considered for regional anesthesia. The natural history of multiple sclerosis in pregnancy is characterized by remission during gestation [18, 19] because of a presumed immunomodulatory protective effect [20]. This is also seen in other parturients with other autoimmune disorders such as rheumatoid arthritis. In fact, patients who have had a full-term pregnancy have a tendency toward an increased time interval to sustained disability. Patients are likely to have more multiple sclerosis relapses in the first 3 months postpartum regardless of whether they received an epidural [20].

Neuraxial, and in particular spinal, anesthesia has been implicated as a potential [21] cause of exacerbations in these patients even though contradictory retrospective studies and case reports exist [22, 23]. Theories to explain any exacerbation of multiple sclerosis symptoms by spinal anesthesia, focus on the potential for an increased susceptibility of demyelinated areas of nerves to the neurotoxic effects of local anesthetics [22]. The three to four times higher concentration of local anesthetic reaching the spinal cord white matter with subarachnoid as opposed to epidural anesthesia could explain the higher risk of exacerbation posed by this modality [24]. Schapira [24] demonstrated that diagnostic lumbar puncture alone did not appear to induce relapses in patients with multiple sclerosis, lending support to the theory that any effects of spinal anesthesia on multiple sclerosis are related to local anesthetic neurotoxicity. In addition, intrathecal morphine has also been used successfully without exacerbation anecdotally in patients with multiple sclerosis.

Bader et al. [22] performed a retrospective and partially prospective review of all obstetric multiple sclerosis patients at the Brigham and Women's Hospital between 1982 and 1987 and noted no significant difference in exacerbation rates between patients receiving epidural anesthesia and local infiltration for vaginal delivery. The total number of pregnancies in patients with multiple sclerosis in this study was 32. However, all of the women who did experience a relapse within 3 months postpartum had received epidural anesthesia with a concentration of bupivacaine greater than 0.25 %. This was a total of three patients. The authors proposed that the use of higher bupivacaine concentrations over a longer period of time (i.e., labor epidurals) may affect the rate of postpartum multiple sclerosis relapse, particularly if multiple local anesthetic boluses are required. Warren et al. [25] also reported minor exacerbations in a patient following two separate epidurals (years apart) for vaginal delivery although a relatively large total dose of bupivacaine was used on the second occasion only. Of note, although these incidents suggest that local anesthetics may potentially produce neurologic symptoms in demyelinated areas of patients with multiple sclerosis, these effects have not been permanent and generally gradual recovery over time is the rule [26].

Despite these concerns, there are many reports of successful use of epidural anesthesia in multiple sclerosis patients without evidence of relapse. Capdeville and Hoyt [27] performed a retrospective review of all obstetric patients with multiple sclerosis admitted to University Hospitals of Cleveland from 1986 to 1993. Over this 7-year period, eight women with multiple sclerosis underwent eight vaginal deliveries, one cesarean delivery, and five obstetric-related procedures. The anesthetic techniques used were five epidurals, two general anesthetics, one pudendal block, and one narcotic technique. Only two exacerbations of multiple sclerosis were noted by chart review. One of these occurred after a general anesthetic, and the other was noted in a patient receiving a pudendal block. No exacerbations were seen in patients receiving epidural anesthesia. Confavreux et al.

evaluated 254 women with MS and 256 pregnancies in 12 European countries [28]. They confirmed that the rate of relapse during pregnancy is reduced and found a relapse rate of 1.2 per woman per year in the first 3 months postpartum. They found that epidural anesthesia had no adverse effect on the rate of relapse. In a 2-year postpartum analysis of this study, this was also confirmed that epidural anesthesia did not have an effect on the relapse rate. The authors though state that the study was not designed to assess this risk specifically [29].

Crawford et al. [23] documented only one perioperative relapse in 50 non-obstetric and seven obstetric patients with multiple sclerosis receiving lumbar epidural anesthesia. In another series involving urologic surgery 14 spinal anesthetics were utilized with only one case of transient worsening of symptoms similar to patients receiving general anesthesia [30]. Again, the numbers are too small to lead to generalized recommendations but do indicate anecdotal success without complication involving the use of neuraxial anesthesia in patients with multiple sclerosis.

A significant concern in patients with multiple sclerosis is the presence of autonomic dysfunction and the potential for chronic hypovolemia in these patients, especially when considering employing a neuraxial technique. Episodes of marked hypotension with epidural and spinal anesthesia in MS patients with a reduced response to intravenous fluids and vasopressor therapy have been reported [31]. Racosta et al. performed a meta-analysis on cardiovascular autonomic dysfunction in MS looking at 16 studies with 611 patients and concluded that there was a wide variation in diagnosis and that using one abnormal autonomic test compared to at least two dropped the diagnosis rate from 42.1 to 18.8 % [32]. They also concluded that consensus is needed to define autonomic dysfunction in this patient group [33]. Regardless of the criteria used, autonomic dysfunction is present in many MS patients and meticulous preoperative evaluation needs to be completed when considering a regional technique.

The use of regional anesthesia in patients with multiple sclerosis can be safely conducted but can be controversial with some techniques particular with spinal anesthesia. Multiple case reports support its successful use, particularly in obstetric patients. Other case reports suggest a risk of perioperative symptom exacerbation and hemodynamic instability. If regional anesthesia is considered, the risk and benefits must be fully discussed with the patient. Special note during these discussions must be made of the potential for exacerbations of multiple sclerosis related to stress and temperature changes associated with the perioperative period regardless of the anesthetic technique used. In addition, parturients have a particular issue with increased incidence of multiple sclerosis relapse early in their postpartum period regardless of epidural use.

Regional Anesthesia and Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a degenerative disease of the upper and lower motor neurons involving the brainstem and multiple spinal cord regions. There are multiple phenotypes such as bulbar presenting with speech and swallowing difficulties, limb-onset with combination of upper motor neuron (UMN) and lower motor neuron (LMN) signs in the limbs, primary lateral sclerosis with only UMN involvement, and progressive muscular atrophy with only LMN involvement [34, 35]. The etiology remains unclear, and the disease affects males more than women with lifetime risk for men of 1:350 and for women of 1:400 with peak age of onset of 58–63 for sporadic disease and 47–52 for familial disease [35].

The clinical features of ALS involve progressive muscular atrophy with weakness and fasciculations of skeletal muscles. Bulbar muscle weakness often predominates with an associated risk of aspiration. A characteristic emotional lability and frontal lobe type cognitive dysfunction is seen [34, 35]. Autonomic nervous system dysfunction is common with the associated risk of exaggerated hemodynamic responses during anesthesia. Death from myocardial or respiratory failure ensues, often within 6 years of the onset of symptoms.

Epidural anesthesia has been successfully used in patients with ALS. Kochi et al. reported three cases in which lumbar epidural anesthesia was used, emphasizing the advantage of avoiding tracheal intubations [36]. Combined spinal epidural has also been successfully used for femur fracture in a woman with ALS and significant respiratory compromise due to ALS. Sertoz and Karaman utilized a lumbar plexus and a sciatic block in this patient with ALS and a collum femoris fracture in order to avoid general anesthesia [37]. Finally, a report of paravertebral block for breast surgery was reported by Agnoletti et al. [38]. Regional techniques can be advantageous in this patient population as any duration of mechanical ventilation could accelerate the loss of muscle tone, and weaning from the ventilator could be quite a challenge. However, a high epidural or spinal block as well as epidural spread from a PVB can affect muscle function with detrimental effects in patients with severe restrictive lung disease and minimal ventilatory reserve.

Regional Anesthesia and Spinal Cord Injuries

Spinal cord injury has classically been divided into two distinct stages. Initial injury is classified as spinal shock which consists of a 1- to 3-week period of flaccid paralysis including loss of sensation temperature regulation, and spinal cord

reflexes below the level of injury [39]. Hypotension, bradycardia, and changes in the electrocardiogram (premature ventricular contractions, nonspecific ST-T wave changes) are characteristic. Regional anesthesia is not frequently used during this stage of spinal shock because of the evolving neurologic injury. There is also a risk of hemodynamic instability as well as hypothermia.

The chronic stage of spinal cord injury is characterized by skeletal muscle spasticity and the return of spinal and autonomic reflexes below the level of injury. Autonomic hyperreflexia is seen in approximately 85 % of patients with lesions at or above T6. In this setting, a reflex response may be produced by a cutaneous (incision) or visceral (bladder distension, uterine contraction) stimulus below the level of injury. This afferent stimulus activates preganglionic sympathetic nerves, resulting in severe hypertension because of intense vasoconstriction below the level of the lesion. Under normal conditions, this response is modulated by inhibitory impulses from higher central nervous system centers. With a spinal cord lesion, this inhibitory input is lost and the vasoconstriction proceeds unimpeded. The resulting hypertension stimulates the carotid sinus baroreceptors, leading to reflex bradycardia and vasodilation above the level of injury [39].

Prevention and early treatment of autonomic hyperreflexia is critical. Both general and regional anesthesia have been used effectively. Broecker et al. noted that spinal and epidural anesthesia were logical choices to prevent autonomic hyperreflexia because the afferent limb of the reflex would be blocked [40]. Spinal anesthesia has been shown to be particularly useful [41], but epidural blocks are less reliable [40]. Parturients at risk for autonomic hyperreflexia from uterine contractions are likely to benefit from the early use of continuous lumbar epidural analgesia after the onset of labor [42]. In addition to its prophylactic use, regional anesthesia has been used therapeutically in patients with autonomic hyperreflexia [42].

Concerns often raised regarding the use of spinal anesthetics in this group of patients with spinal cord injury include potential difficulty in placement, difficulty in control or examination of block level, difficulty in evaluating for complications, and a potential increased risk of hypotension [43]. Lambert et al. performed a retrospective review of 78 procedures in 50 spinal cord-injured patients considered "at risk" for autonomic hyperreflexia [41]. No significant differences were seen in intraoperative blood pressure between those receiving spinal or general anesthesia. Both techniques seemed to protect equally against intraoperative hypertension. Several other studies describe successful use of neuraxial anesthesia for treatment or prevention of autonomic hyperreflexia.

Peripheral regional techniques can be utilized in patients with spinal cord injuries but present unique challenges as well. Interscalene or supraclavicular blocks can result in temporary phrenic nerve paralysis and can worsen respiratory function in patients that have compromised respiratory dynamics. Placement of peripheral blocks should utilize ultrasound technique as nerve stimulation may be altered in these patients in addition to potential altered anatomy.

Regional Anesthesia and Post-polio Syndrome

In 1952–1954 at the peak of the polio crisis in the United States approximately 40,000 cases of polio per year were reported in the United States with an incidence of approximately 15/100,000. It mostly affected children and young adults. Following the introduction of the Salk vaccination in 1955 the incidence of polio decreased dramatically and by 1963 the incidence was 0.04/100,000 [44]. The last natural virus confirmed infection in the United States resulting in paralysis was in 1979. Although eradicated in the United States, there are still many countries where polio cases continue to be reported. The Centers for Disease Control, the World Health Organization, and the Bill and Melinda Gates foundation are working toward worldwide eradication in the last few polio-infected countries including Afghanistan, Cameroon, Equatorial Guinea, Ethiopia, Iraq, Nigeria, Pakistan, and the Syrian Arab Republic. In March 2014, India along with ten other countries in the South East Asian Region was certified as polio-free [45]. Approximately 12–20 million people worldwide and 640,000 in the United States have sequelae of poliomyelitis thus it remains one of the most prevalent neuromuscular diseases in the United States [44, 46].

Post-polio syndrome (PPS) is characterized by new onset of weakness that occurs in polio survivors many years after their initial illness. The weakness can occur in previously affected muscles but also in muscles thought to be uninvolved in the initial illness. The first description appeared in 1875. It wasn't until 1984 when the first international conference of PPS was held that clarified the nature, pathogenesis, and treatment of PPS [44]. While it appears that PPS is more common in individuals who suffered more severe paralysis, studies have shown that up to 64 % of polio survivors may develop new symptoms [47].

The pathophysiology of PPS is complex but it is believed to involve an ongoing denervation-reinnervation process. After much time the reinnervation process is no longer possible. Several hypotheses have been proposed including stress and overuse, aging, persistent virus, and immunologic and genetic factors [46]. Symptoms of PPS most commonly appear 30–50 years after the initial infection. Other symptoms associated with PPS include fatigue, joint pain, muscle pain, cold intolerance, and breathing and swallowing difficulties [44].

There are few case reports of regional anesthesia in patients with post-polio syndrome. Higashizawa et al. reported a successful spinal anesthetic with tetracaine in a 70 year-old man with hemiparesis from post-polio syndrome undergoing transurethral resection of the prostate [48]. There was no progression of neurologic deficits following surgery. In a retrospective study, Hebl et al. reviewed medical records of 79 patients with post-polio syndrome that received a spinal, epidural, or combined spinal epidural with primarily bupivacaine [8]. Not one patient in this study suffered from new or worsening postoperative neurologic symptoms. Regional anesthesia can be performed on individuals with post-polio syndrome; however, detailed discussion with the patient concerning the risks and benefits should be conducted and documented in the patient's chart.

Regional Anesthesia and Peripheral Neuropathies

Peripheral neuropathies result from either the disruption of axons with distal degeneration or segmental demyelination caused by Schwann cell degeneration. They classically start distally and spread proximally resulting in a "glove and stocking" distribution of decreased sensation, weakness, and reduced reflexes. Some, such as diabetic and alcoholic neuropathy, can be associated with tender muscles. The etiologies of peripheral neuropathies are considerable, including metabolic disorders (diabetes mellitus, renal failure, hepatic failure, porphyria, and nutritional deficiencies), connective tissue disorders, infection, toxins, malignancy, endocrine disorders, and Guillain–Barré syndrome. Diagnosis depends on metabolic screening tests, serology, infection, and autoimmune evaluations. Electromyogram studies reveal evidence of denervation and a reduction in nerve conduction velocity.

Diabetic peripheral and autonomic neuropathies are encountered frequently in patients presenting for anesthesia and surgery. Clinically, the peripheral neuropathy predominantly affects the lower extremities with paresthesias, weakness, and sensory loss more distally. Occasionally, the neuropathy of diabetes may present as a mononeuropathy causing transient pain and weakness in an isolated nerve distribution. The associated autonomic neuropathy may be significant, with anesthetic implications related to an increased risk of intraoperative hemodynamic instability.

The use of regional anesthesia in patients with preexisting peripheral neuropathies depends on a thorough analysis of the risks and benefits for each individual patient. The diabetic patient with a propensity toward perioperative cardiovascular complications might benefit from a regional, particularly spinal, technique that allows the patient to be more awake or lightly sedated. Another purported advantage of epidural or spinal anesthesia in diabetic patients relates to an improved ability to maintain blood glucose control with the inhibition of the surgical stress response [34]. Certainly, some patients may have exaggerated hypotension with respect to their preexisting autonomic neuropathy. This must be weighed against other risks and benefits that would affect the patient. Furthermore, large doses of local anesthetics have been associated with myocardial depression in diabetic patients [49].

Regional Anesthesia and Guillain–Barré Syndrome

Guillain–Barré syndrome is an acute inflammatory demyelinating disease of the peripheral nervous system with an incidence of approximately 1:100,000 persons per year [50]. There are several subtypes that involve T cell interactions against myelin proteins as well as antibodies to gangliosides on the axolemma. Although there are many suspected etiologies such as recent vaccinations, history of surgery, and recent respiratory infection, approximately 25 % of the cases are in individuals with recent Campylobacter jejuni infection [51]. Patients present with the acute onset of lower motor neuron paralysis including flaccid paralysis and reduced reflexes. It begins in the lower extremities and progresses cephalad over hours to days [52]. Bulbar dysfunction and intercostals muscle weakness may ensue, with resultant respiratory failure and the patient's inability to protect their airway. Painful distal extremity paresthesias are common. Autonomic dysfunction occurs in a significant number of patients [53], which results in hemodynamic instability, tachycardia, and cardiac conduction disturbances. Ninety percent of patients will have the most progressive symptoms within 2 weeks. Persistent disability occurs in approximately 20 % of these patients [51].

The treatment of Guillain–Barré is either intravenous immunoglobulins or plasma exchange which are considered to be equally efficacious. Steroids are not beneficial [51]. Some patients may require endotracheal intubation and mechanical ventilation secondary to the respiratory weakness and bulbar dysfunction. Management of hemodynamic variability associated with autonomic dysfunction can be very challenging. Guillain–Barré usually resolves spontaneously over weeks to months, but approximately 20 % of patients will have residual neurologic deficits. The mortality rate is estimated at approximately 4 % within a year of diagnosis [54].

Regional anesthesia has been used successfully in patients with Guillain–Barré syndrome. In particular, epidural anesthesia has been used in parturients with Guillain–Barré without adverse effects [55]. These patients had some residual effects from an episode of Guillain–Barré in the past, but did

not have an acute episode of the disease. Epidural narcotics have been used without complication in the acute phase of the disease in an attempt to control painful paresthesias [56, 57]. Although the case reports are infrequent, this is another example that narcotics have not been shown to cause toxicity administered neuraxially in patients with neurologic disease [58]—even in the setting of acute demyelination. However, no patients received local anesthetics in the acute phase of Guillain–Barré. When considering regional techniques, patients can have exaggerated responses to indirect vasopressors because of their autonomic dysfunction.

Regional Anesthesia and Myotonic Dystrophy

Myotonic dystrophy is the most common of the myotonic disorders and includes two subtypes, type 1 and type 2 [59]. The disorders are characterized by persistent contraction and delayed relaxation following muscle stimulation which is unrelieved by denervation or paralysis [60]. Both types of myotonic dystrophy are inherited as an autosomal dominant with symptoms becoming chronically evident in the second or third decade [61]. Type 1 has multiple subtypes including adult onset, childhood onset, and congenital. Type 2 is adult onset but typically presents later than adult onset type 1. In general, there is progressive deterioration of skeletal, cardiac, and smooth muscle function. Initially, involvement of the intrinsic hand and facial muscles progresses to proximal limb musculature as well as bulbar dysfunction with weakness of pharyngeal and laryngeal muscles. Diaphragmatic involvement is common. Cardiomyopathy is common as well. The cardiac conduction system is particularly affected with a significant risk of dysrhythmias and atrioventricular block primarily in type 1 patients [62, 63]. Bulbar dysfunction and delayed gastric emptying place these patients at high risk for pulmonary aspiration. Associated endocrine disorders also occur, including diabetes mellitus, adrenal, and thyroid dysfunction. Ultimately, death occurs as a result of dysrhythmias, respiratory, or cardiac failure. Treatment is mostly supportive, but can involve the use of quinine or procainamide for myotonic symptoms [63]. Type 1 patients have a decreased life expectancy while type 2 patients have a normal life expectancy.

When patients with myotonic dystrophy present for anesthesia, the preoperative evaluation of pulmonary function is critical. Pulmonary function tests usually reveal a restrictive deficit with mild arterial hypoxemia on a blood gas. A preoperative measurement of baseline negative inspiratory force may be a useful guide to perioperative management. A baseline electrocardiogram should be obtained to assess for cardiac conduction abnormalities. Any underlying respiratory infection should be treated.

General anesthesia presents unique problems in the patient with myotonic dystrophy. Succinylcholine may result in exaggerated contraction of muscles resulting in more difficulty with the placement of an endotracheal tube as well as ventilation. The use of neostigmine to reverse neuromuscular blockade may precipitate myotonic contractions. These patients, especially type 1, tend to be extremely sensitive to the respiratory depressant effects of sedatives, opioids, and general anesthetics [64]. An underlying component of central sleep apnea is often present, which further complicates airway management and necessitates added caution in the use of sedatives.

The use of regional anesthesia in patients with myotonic dystrophy is attractive because of the avoidance of neuromuscular blocking agents and their reversal drugs. In addition, the use of sedatives and other anesthetics that may produce respiratory depression can be minimized. Regional anesthetics can present a different set of concerns. Myotonic contractions are not relieved by spinal or epidural anesthesia—only direct infiltration of an affected muscle with local anesthetic will relieve myotonia. In patients with marginal ventilatory reserve, the effect of high epidural or spinal blockade on intercostals muscle function must be considered, especially because many of these patients may have diaphragmatic dysfunction. When performing regional anesthesia, additional sedatives and anxiolytics should be used with caution. Respiratory status should be continuously assessed for signs of hypoventilation or apnea.

Pregnant patients with myotonic dystrophy may require anesthesia for labor and delivery. General, spinal, and epidural anesthetics have been used successfully in these patients for caesarean delivery [65, 66]. However, myotonia and weakness may be exacerbated during pregnancy. Patients with myotonic dystrophy are at increased risk for caesarean delivery because of prolonged labor, as well as postpartum hemorrhage from uterine smooth muscle dysfunction [65, 66]. Others have reported successful regional anesthesia using epidural and caudal approaches in patients with myotonic dystrophy type 1. A case series of 35 patients with type 2 myotonic dystrophy found no anesthetic complications with general and in two cases regional anesthesia [67].

Cold is a well-known trigger for myotonic contractions. Therefore, no matter what technique is used, normothermia is required throughout the perioperative period [68]. This is particularly important if spinal anesthesia is provided due to potential risk of increased heat loss due to vasodilation [69].

Regional Anesthesia and Myasthenia Gravis

Myasthenia gravis is an autoimmune disorder affecting the neuromuscular junction with a decrease in the number of acetylcholine receptors and the presence of antireceptor anti-

bodies in 70–90 % of patients [70]. Skeletal muscle weakness is characteristically worsened by activity. Although smooth and cardiac muscle are uninvolved, myocarditis and dysrhythmias may be present [71]. Treatment modalities include cholinesterase inhibitors, corticosteroids, immunosuppressants, plasmapheresis, and thymectomy. Progressive weakness may be associated with progression of the disease (myasthenic crisis) or may reflect excessive muscarinic effects of anticholinesterase drugs (cholinergic crisis). Evaluation of the patient's response to the administration of edrophonium allows differentiation between the two phenomena.

The major anesthetic consideration in myasthenia gravis relates to the use of neuromuscular blockers with affected patients displaying extreme sensitivity to nondepolarizing blockers is unpredictable. Preexisting skeletal muscle weakness, which is present in varying degrees in these patients, may be potentiated by the relaxant effects of volatile anesthetic agents. Finally, ester local anesthetics may display a prolonged elimination of half-life because of reduced plasma cholinesterase activity in patients treated with anticholinesterases [68], suggesting that amide local anesthetics may be preferable when high or repeated doses are anticipated.

Patients with myasthenia gravis need preoperative assessment of both pulmonary function and aspiration risk because of bulbar dysfunction. Patients with preexisting respiratory compromise are predisposed to significant respiratory depression from anesthetic agents. Therefore, sedatives should be used with caution.

Patients should be monitored closely throughout the perioperative period for myasthenic or cholinergic crisis as well as for gradual deterioration in respiratory function precipitated by stress, infection, missed or excessive anticholinesterase doses, electrolyte abnormalities, or aminoglycoside antibiotics. Identifying patients at particular risk for perioperative compromise and the need for postoperative ventilation was delineated by Leventhal et al. [72] as the following:

1. A history of myasthenia gravis for more than 6 years.
2. A history of unrelated chronic obstructive airway disease.
3. A pyridostigmine dose greater than 750 mg/day during the 48 h immediately preoperative.
4. A vital capacity of less than 2.9 L.

Regional anesthesia has been used successfully in patients with myasthenia gravis. It is the preferred analgesic technique in laboring parturients with the disease who are planning a vaginal delivery [73]. The use of regional anesthesia may reduce respiratory risk by avoiding the depressant effects of opioids as well as inhaled agents and neuromuscular blockers. Careful consideration should be made when considering brachial plexus blocks utilizing interscalene or supraclavicular blocks as some of these patients may not tolerate phrenic nerve paralysis. In addition, postoperative analgesia and chest physical therapy can also be managed better with neuraxial analgesia. Once again, there is the potential risk of intercostal blockade resulting in respiratory compromise. As is also present in some of the preceding disease states, the combination of bulbar dysfunction with respiratory compromise makes securing the airway with an endotracheal tube somewhat advantageous to avoid potential aspiration.

Conclusion

Regional anesthesia has been used successfully in many patients with neurologic disease. Controlled clinical studies with regional anesthesia in these patients are still lacking; however, there is an increasing number of anecdotal reports indicating the safety of utilizing regional anesthesia in these patients. Despite these reports, many anesthesiologists are still apprehensive due to the medicolegal issues. There are distinct benefits in avoiding the side effects of neuromuscular blockers, general anesthetics, and opioids. The whole patient should be evaluated and examined before any type of anesthetic to document disease progression and effects on other organ systems. An informed decision should be made by the patient and clinician and this should be carefully documented in the patient's chart. A regional technique should probably be avoided in the setting of an acute inflammation of the nerves. If a regional technique is used, lower concentrations of local anesthetics should be considered. Neuraxial narcotics with careful attention to dosing and postoperative monitoring may be a safe alternative.

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Evaluation of Neurologic Injury Following Regional Anesthesia

7

Quinn Hogan, Keith McCollister, Matthew Harmelink, Laura Kohl, and Michael Collins

Key Points

- Neurologic injury associated with regional blockade is rare but does occur. Upon suspicion or discovery of a neurologic injury following a nerve block, factors including preexisting conditions, surgical or anesthetic events, and development/course of the injury should be investigated.
- Physical examination of neurologic, cognitive, motor, sensory, and reflex function, as well as electrodiagnostic studies, can yield clues as to the source and site of nerve injury following regional anesthesia.
- Examination of nerve conduction can help evaluate the degree of the injury but can be limited by factors including accessibility and size of the nerve, technical difficulties of electrode placement and response measurement, nature of the injury, and presence of preexisting neuronal damage.
- Electromyography (EMG) can help determine the location and type of neuronal injury, be it neuropraxia, axonotmesis, or neurotmesis, and prognosis for nerve regeneration or reinnervation. The value of EMG findings is dependent on the skill of the examiner.
- Imaging technologies, including conventional radiography, computed tomography, magnetic resonance imaging, magnetic resonance neurography, angiography, and ultrasonography, can be used to identify and evaluate neurologic injury.

Q. Hogan, MD (✉)
Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI, USA
e-mail: qhogan@mcw.edu

K. McCollister, MD
Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, USA

X-Ray Consultants, Inc., South Bend, IN, USA
e-mail: kbmccollister@gmail.com

M. Harmelink, MD
Division of Pediatric Neurology, Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA
e-mail: mharmelink@mcw.edu

L. Kohl, MD
Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, USA

Madison Radiologists SC, Madison, WI, USA
e-mail: Lkohl5711@gmail.com

M. Collins, MD
Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA
e-mail: mcollins@mcw.edu

Introduction

Modern anesthesia is a highly predictable undertaking with a very low failure rate. The ability to produce successful anesthesia is a less important characteristic of excellent anesthetic practice than the ability to recognize and treat adverse perioperative events. Recognition of mycardial ischemia and prompt treatment of catastrophic bleeding are examples of situations requiring careful diagnosis and calm, decisive action. This same approach should prevail when the adverse event is a neurologic complication of regional anesthesia, only there is an added difficulty. At few other times in the practice of anesthesia will a practitioner be so directly confronted with responsibility for an adverse outcome as with a complication from neural blockade since, in a sense, the "smoking gun" is clearly in our hands. Additional opprobrium may stem from the common misconceptions that complication rates should be zero in the practice of anesthesiology, and that the complication would not have occurred if only a general anesthetic had been performed or the supplemental pain block hadn't been provided.

The goal for this chapter is to provide a framework for evaluation of neurologic injury during regional anesthesia. Because other chapters address the details of various types of injury, diagnosis of specific complications will not be the focus here. Rather, the means of diagnosis are discussed in

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_7

sequence, specifically: gathering of pertinent history; physical examination, especially of the neurologic system; clinical neurophysiologic analysis, including nerve conduction study and electromyography; and radiologic imaging. Only rarely are other methods used to determine the presence or cause of neurologic injury, such as surgical exploration, or biopsy. Occasionally, blood tests may be necessary, including blood cell count (to identify leukocytosis from infection), glucose (to test for diabetes mellitus), erythrocyte sedimentation rate (indicative of infection such as Lyme disease or connective tissue disease, if elevated), and blood serology (syphilis, human immunodeficiency virus).

Knowledge of the patient's baseline neurologic status before anesthesia is a key element that is often missing and impossible to recover at the time of evaluation of a neurologic injury. A missing reflex or an anesthetic patch of skin, for instance, has ominous implications only if they are absent before neural blockade. It is therefore valuable to do a brief neurologic examination focused on the area of blockade before performing regional anesthesia.

History

Identifying the Complication

The initial step in diagnosis of neural injury is identification and delineation of neural dysfunction. This is often vexing in the context of regional anesthesia because temporary nerve blockade is the desired goal of uncomplicated regional anesthesia. Therefore, a distinction must be made between unexpectedly prolonged effects of local anesthetic and a pathologic event.

The duration of local anesthetic effect is often confusingly specified without consideration of the site of blockade. Whereas lidocaine may produce only an hour of anesthesia in the subarachnoid space, peripheral neural blockade can be expected to last much longer, particularly if high volumes are administered and epinephrine is coinjected. Another source of confusion comes from the definition used in published sources for anesthetic duration. Whereas the duration of predictable surgical anesthesia after a peripheral nerve block may be specified as perhaps 3 h for 0.5 % bupivacaine, a residual component of block may persist for more than 8 h. The duration of neuraxial blockade is usually specified as the time before the upper limit of skin analgesia recedes two dermatomal segments. Sensory changes may be expected to persist for a much greater time at sites close to the level of spinal or epidural injection. In these cases, continued anesthetic effect may mistakenly be interpreted as neural injury.

Certain features of neural change may suggest injury rather than anesthetic effect. Resolving anesthesia should show a pattern of steady regression of block, so any irregularity in this expected pattern and rate of recovery should prompt concern for a complication of the procedure [1]. Any new or intensifying neural dysfunction in the absence of further anesthetic injection must be considered to represent neural injury. Sensory or motor defects produced by neural injury are usually patchy rather than uniform in distribution because of uneven damage among the components of a plexus or nerve roots. Mechanical damage by catheter or needle is typically restricted to a single nerve root or peripheral nerve.

Preexisting Conditions

If neural damage is suspected, information obtained preoperatively about the patient's baseline neurologic status should be supplemented by a thorough postoperative inquiry. Reactivation of reflex sympathetic dystrophy and herpetic neuralgia are examples of conditions that may be revealed by thorough questioning. Spinal stenosis, which is a risk factor for neurologic sequelae after epidural anesthesia [2], may be discerned by a history of neurogenic claudication. Conditions that might undergo exacerbation in the postsurgical setting include polyneuropathies, peripheral nerve entrapments, radiculopathies, myopathies, or relapsing-remitting disorders, such as multiple sclerosis, myasthenia gravis, and various autoimmune nerve and muscle diseases.

History should also focus on symptoms and past events suggestive of a preexisting neuromuscular disease even in the absence of such a diagnosis. Previously undiagnosed acquired or hereditary neuromuscular disorders might have produced symptoms in the past that are similar to the new condition. Patients should be questioned about remote, episodic, or ongoing numbness, tingling, weakness, neuropathic pain, muscle cramps, and muscle fasciculations. Inquiries into prior changes in gait, tripping, falling, and in coordination (e.g., impaired ability to button shirt or tie shoes) provide insight into the possibility of previous motor abnormalities. Risk factors for premorbid subclinical neuropathies should also be identified, including but not limited to diabetes mellitus, chronic kidney disease, cancers, alcohol abuse, systemic autoimmune-inflammatory conditions, and medications with known peripheral neurotoxicity.

Surgical Events

Discussion with the surgeon regarding possible etiologies for a new neural deficit is imperative in order to ascertain the presence or absence of intraoperative events (surgical or local anesthetic) that might have caused new neurological symptoms. Nerve injury in the wound may not have been mentioned to the anesthetist, or long-acting local anesthetic

Table 7.1 Examples of surgical and obstetric entrapments

Procedure or positioning	Nerve(s) compressed	Symptoms
Arthroscopic surgery of the elbow [3]	Posterior interosseous nerve	Wrist drop
Abduction, dorsal extension, and external rotation of the arm [4]	Brachial plexus	Variable
Elbow abduction to 90*with a sagging armboard [4]	Brachial plexus	Variable
Trendelenburg positioning with shoulder braces [4]	Brachial plexus	Variable
Open heart surgery [5]	Lower brachial plexus	Ulnar nerve distribution numbness and weakness with finger extensor weakness
Arm abduction without elbow pad [4]	Ulnar	Numbness in digits III–V, weakness in ulnar innervated muscles
Lithotomy [6]	Peroneal nerve	Foot drop
Lithotomy [6]	Femoral nerve	Quadriceps weakness, loss of patellar reflex
Semilateral position [4]	Sciatic	Peroneal and tibial innervated nerves as well as hamstring muscles

may have been injected by the surgeon. Compression by dressings or casts may compromise neural function, as may a compartment syndrome from edema or bleeding around the wound. Vascular injury during the operation could result in neurologic complications, most dramatically with spinal cord injury after thoracic aneurysm repair. Because of this, it is probably desirable to let the local anesthetic blockade abate after aortic surgery and before continuous postoperative blockade to allow confirmation of normal intact neurologic function. Neuraxial opioid analgesia can be continued during this period of observation.

Positioning of the patient should be reviewed because direct pressure (e.g., peroneal nerve at the fibular head) or tension on nerves (e.g., traction on the brachial plexus from hyperextension of the shoulder during thoracotomy) may produce nerve injury that might otherwise be attributed to a regional anesthetic mishap. Table 7.1 contains examples of focal neuropathies that can develop during and after surgical and obstetric procedures.

Anesthetic Events

The details of anesthetic management should be thoroughly reviewed, especially if portions of the anesthetic care were delivered by other anesthetists. Drug choice, dose, and last time of administration are of obvious importance. Long duration of blockade and high concentration of agents probably increases the risk of neural complications. The development of hypotension or hypertension should be identified, since these can be a source of CNS injury. Examples include (1) malignant hypertension-induced posterior reversible encephalopathy syndrome [7], the lesions of which are typically occipital but can occur elsewhere in the brain; (2) hypotension-induced spinal cord infarct, especially in the setting of thoracoabdominal aortic interventions [8]; and (3) hypotension-associated cerebral watershed stroke leading to a "Man in the Barrel Syndrome" characterized by bilateral arm weakness or paralysis with intact leg function [9].

Blood return through the needle at the time of performing the blockade, although sometimes intended, indicates the possibility of hematoma as mechanism of neural compromise. Undesired entry into the subarachnoid space may be evident only after doses suitable for epidural anesthesia have been injected, increasing the risk of local anesthetic toxicity. Attempted aspiration of cerebrospinal fluid (CSF) before each epidural injection should be a standard maneuver. Observation of a gradual development and expected sequence of blockade and hemodynamic changes offer some reassurance that the proper site of drug deposition has been achieved. Conversely, maldistribution will not only lead to possible toxic results but also fail to produce desired anesthetic effects. Examples include accumulation of hyperbaric subarachnoid lidocaine in the terminal dural sac or injection through a catheter intended for the epidural space but placed in or adjacent to a spinal nerve in the intervertebral foramen.

The presence of paresthesia or pain during needle placement may herald mechanical injury or injection within a nerve fascicle, increasing the likelihood of mechanical or chemical injury to individual nerve fibers. Because sedation or general anesthesia precludes the observation of pain and paresthesias, the exact timing of needle placement and injections relative to systemic medication may be critical, and the depth of sedation or presence of general anesthesia at the time of neural blockade should be noted. Injection into the spinal cord is unlikely to take place in a patient who is awake and can report the accompanying intense sensory event. However, injection into the cord, or even into a peripheral nerve with longitudinal passage of solution into the cord [10], may go unrecognized in an unresponsive patient, resulting in catastrophic myelopathy. Sudden hypotension may accompany the cord injury. Such events are most likely to occur

during thoracic epidural injections or subarachnoid injections in obese patients in whom the surface landmarks mistakenly lead to high lumbar needle placement.

Development of Neurologic Dysfunction

The sequence and timing of the onset of symptoms related to the nerve injury should be determined to provide clues to the etiology and best treatment. The onset of pain, weakness, sensory deficit, and changes in sphincter control may be obtained from the patient, although sedation in the early postoperative period may compromise recollection of the details. Nurses are important sources of information, as are family members if the patient has already been discharged home. The ideal is frequent and complete postoperative visits by the anesthetist.

Physical Examination

General Examination

The general examination may yield clues to the etiology of a suspected postanesthetic nerve injury. For example, a local hematoma or ecchymosis will draw attention to the possibility of a focal compressive or traumatic nerve injury. Even in the absence of such superficial signs, focal nerve compression by a deeper limb or spinal hematoma should be considered if other manifestations of a coagulopathy are identified (e.g., bleeding at multiple sites). The presence of distal vascular insufficiency raises concern for a monomelic ischemic neuropathy. Abnormal function of the gastrointestinal or urologic system is a "red flag" for possible spinal cord injury or cauda equina syndrome. A postprocedural abscess should be excluded in the setting of fever or local erythema, tenderness, induration, fluctuance, or gross purulence. The presence of a fever, especially in the absence of another obvious source, should raise the question of a deep infection such as in the epidural space, although fevers are often absent. Tenderness and spasm of the muscles may result from bleeding, infection, or neural injury. A distended bladder may indicate a dysfunctional sphincter.

Neurologic Examination

A detailed evaluation is essential for identifying signs of dysfunction, monitoring for progression, and tracking recovery from regional anesthesia. In patients who have seen a neurologist in the past for an established diagnosis or evaluation of neurologic complaints, the previous neurologic examination should be employed as baseline against which the current examination is compared to objectively differentiate new from old findings. The neurologic examination should encompass all of its usual subcomponents, including cranial nerves and mental status, as abnormalities in these realms will redirect attention away from the site of regional anesthesia to more cephalad areas of the CNS. Additionally, examination of the muscles, skin, and hair in the extremities can help to determine if the patient has had a previous neurologic injury in the acutely symptomatic region. Muscle atrophy, cutaneous atrophy, loss of hair, anhidrosis, hyperhidrosis, scarring, or ulcers in a distribution similar to the current complaints may signify the presence of a preexisting, chronic neurogenic process. In patients with unilateral symptoms, examination of the contralateral side of the body should be done and may provide additional clues to the location and extent of injury.

When evaluating a potential neurologic injury, diagnosis and treatment hinge on first localizing the lesion in the neurologic system. The process of localization commences with the differentiation between central (brain and spinal cord) and peripheral (peripheral nerves, muscles, and neuromuscular junctions) lesions. In the acute setting, both central and peripheral injuries tend to suppress stretch reflexes. Moreover, such lower motor neuron signs as muscle atrophy and fasciculations are generally delayed in appearance. Hence, shortly after the procedure and the onset of new neurological deficits, careful mapping of the patterns of motor and sensory abnormalities, combined with the presence versus absence of Babinski signs, is critical to the central versus peripheral differentiation. Once this distinction is made, further attention to the precise nature and distribution of the motor and sensory deficits permits the region of injury to be localized to specific areas of the central nervous system (CNS), nerve roots, nerve plexuses, peripheral nerves, and/or muscles. After the site of injury is determined, a refined etiologic differential diagnosis can be designed and investigated with focused diagnostic testing. (With the advent of the smart phone, localization can now be aided by applications that provide a provisional localization based on input data comprising regions of affected versus intact strengths.) [11].

Mental Status/Cranial Nerves

Abnormal mentation (e.g., confusion or aphasia) or cranial nerves should prompt concern for an intracranial rather than peripheral process. Postoperative altered mental status has a broad differential diagnosis but most commonly results from metabolic, toxic, and systemic infectious causes. When focal neurologic deficits are accompanied by altered mentation, a cerebrovascular event is more likely than a peripheral regional injury. However, two (or more) processes may be concurrent.

Motor Examination

To evaluate any neurologic complaint, manual muscle testing should be performed. In manual muscle testing, the primary action of the tested muscle is identified and its action isolated, with the understanding that confounding by other muscles with similar actions is inevitable. As such, grading of strengths should be assigned to the action (e.g., elbow flexors) rather than the muscle (e.g., biceps brachii). Once the active joint and muscle are isolated, the joint is stabilized and the patient is instructed to perform a maximal isometric contraction against the examiner's resistance. Strength is then graded on a standard 0–5 scale originally defined by the United Kingdom's Medical Research Council (MRC) as shown in Table 7.2. While other scales exist, this is the most commonly used method of grading muscle strengths [12]. For regional injuries that appear to involve a single extremity, it is important to test not only ipsilateral but also contralateral muscles. The sensitivity of individual muscle strength assignments is enhanced by interside comparisons. Moreover, a bilateral examination may reveal unexpected deficits in the "unaffected" side, thereby altering the neurological localization.

In patients who complain of weakness despite intact manual muscle testing, other examination techniques may detect more subtle weakness. Examples include assessment of fine finger movements, such as those required with repetitive tapping or buttoning tasks, observation for a pronator drift of one arm with both upper arms forward flexed and eyes closed, and rolling of the forearms around each other (also known as "disco dancing"). Of note, asymmetries in arm rolling and rapid finger tapping amplitude and rate can ensue not only from subtle weakness but also handedness, bradykinesia, or ataxia. Moreover, findings in these tasks are more difficult to localize than those revealed in manual muscle testing because multiple muscles contribute to these complex movements.

Once the distribution of motor deficits has been determined by muscle strength testing, the resulting pattern should be analyzed for lesion localization. If true injury has occurred, the pattern of weakness should conform to an upper motor neuron, spinal nerve root, plexus, or peripheral nerve process. Typical motor deficits observed in patients with cervical or lumbosacral nerve root injuries are itemized in Table 7.3.

Table 7.2 UK medical research council manual muscle grading scale

Grade	Exam finding
5	Unable to overcome a patient's antigravity positioning with an examiner's muscle of similar strength
4+	Able to overcome with much effort a patient's antigravity positioning with an examiner's muscle of similar strength
4	Able to overcome with moderate effort a patient's antigravity positioning with an examiner's muscle of similar strength
4–	Able to overcome with minimal effort a patient's antigravity positioning with an examiner's muscle of similar strength
3	Patient has full range of motion against gravity but cannot exert any power against the examiner
2	Full range of motion when gravity eliminated (action of muscle must be observed in plane perpendicular to gravity)
1	Contraction of muscle felt or seen without movement of joint
0	No movement of muscle

Table 7.3 Clinical findings in nerve root lesions

Root	Sensory loss	Reflex arc	Motor deficits
C5	Lateral shoulder	Biceps	Shoulder abduction/external rotation, elbow flexion
C6	Lateral forearm, thumb	Biceps, brachioradialis	Supination, elbow flexion, pronation, wrist extension
C7	Dorsal arm and forearm, middle finger	Triceps	Elbow extension, wrist flexion/extension
C8	Medial hand, small finger	Finger flexors	Finger extension, abduction, and flexion
T1	Anteromedial forearm	–	Thumb abduction
L2–3	Anterolateral thigh (L2), distal medial thigh/knee (L3)	Adductor, patellar	Hip flexion/adduction
L4	Anteromedial lower leg	Patellar	Knee extension/adduction, hip flexion
L5	Lateral lower leg, dorsal foot, great toe	Medial hamstrings	Ankle dorsiflexion, eversion, and inversion; great toe extension; hip abduction
S1	Posterior thigh and lower leg, lateral foot, sole	Achilles	Ankle plantar flexion, hip extension

Sensory Examination

The sensory examination involves evaluation of multiple sensory modalities (pain, cold, heat, light touch, vibration, and proprioception), but not all modalities need to be tested in every patient. Testing of nociception with a truly sharp object (i.e., pin) and light touch with a finger or cotton wisp should be routinely performed. Similarly sized small myelinated and unmyelinated fiber types convey both temperature and pain sensation to the CNS. Within the spinal cord, primary afferents subserving pain and temperature cross over at their level of entry into the spine and then jointly ascend in the contralateral spinothalamic tract. Therefore, evaluation of cold and hot sensation need not be undertaken in every patient already evaluated for pain sensation, but thermal sensation testing may help to confirm a region of abnormal sensation suggested by the pinprick examination.

Vibration and proprioception sensation should also be examined. Unlike pain and temperature, these sensory modalities are carried by larger myelinated fibers, which ascend ipsilaterally (no cross-over) in the posterior part of the spinal cord (posterior columns). Loss of dorsal column function may lead to an abnormal "sensory ataxic" gait, as the patient loses their ability to sense the placement of their lower extremities in space. Spinal cord infarcts are usually caused by occlusion of the anterior spinal artery, which supplies the spinothalamic tracts but not the dorsal columns. Hence, vibration and proprioception are usually spared in ischemic spinal cord injuries.

In all modalities, testing should not only be distal but also delineate possible peripheral nerve, brachial or lumbosacral plexus, nerve root, and spinal sensory tract lesions. Key dermatomes (areas of sensory loss resulting from nerve root lesions) are detailed in Table 7.3.

Reflexes

Muscle stretch reflexes should be tested in all extremities in all patients. Normal reflexes range from 1+ (hypoactive) to 2+ (normal) to 3+ (brisk) depending on age, level of consciousness, medications, and past medical history. Reflexes are abnormal if they are asymmetric, absent ("0"), clonic ("4+"), or incongruent with reflexes in other extremities. Crossed adductor reflexes are also abnormal after a few months of age. Localization can be assisted by understanding the pathway of a reflex arc. Table 7.3 includes commonly tested reflexes and the nerve roots through which they are mediated.

Coordination/Gait

Coordination is dependent not only on CNS control but also intact peripheral motor and sensory function. Patients with peripheral weakness or large fiber sensory loss can be as clumsy and "ataxic" as those with cerebellar pathway lesions. Similarly, tremors are centrally generated but modified by peripheral sensorimotor function. As another confounding factor, objective weakness of the extremities can produce "tremulous," impersistent movements mimicking tremors and cerebellar or sensory ataxia. Retesting with the involved joint isolated from gravity (e.g., testing finger–nose–finger with the elbow supported) sometimes clarifies the source of the impairment. If the ataxia and tremor then resolve, the impersistent, clumsy movements are probably due to weakness rather than an intracranial process.

In patients with complaints of leg weakness or disturbed ambulation, evaluation of gait is mandatory. The patient should be observed walking down a long hallway. Gait is assessed with respect to multiple parameters including rate, fluidity, stability, symmetry, step height, stride length, base, arm swing, truncal posture, and extraneous movements. There are characteristic features of abnormal gait due to peripheral weakness (e.g., foot drop leading to steppage), sensory ataxia, cerebellar ataxia, spasticity, Parkinsonism, truncal weakness, hyperkinetic movement disorders, and higher level cerebral dysfunction that are beyond the scope of this chapter [13]. Toe and heel walking may reveal mild posterior and anterior distal leg weakness occult to manual muscle testing. Finally, an ataxic or Parkinsonian gait may be misconstrued by some patients and providers as resulting from leg weakness.

Electrodiagnostic Evaluation

Injuries to peripheral nerves are routinely evaluated by electrodiagnostic studies that comprise electromyography (EMG) and nerve conduction studies (NCS). These investigations assess the electrophysiological function of the larger diameter motor and sensory fibers, which is generally sufficient for regional anesthesia-related nerve injuries, almost all of which involve larger nerves to a greater or lesser extent. For evaluation of those rare anesthesia-induced injuries restricted to small cutaneous nerve fibers alone, autonomic nervous system studies such as the quantitative sudomotor axon reflex test (QSART) and thermoregulatory sweat test (TST) can be performed [14].

The goals of electrodiagnostic testing in the setting of a regional anesthesia-related nerve injury are to (1) confirm the

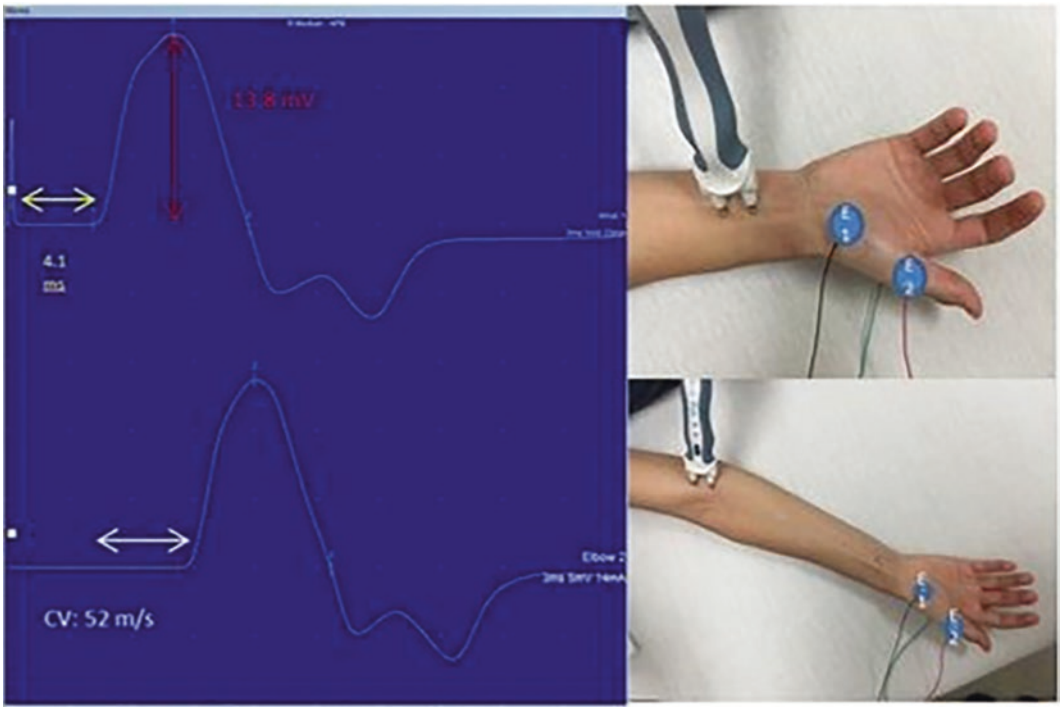

Fig. 7.1 Median nerve motor conductions. The CMAPs are on the *left* with placements of the distal stimulator (above *right*) and proximal (below *right*) shown. The *yellow arrow* highlights the onset latency, the *white arrow* highlights the conduction velocity (CV), and the *red* highlights the amplitude. E1 is the recording electrode and E2 is the reference electrode. The ground electrode is not visible on the posterior hand

presence of a neurogenic lesion; (2) anatomically localize the lesion; (3) characterize the lesion with respect to attributes of diagnostic and prognostic significance, such as the primarily axonal versus demyelinating nature of the injury; and (4) monitor the evolution and progression of the lesion, with the understanding that some NCS and EMG markers of nerve injury are delayed in onset. Specific pathogenic processes tend to exhibit preferential types of injury. For example, chronic nerve compression usually produces demyelination/remyelination whereas direct trauma (e.g., intrafascicular injections), most neurotoxic drugs, and ischemic insults cause predominantly axonal damage. Autoimmune inflammatory nerve diseases can be either axonal or demyelinating depending on the target of the immune attack.

Nerve Conductions

Motor Conductions

Motor nerve conductions are performed by stimulating a motor nerve at two separate locations along its course and recording from a surface electrode placed over the belly of a muscle supplied by that nerve. The amplitude of the evoked compound muscle action potential (CMAP), distal latency (time from the distal stimulation to the onset of the corresponding motor response), and conduction velocity between the two stimulation sites are then calculated (Fig. 7.1). Based on comparisons to normative data, these values are then used to determine if the motor NCS is normal or shows evidence of a demyelinating or axonal lesion. As a general rule, motor NCS in axonal neuropathies (with intact myelination) exhibit reduced CMAP amplitudes with preserved conduction velocities and distal latencies, whereas demyelinating neuropathies feature slow nerve conductions, prolonged distal latencies, and normal or relatively normal CMAP amplitudes. Focal demyelination can also block conduction in some (partial) or all (complete) axons at the affected site despite the presence of structurally preserved axons. Similar to axon loss, motor conduction block produces clinical weakness. In a motor NCS performed on a nerve affected by a partial demyelinative conduction block, the CMAP evoked by stimulation above the site of block has significantly smaller amplitude than that evoked by stimulation below the block (Fig. 7.2). If the block is complete, no CMAP is evoked with proximal stimulation. A partial motor conduction block is the hallmark of an acquired demyelinating neuropathy.

Late Responses

A suprathreshold motor nerve stimulation evokes both an orthodromically (proximal to distal) and antidromically (distal to proximal) conducted neural impulse. The routine motor

NCS depends on the orthodromic response. The antidromic impulse depolarizes the anterior horn cells of the constituent motor axons. If one or more of these cells is depolarized to or above its threshold, a recurrent discharge is generated that travels back down the nerve orthodromically resulting in "late" reactivation of the muscle, the F-wave response. In a single stimulation, only a small subset of motor neurons generates an F-wave. With multiple stimulations, consecutive F-waves are usually generated by different motor neurons, resulting in F-waves of varying latency and morphology (Fig. 7.3). If, on the other hand, the large Ia afferent sensory fibers are preferentially activated, typically by a lower intensity, longer duration stimulus, the evoked antidromically conducted impulse will synapse with and depolarize a pool of anterior horn cells in the spinal cord. These monosynaptic connections result in reflex activation of an orthodromically conducted motor impulse, which is recorded from the innervated muscle as the H-reflex. Unlike an F-wave, the latency of an H-reflex does not vary between stimulations, but its amplitude increases with progressively higher stimulus intensities until reaching a maximum. Then, with still higher stimulus intensities, the H-reflex decreases in amplitude and eventually disappears (Fig. 7.4). Whereas F-waves can be generated from all motor nerves and recorded from all muscles, H-reflexes are only consistently recorded from the soleus muscle after stimulation of the tibial nerve and more inconsistently recorded from the flexor carpi radialis muscle after stimulation of the median nerve.

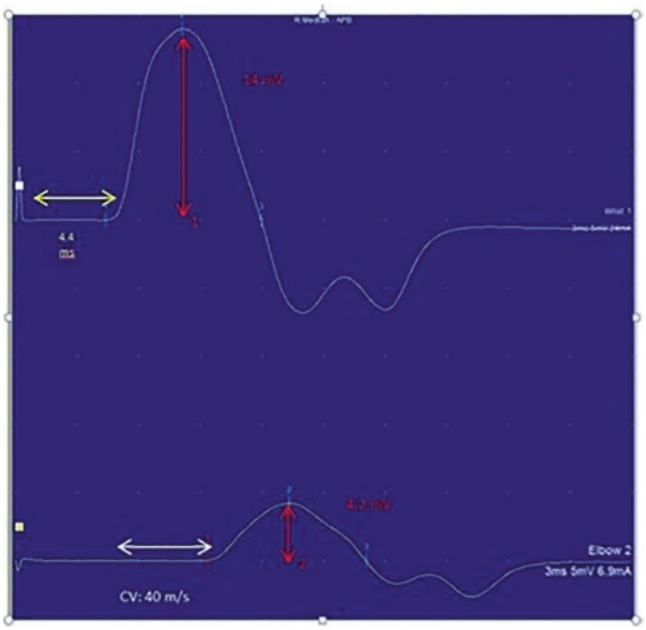

Fig. 7.2 Conduction block of the median nerve. In this patient, there is demyelination between the distal and proximal stimulation sites resulting in a drop in amplitude and conduction velocity. The superior waveform is the distal recording and inferior recording is from a proximal site. The *yellow arrow* highlights the onset latency, the *white arrow* highlights the conduction velocity (CV), and the *red* highlights the amplitude. Please note the differences between amplitude 1 (distal stimulation) and amplitude 2 (proximal stimulation)

Clinically, F-waves and H-reflexes are used to evaluate the proximal portions of peripheral nerves not amenable to standard motor NCS. Whereas, prolonged F-wave and H-reflex latencies generally occur in demyelinating lesions, absent F-waves and H-reflexes can result from both axonal and severe demyelinating insults. F-waves that "repeat," i.e., recur with the same latency and waveform morphology sug-

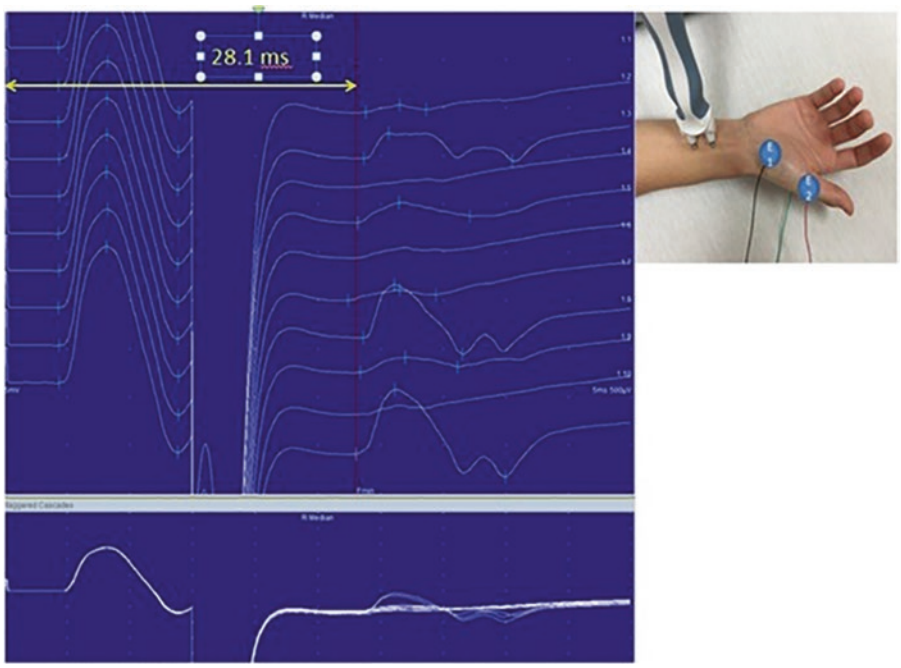

Fig. 7.3 F-Waves. The F-waves are located to the right of the *red line*. Please note the variable morphologies and latencies of these waveforms which indicate different motor neurons involved in each stimulation. The most common parameter measured is the minimum F-wave latency (*yellow line*)

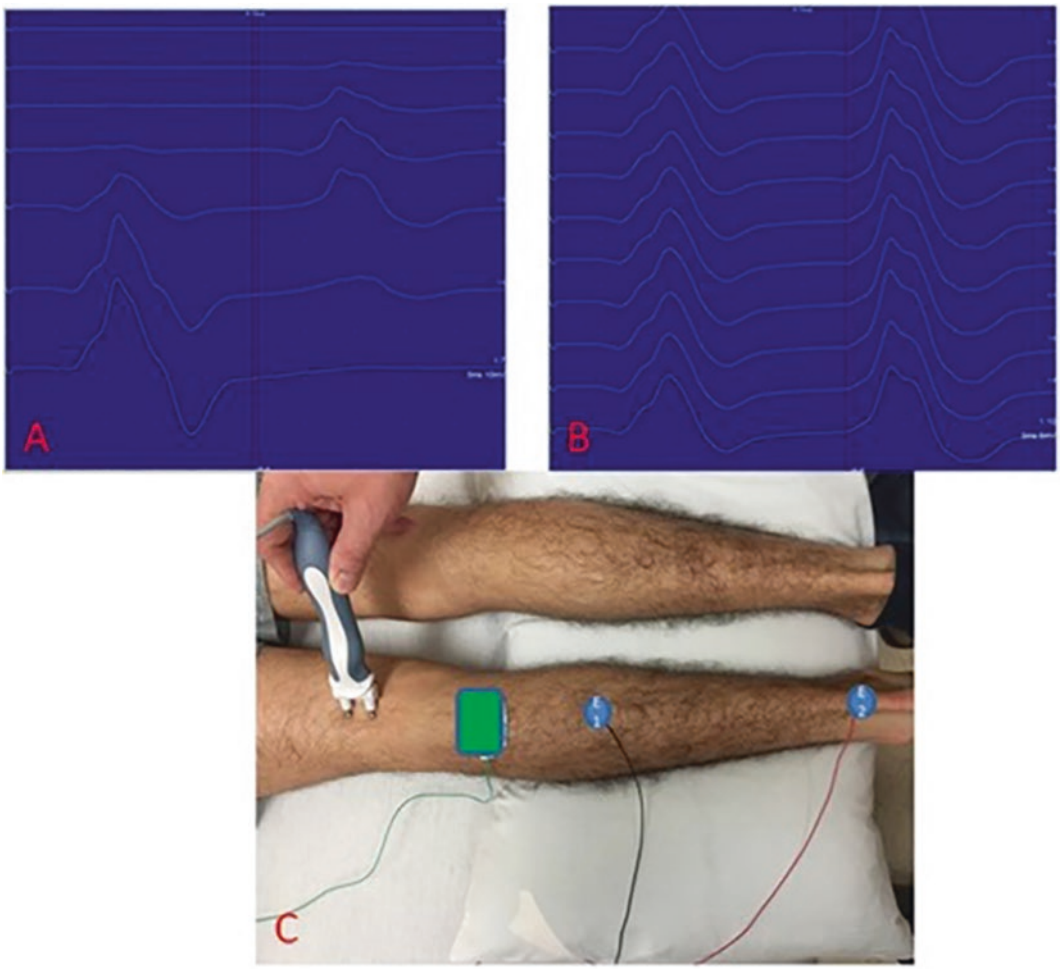

Fig. 7.4 Tibial H-reflex. The H-reflex is seen to the right of the *red line* in (**a**, **b**); the CMAP is to the left. From *top to bottom*, (**a**) shows sequential increasing levels of stimulation; the H-reflex gradually increases in amplitude and then decreases in amplitude as stimulation increases. (**b**) Shows a series of reflexes at unchanged levels of stimulus intensity; notice the uniform morphology and latency morphology (different from F-waves). (**c**) Shows montage with stimulator, ground (*green*), recording electrode (E1) and reference electrode (E2)

gest a dropout of the original number of anterior horn cells or their motor axons. Focal or multifocal demyelinating lesions frequently produce variable effects on different nerve fibers in the same motor nerve, resulting in an increased spectrum of conduction velocities within individual motor fibers and hence an increased range of F-wave latencies.

Sensory Conductions

A sensory nerve conduction study is performed by stimulating a sensory nerve at one or more sites along its course and recording from a surface electrode placed over the same nerve distal or proximal to the stimulation site. Sensory conductions can be performed either antidromically or orthodromically. The evoked sensory nerve action potential (SNAP) is then evaluated with respect to amplitude, onset latency (time from stimulus to onset of the evoked potential), peak latency (time from stimulus to peak amplitude of the evoked potential), and conduction velocity (Fig. 7.5).

Sensory responses are generally much smaller than motor responses. As such, sensory NCS are more technically challenging and produce more variable results than motor NCS. Similar to motor studies, SNAPs in axonal neuropathies are reduced in amplitude or absent with normal or only mildly abnormal latencies and conduction velocities. Sensory responses can be slowed in demyelinating neuropathies, but they more commonly lose amplitude because of the increased range of individual nerve fiber conduction velocities. This widened spectrum of velocities results in decreased synchrony and increased phase cancellation of the waves generated by single fibers at the site of the recording electrode. Peripherally directed sensory nerve axons originate from cell

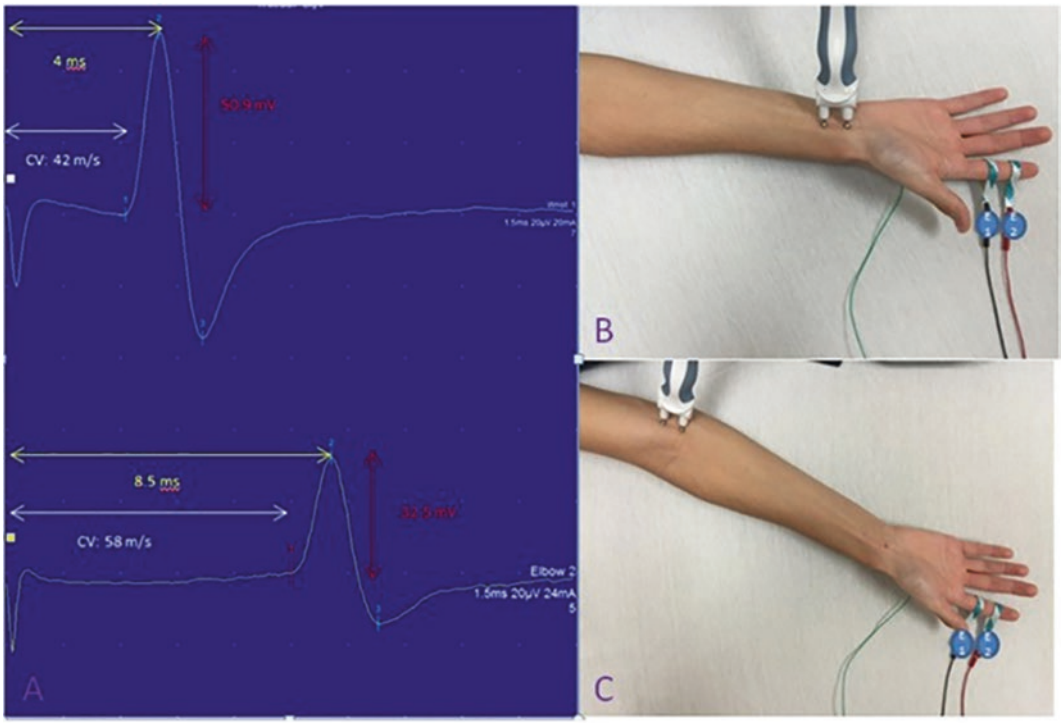

Fig. 7.5 Median sensory nerve conduction. (**a**) Shows the wave forms of distal (*upper*) and proximal (*lower*) waveforms. The *yellow arrow* highlights the peak latency, the *white arrow* highlights the conduction velocity (CV), and the *red* highlights the amplitude. The peak latency is measured from the stimulus to the peak of the wave whereas the time for the conduction velocity is measured from the stimulus to the onset of the wave (onset latency). This is an example of a normal median sensory conduction study. In (**b**, **c**) E1 is the recording electrode, E2 is the reference electrode and the ground electrode is on the posterior hand not visible in these photographs

bodies of primary sensory neurons located in the dorsal root ganglia. They only degenerate with corresponding loss of SNAP amplitude when lesions damage the dorsal root ganglion or the sensory axons themselves, i.e., neuropathies or plexopathies. On the other hand, peripheral sensory nerves and thus SNAPs are preserved in most radiculopathies, in which centrally directed sensory axons in the dorsal root proximal to the dorsal root ganglion are primarily affected.

Limitations of Nerve Conduction Studies

There are some limitations to NCS. First, the nerve must be readily accessible to superficial stimulation with an equally accessible recording zone. This precludes NCS of most proximal nerves and plexus structures. Spinal nerve roots can be stimulated percutaneously with a needle electrode, but root stimulation is painful, technically difficult, and generally unreliable. Second, NCS only evaluate large sensory and motor fibers, so any process that is restricted to small-diameter nerve fibers may remain undetected with standard NCS. Third, sensory conductions can be technically difficult because of the inherently low amplitude of the evoked responses, especially in patients with extra tissue between the recording site and nerve (obesity and peripheral edema). Their performance requires utmost attention to proper technique to ensure the presence of a reproducible response. Undesired motor responses are not infrequently mistakenly identified as sensory responses when the SNAP is truly absent. Fourth, small cutaneous nerves—whether proximal or distal—cannot be reliably studied due to their inherently small surface recorded potentials (e.g., medial femoral cutaneous nerve). Fifth, the electrodiagnostic consultant needs to be attuned to the possibility of anomalous innervation pathways, e.g., Martin–Gruber (median-to-ulnar) anastomosis in the forearm, accessory peroneal branch in the lower leg, and aberrant course of the superficial peroneal sensory nerve. Sixth, CMAP amplitudes are exquisitely dependent on proper placement of the recording electrode over the "motor point" of the muscle, since the amplitude can change significantly with even minor relocations of this electrode. Seventh, preexisting conditions always need to be considered, since preexisting polyneuropathies and nerve entrapments are common and may confound interpretation of a postinjury NCS.

Another salient limitation is the delayed onset of NCS changes in response to acute axon-loss lesions. In traumatic nerve lesions resulting in Wallerian degeneration of the transected axons, which includes most needle injuries, the portion of the axon distal to the injury remains structurally intact

and capable of transmitting a distally directed nerve impulse for the next 2–3 days prior to undergoing Wallerian degeneration (which will last up to 1 week). As such, CMAP and SNAP amplitudes do not begin to decrease until 2–3 days after the injury. CMAP amplitudes do not reach their nadir until 9 days after the insult. Sensory nerves degenerate at a slightly slower rate than motor nerves; accordingly, SNAP amplitudes do not achieve their nadir until 10–11 days postinjury [15]. Hence, NCS performed immediately after the injury serve as a preinjury baseline against which a follow-up study performed after 12 days can be compared to capture the true injury-related effects on the NCS.

There are also several practical limitations to the clinical utility of late responses. F-waves and H-reflexes are often normal in incomplete proximal axon-loss lesions due to the presence of many unaffected motor and sensory fibers that are capable of generating a normal response. These late responses are also often normal in proximal demyelinating lesions wherein focal slowing is limited to a small segment of the entire nerve pathway or conduction is preserved through the affected region by nondemyelinated nerve fibers. Moreover, F-waves are typically mediated by two or more nerve roots. As such, they tend to be normal in axonal or demyelinating mono-radiculopathies in which adjacent roots are spared. Unlike F-waves, H-reflexes are restricted in distribution and can only be recorded from the soleus (and occasionally the flexor carpi radialis) muscle in adults. H-reflexes tend to disappear in elderly individuals without known focal neurologic injuries.

Electromyography

For EMG, a needle electrode is inserted into a muscle for the purpose of directly recording the electrical activity (voltage changes) of the muscle fibers. In current EMG practice, two types of recording needle electrode are used, the concentric and the monopolar. A concentric needle consists of a cannula (reference electrode) and a core (active electrode), which are generally made of different materials. A monopolar needle consists of the active electrode alone covered with an insulating material except for its sharpened tip, which is the conductive area of the needle. When employing a monopolar recording electrode, the reference electrode is a surface electrode placed on the skin in close proximity to the active monopolar needle.

There are three separate phases of the evaluation. First, the electrical activity is evaluated during insertion of the needle electrode (i.e., "insertional activity"). In the second phase, the consultant searches for abnormal "spontaneous activity" within the muscle which occurs when the electrode is stationary in the resting muscle. Multiple sites are assessed in each examined muscle. The type of abnormal spontaneous activity of greatest relevance to regional anesthesia-related nerve injury is the so-called fibrillation potential. A fibrillation potential is an EMG waveform generated by spontaneous firing of a single muscle fiber. Most fibrillation potentials discharge at a regular rate (Fig. 7.6). Positive sharp waves have the same origin and significance as fibrillation potentials. Fibrillations develop in acutely denervated muscle fibers, which become supersensitive after a short delay following the injury. They also occur in many muscle diseases associated with segmental necrosis of muscle fibers or primary electrical instability of the muscle fiber membrane.

The final stage is devoted to analysis of motor unit potentials (MUPs). The motor unit is defined as a single motor nerve and all of its innervated muscle fibers. When the patient voluntarily activates a motor nerve, a nerve impulse is generated at the level of the spinal anterior horn cells that travels down the individual motor axons within that nerve to their points of contact with many individual muscle fibers, i.e., the neuromuscular junctions. Action potentials are then, in turn, elicited in all of the muscle fibers supplied by each of the constituent motor axons. The MUP is the sum of all the single muscle fiber action potentials triggered by activation of a single motor nerve as recorded by the needle electrode. The patient is asked to slowly activate the muscle from rest in incremental steps to full effort. With stronger and stronger contraction, more and more motor units are recruited and the recorded MUPs begin to overlap and interfere with one other, creating a so-called interference pattern (Figs. 7.7 and 7.8). The assessment of the manner whereby individual MUPs increase their firing rates and new MUPs are recruited as the patient slowly increments activation of the muscle is termed "recruitment." MUPs are analyzed at low effort when only a few are discharging so that they can be easily and individually identified. Unlike fibrillation potentials, MUPs always fire irregularly (Fig. 7.9). The salient morphological attributes of each MUP are its duration, amplitude, complexity, firing rate, and stability.

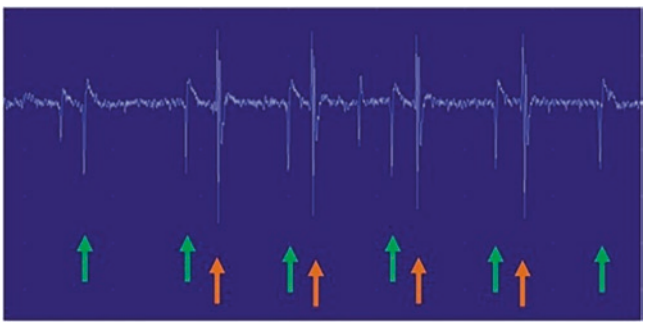

Fig. 7.6 Fibrillation potentials (settings at 100 ms per horizontal division and 100 μV per vertical division) recorded while the muscle was at rest (i.e., no voluntary muscle activity) without needle electrode movement. There are two fibrillation potentials recorded (denoted by *arrows*: *orange and red*). Please note that the regular firing frequency of these spontaneous potentials contrast with the irregularly firing MUPs seen previously

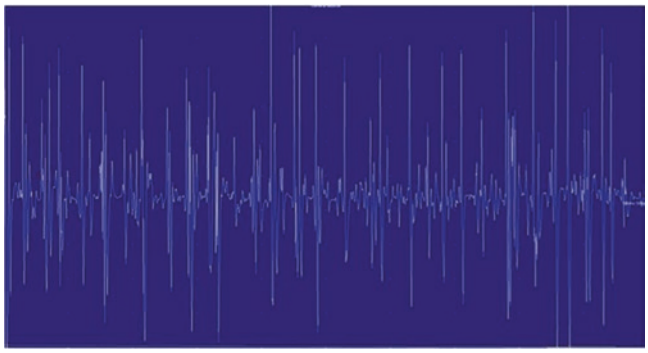

Fig. 7.7 Normal Interference pattern (settings at 100 ms per horizontal division and 500 μV per vertical division). The baseline is obscured with MUPs. This is done when the patient fully activates the muscle against isometric resistance

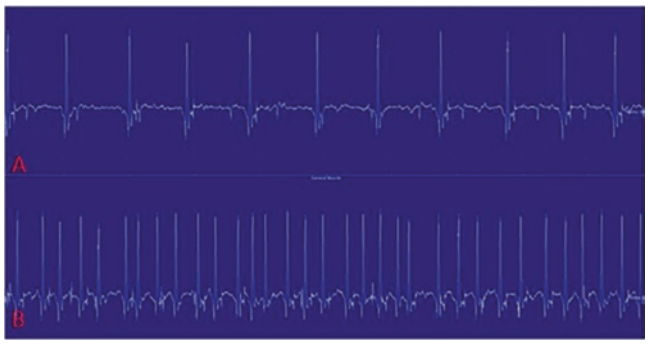

Fig. 7.8 (**a**) Decreased recruitment (settings at 100 ms per horizontal division and 200 μV per vertical division). Despite the MUP firing at 11 Hz, no other motor units have been recruited. This MUP is also normal in size reflecting a recent-onset or purely demyelinating lesion. On close inspection the firing irregularity of the MUPs can be appreciated (i.e., variance I time intervals between the MUP discharges). (**b**) The same normal-sized MUP shown at the highest level of activation (interference pattern). Although more discharges of this MUP are seen (now firing at 35 Hz) no other motor units have been recruited (settings at 100 ms per horizontal division and 200 μV per vertical division). This is a reduced interference pattern in the setting of a recent-onset or purely demyelinating lesion. In a chronic axonal lesion (i.e., months post onset), a similar recruitment and interference pattern might be seen, but the MUP would be enlarged due to reinnervation

The needle electrode records from muscle fibers lying within a radius of about 1.5–2.0 mm from the recording tip of the electrode. On the other hand, the diameter of the circular (in cross section) motor unit territory in most muscles ranges from 5 to 10 mm [16]. As such, these electrodes selectively record from only a fraction of the total number of muscles fibers contributing to the MUP in the normal state. The muscle fibers belonging to a specific motor unit are distributed in the muscle in a patchy, noncontiguous pattern. In a low-power cross section of muscle, muscle fibers from up to 40 motor units may be represented [17]. Thus, the needle electrode records MUPs from muscle fibers of several different motor units within the limited recording area of the electrode tip, but it does not sample every motor unit in the muscle.

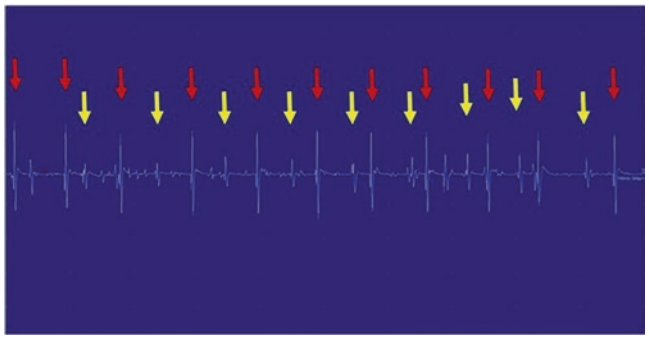

Fig. 7.9 Normal recruitment (settings at 100 ms per horizontal division and 500 μV per vertical division). The larger amplitude MUP (*red* arrow) is firing at a rate of 11 Hz with a smaller amplitude MUP (*yellow* arrow) firing at almost the same rate (10–11 Hz). The variance in the time interval between discharges of the same MUP (i.e., interpotential interval) demonstrates how a MUP normally fires in a slightly irregular manner

In neuromuscular disorders, the muscle fibers and their organization within the motor unit territory may be altered, resulting in corresponding changes in the EMG recording from the affected muscles. In this chapter, only those changes observed after neuropraxia and partial to complete denervation will be summarized. EMG findings in other neuromuscular processes, such as myopathy, polyneuropathy, and neuromuscular transmission disorders have been recently reviewed [18].

The Seddon classification divides nerve injuries into three categories: neuropraxia, axonotmesis, and neurotmesis [19]. Neuropraxia is defined as functional or demyelinative conduction block without structural damage to the axon. The ensuing loss of conduction is always transient, and prognosis for complete recovery is excellent. In axonotmesis, axons are damaged and the distal segments subsequently undergo Wallerian degeneration, but the perineurium, epineurium, and other supporting connective tissues are preserved, and the nerve itself remains in continuity. If all axons in the nerve degenerate, the supplied muscles fibers are completely denervated. If only a subset degenerate, denervation is partial and incomplete. Recovery from axonotmesis depends on the slow process of axonal regeneration. Prognosis for full recovery is fair but variable. Neurotmesis refers to injuries in which the entire nerve and all its supporting connective tissue are physically separated into distal and proximal segments. Denervation is complete. Prognosis for successful regeneration of the nerve is poor.

In an injury not resulting in denervation (axon loss), i.e., neuropraxia, the first and only EMG change is a decreased number of rapidly firing MUPs reflecting the functional but not anatomic loss of motor units (Table 7.4). This is referred to as "decreased recruitment" (Fig. 7.8). In mild neuropraxic lesions, MUP dropout may not be detectable in the EMG recording and recruitment remains essentially normal. An injury of this nature is felt to result from damage to the

Table 7.4 Types of neuronal injury

Type of injury	Time after lesion	Fibrillations	MUP size	MUP stability	Recruitment
Neuropraxia	<3–4 weeks	No	Normal	Stable	Variably reduced
	1–6 months	No	Normal	Stable	Normal
	6+ months	No	Normal	Stable	Normal
Partial denervation	<3–4 weeks	No	Normal	Stable	Variably reduced
	1–6 months	Yes	Increasing in amplitude, duration, and complexity	Unstable	Variably reduced
	6+ months (reinnervation complete)	No	Increased amplitude, duration, and complexity	Stable	Variably reduced
	6+ months (reinnervation incomplete)	Yes (low amplitude)[a]	Increasing in amplitude, duration, and complexity	Unstable	Variably reduced
Complete denervation	<3–4 weeks	No	No MUPS recorded	Since no MUPS, cannot measure	Absent
	1–6 months	Yes	Increasing in amplitude, duration, and complexity	Unstable	Variably reduced
	6+ months (reinnervation complete)	No	Increased amplitude, duration, and complexity	Stable	Variably reduced
	6+ months (reinnervation incomplete)	Yes (low amplitude)[a]	Increasing in amplitude, duration, and complexity	Unstable	Variably reduced

[a]May also see complex repetitive discharges, myokymic discharges, decreased insertional activity.

myelin sheath or minor functional/structural disturbances at the nodes of Ranvier that usually recover within minutes to a few months. As the myelin sheaths and nodes of Ranvier are repaired, MUPs begin to show more normal recruitment patterns. In the absence of denervation and hence reinnervation, fibrillation potentials do not occur and MUPs are unchanged in their morphology (i.e., amplitude, duration, complexity).

The electrophysiologic changes in the acute phase (<21 days) following partial denervation (axonotmesis) are similar to those of neuropraxia, i.e., decreased recruitment of rapidly firing MUPs of normal morphology. At about 14–21 days, increased insertional and spontaneous activity (fibrillation potentials and positive sharp waves) begin to appear. Muscles supplied by shorter nerves (proximal) exhibit these changes sooner than muscles supplied by longer nerves (distal). Fibrillation potentials are larger in amplitude during the acute phase of injury when the muscle fibers are still normal in diameter. Muscle fibers that remain denervated eventually atrophy (seen pathologically as small angular muscle fibers in routine H&E staining). As a single muscle fiber action potential's amplitude is proportionate to fiber diameter, the amplitudes of these potentials decrease as fiber diameters decrease. Hence, in the weeks following the injury, fibrillation potentials become reduced in amplitude.

In partial motor axonal loss, reinnervation occurs primarily via collateral sprouting. This is a process whereby terminal axons of nondamaged fibers supplying the affected muscle issue additional distal branches to innervate orphaned muscle fibers that have lost their motor axon. Collateral sprouting occurs within the preexisting motor unit territory of that surviving motor unit. Thus, as reinnervation proceeds, the density of muscle fibers supplied by a particular motor neuron increases (i.e., innervation ratio), but the size of the corresponding motor unit territory remains unchanged. Muscle fibers supplied by a single motor axon become more contiguously than randomly distributed within the motor unit territory. The muscle biopsy correlate of this process is grouping of fiber types. The efficiency of the reinnervational process depends on a number of factors, such as the mechanism of injury, severity of injury, patient age, premorbid conditions (e.g., preexisting polyneuropathies), and length of nerve involved in recovery.

As collateral sprouting and neural regeneration following partial denervation proceed, more and more previously denervated muscle fibers become reinnervated and fibrillation potentials become less and less prevalent. In most cases of axonotmesis characterized by only partial denervation, denervated muscle fibers are successfully reinnervated and fibrillation potentials eventually disappear. As concerns MUP morphology, the increase in innervation ratio arising from reinnervation evolves over weeks to months. The increased density of terminal axonal sprouting and muscle fibers within a single motor unit territory is reflected in the corresponding MUP by increased amplitude, longer dura-

tion, and increased complexity (i.e., increased phases, turns, or satellites; Figs. 7.10, 7.11, and 7.12).

If an EMG performed before 21 days following an injury shows enlarged MUPs or well-developed fibrillation potentials, one can infer that these abnormalities resulted from a preexisting radiculopathy or neuropathic disorder. Examples might include a patient with an underlying distal symmetric diabetic polyneuropathy or history of a spondylosis-related radiculopathy who then develops an acute focal neuropathy following regional anesthesia affecting nerve fibers already damaged by the preexisting polyneuropathy or radiculopathy. If an EMG is routinely performed only a few days postinjury, these preexiting, confounding conditions will be identified. This immediate postinjury EMG will then serve as a baseline against which follow-up EMGs can be compared to more accurately attribute abnormal spontaneous activity and MUP remodeling to the nerve injury itself.

In cases of complete denervation, no activation of MUPs within the affected muscles will occur in the early and subacute phases of the injury. As in partial denervation, fibrillation potentials will emerge at about 21 days. In this more severe type of injury, recovery is typically incomplete. All of the muscle fibers are denervated and require reinnervation. Reinnervation is accomplished primarily by axonal regeneration from the point of injury. This is a slow (approximately 1 mm/day or inch/month) and inefficient process. Recovery is contingent on how many motor axons grow back into the muscle to reinnervate the orphaned muscle fibers. Important prognostic factors include the integrity of the damaged nerve's supporting connective tissue structures (axonotmesis versus neurotmesis) and the distance from the site of injury to the muscle (length that the regenerating axons must traverse for successful reinnervation of the target muscle). The reinnervational MUPs encountered in this type of lesion tend to be complex and long in duration rather than large in amplitude.

As reinnervation reaches completion following any degree of axon-loss lesion, MUPs become enlarged and stable (Fig. 7.12). Stability ensues as the de novo neuromuscular junctions mature. Grossly unstable MUPs are readily recognized by an experienced electrodiagnostic consultant. To detect minimal to moderate instability, individual MUPs are assessed at special instrument settings as used for jitter analysis in a single fiber EMG. If an EMG is performed months after the injury, the presence of fibrillation potentials and unstable MUPs indicates that reinnervation is still incomplete and ongoing. Conversely, the absence of fibrillation potentials and presence of stable MUPs indicate that reinnervation is complete.

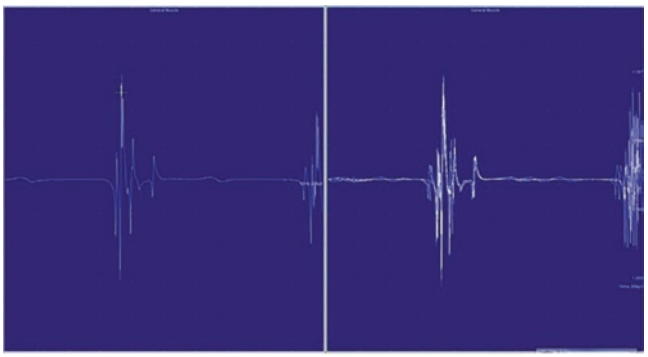

Fig. 7.11 Complex, unstable MUP (settings at 10 ms per horizontal division and 500 μV per vertical division). The *left screen* shows a single MUP and the *right* shows the same MUP superimposed after four discharges. This MUP is complex due to the increased number of phases. The variation between discharges indicates that this MUP is unstable

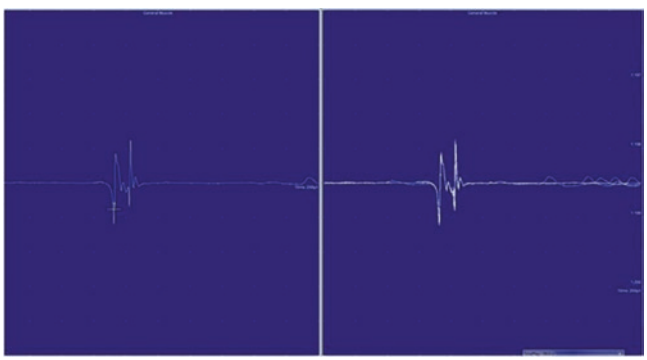

Fig. 7.10 Complex, stable MUP (settings at 10 ms per horizontal division and 500 μV per vertical division). The *left screen* shows a single MUP and the *right* shows the same MUP superimposed after four discharges. This unit is complex due to the increased number of phases (deviations above or below the baseline). The lack of variation between discharges indicates that this unit is stable

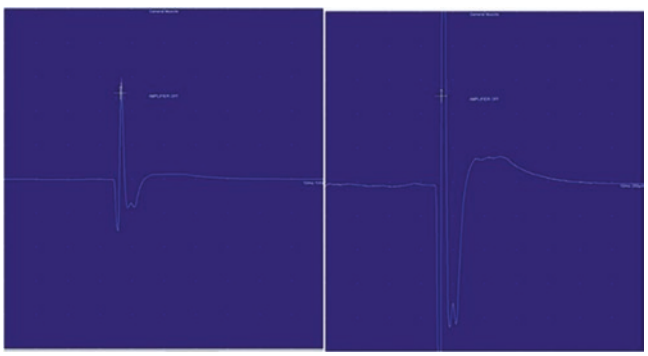

Fig. 7.12 Increased MUP duration and amplitude. The *right and left screens* show the same MUPs displayed at different settings (*right* is 10 ms per horizontal division and 1 mV per vertical division; *left* is 10 ms per horizontal division and 200 μV per vertical division). This MUP has large amplitude (greater than 2 mV) and a prolonged duration (greater than 15 ms). The right display shows standard settings for assessing phases and duration

Limitations and Benefits of EMG

EMG critically depends on the skill of the examiner. The EMG test is a very dynamic process where the examiner needs to choose muscles to test based upon patterns that may evolve during testing. In addition, the abnormal discharges may be very brief or distant, such that they may be misinterpreted or missed by a novice examiner. The ability to identify subtle changes in EMG waveforms in a short period of time (they may only be present on the screen for a fraction of a second), differentiate between multiple concurrent processes affecting the same muscle, and estimate the duration of these processes requires an electromyographer with significant experience. Another limitation of EMG is its failure to determine the etiology of any neurogenic process. The greatest benefit of EMG is its ability to refine the localization of a nerve injury by examining muscles (and hence their innervating nerves) that might otherwise be difficult to test individually on clinical examination or by nerve conduction studies. An added benefit is its potential to provide information on the chronicity of a neurogenic injury. Of course, it is important to remember that EMG findings should always be used as an adjunct to the clinical history and examination.

Practical Approach

In designing the electrodiagnostic study, it is crucial to first obtain a history from the patient, perform a focused general and neurological examination, and then formulate a differential diagnosis regarding lesion localization. Nerves for NCS and muscles for EMG are next selected based on this differential diagnosis. As already noted, if there are preexisting neuromuscular diseases, postinjury studies can be confounded by these conditions. In this setting, a prior comparison study performed in the same EMG laboratory is invaluable. However, if such a premorbid baseline study does not exist, a new study performed with 1–3 days of the putative injury can serve as that baseline, given the delayed onset of all NCS and EMG changes after acute trauma, except for decreased recruitment in the needle EMG examination mediated by axon loss or conduction block, which is not delayed in its appearance. If a repeat study is then performed in 4 weeks, the new NCS and EMG findings can be compared to those obtained in the immediate postinjury study to determine the direct effects of the injury in contrast to those ensuing from the preexisting conditions. In both the baseline and follow-up examination, nerves and muscles should be examined bilaterally, as interside comparisons improve the sensitivity, specificity, and overall accuracy of the findings, especially in a patient with a chronic polyneuropathy.

Imaging

Here, we first describe the various imaging techniques that are relevant to identifying and evaluating injury to nerves (and adjacent structures) caused by regional anesthesia, and thereafter suggest choices of imaging for specific suspected injuries.

Plain Films

Plain films or conventional radiography is a simple, relatively inexpensive method of imaging the bony, and to a limited extent, the soft tissue components of the spine. Spatial resolution is good, but contrast resolution is inferior to that of computed tomography (CT) or magnetic resonance imaging (MRI). Plain film myelography after the administration of intrathecal contrast has largely been supplanted by CT myelography or MRI.

Computed Tomography

Technology

CT has been used for imaging the spine for more than 40 years. CT technology continues to advance with subsequent improved spatial and contrast resolution, decreased scan time, and lower radiation dose. Although MRI is being used increasingly for spine imaging, CT continues to have advantages in some circumstances.

The CT gantry contains an array of X-ray detectors and an X-ray tube that rotates about the patient. An X-ray beam is passed through the patient at multiple different tube positions or projections and the detectors measure the beam attenuation at each projection. This process is repeated at multiple sequential points to allow creation, via data reconstruction programs, of thin cut (often <1 mm) cross sectional images of the scanned anatomy. Each pixel, or picture element, of a CT image is assigned a CT number or Hounsfield unit based on the X-ray attenuation of the corresponding tissue in the patient. To display this digital information as an image, the Hounsfield numbers must be mapped onto a gray scale ranging from white to black. The way in which the digital scale is matched to the display gray scale is termed *window*. The window *width* is the range between the highest and lowest CT number to be displayed, and the window *level* is the median number in the range. By adjusting the window width and level, various tissues may be optimally displayed.

Limitations

Tissues with similar beam attenuations are not well discriminated by CT. The difference in X-ray attenuation of

various soft tissues (excluding fat) is only about 4 %. In spine imaging, the contrast between the soft tissues of the spinal canal including the spinal cord, nerve roots, disc margins, and CSF is low, which limits evaluation. Visualization can be improved by the use of iodinated contrast material within the thecal sac (i.e., CT myelography), but this requires lumbar puncture.

Artifacts are generally related to patient motion, high-density objects, detector malfunction, and the inherent limitations of reconstruction algorithms for portraying objects of geometric complexity. Motion degrades images by producing misregistration artifacts that appear as shading or streaking. Motion is generally less of a problem with CT than with MRI as acquisition time with CT is much faster than MR (seconds rather than minutes). Metallic foreign objects such as aneurysm clips, bullet fragments, and spinal hardware produce radially oriented streak artifact and can limit evaluation of adjacent structures. Beam hardening artifact occurs when dense structures in the field, such as bone, attenuate the lower energy portions of the X-ray beam, resulting in dark streaks in the adjacent tissues.

CT utilizes ionizing radiation during image acquisition, so caution must be exercised to limit radiation exposure, particularly in children and pregnant women. While efforts are being made to reduce dose, the balance of risks and benefits of CT should always be carefully assessed, for which consultation with a radiologist can be helpful.

Indications

CT imaging is well adapted to evaluation of neurologic injury as it can be rapidly obtained and is readily available. Although it provides excellent evaluation of bony anatomy, it has limited contrast resolution, which limits soft tissue evaluation. Furthermore, processes within the spinal canal such as epidural hematoma and spinal cord injury are poorly evaluated with CT.

Degenerative changes of the vertebral column are clearly evident by CT imaging. As the intervertebral disc ages, there is loss of axial height and development of radial bulging. Additional signs of disc degeneration include endplate osteophytes and gas within the disc space—both easily identified on CT. While CT can usually identify disc bulges, MRI is preferred to evaluate smaller disc protrusions and characterize the effects on adjacent structures (i.e., the degree of cord and nerve root compression). CT myelography can improve visualization of the disc margin in patients who cannot have an MRI (due to contraindications such as certain types of cardiac generators). Osseous stenosis of the vertebral canal and intervertebral foramina, hypertrophic bone changes, subarticular bony erosions, and defects of the pars interarticularis are well evaluated with CT.

Magnetic Resonance Imaging

Technology

MRI is based on the phenomenon of nuclear magnetic resonance. Hydrogen, with its single proton nucleus, is by far the most abundant element in living organisms and has a large magnetic moment. At present, virtually all clinical MRI is based on magnetic resonance of the hydrogen nucleus.

When placed in a magnetic field, the hydrogen nucleus (a proton) will process like a gyroscope about the axis of the magnetic field at a frequency specific for the nuclear species and the particular magnetic field strength. A radiofrequency (RF) pulse is applied which results in temporary alignment of the protons and signal production. Subsequently, the protons lose alignment (relaxation) at which time additional RF pulses may be applied in order to realign the protons. Relaxation can be resolved into two separable processes of longitudinal and transverse relaxation, with rates measured by time constants T1 and T2, respectively. Differential rates of relaxation affect the intensity of the signal emitted by a particular tissue and its appearance in the final image.

The patient is positioned within the bore of a large magnet. The most common field strengths are 1.5 and 3 T. A specific sequence of RF pulses is used to excite (align) the protons. A receiver then detects the signal emitted by the relaxing hydrogen protons, which is used to produce an image. Varying patterns of RF pulses can be applied with the goal of differentiating tissues from one another based on the differences in tissue T1 and T2 relaxation rates. This results in images with T1 weighting (Fig. 7.13) or T2 weighting (Fig. 7.14). T1-weighted images provide contrast based on longitudinal relaxation rate. Fat, protein, and blood products are T1 hyperintense (bright). T2-weighted images provide contrast based largely on differences in transverse relaxation rates. Fluid appears bright on T2-weighted images. T1 and T2 weighting is relative and images with components of both can be obtained.

In certain situations, the contrast between tissues can be increased through the intravenous administration of a gadolinium chelate, which results in increased brightness on T1-weighted images of tissues in which gadolinium has accumulated. Although some degree of parenchymal enhancement is normal, gadolinium tends to accumulate in tissues with increased vascularity or vessel permeability, such as infection, tumor, or breakdown of the blood–brain barrier, allowing for increased conspicuity.

Limitations

No definite ill effects of magnetic fields on human beings have been documented to date from exposure to MRI. However, certain devices and ferromagnetic objects

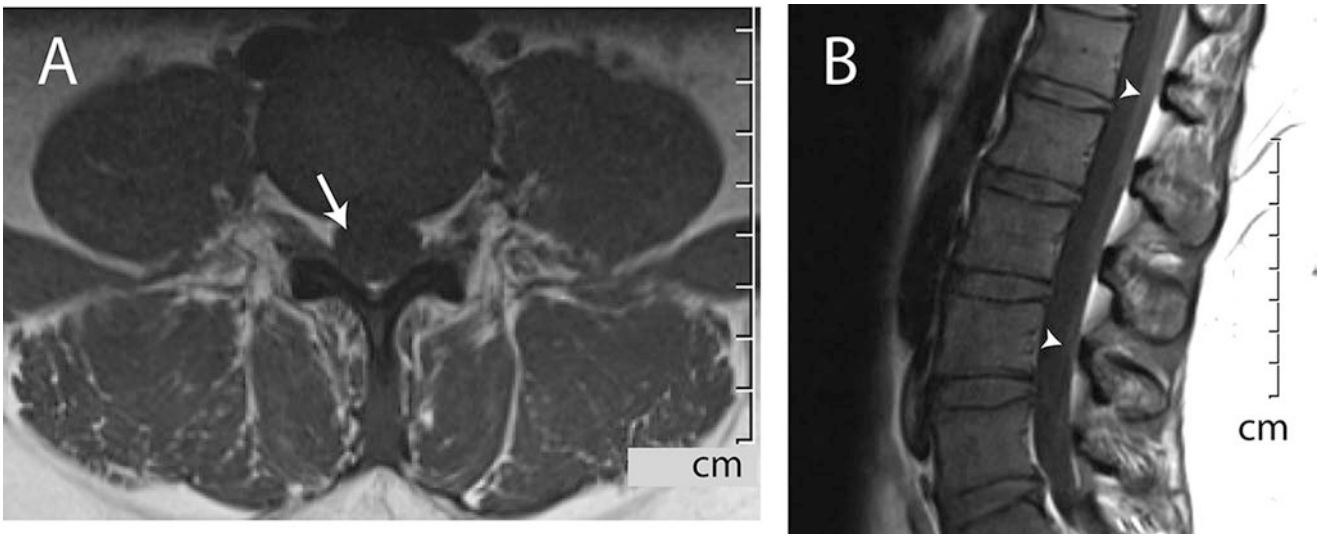

Fig. 7.13 Normal T1-weighted MRIs. (**a**) In the axial plane through a lumbar disc (*anterior up*). (**b**) In the midline sagittal plane of normal lumbar vertebrae (*anterior left*). Fat has a high signal intensity (appears bright), whereas muscle and disc have intermediate signal intensity. Low signal intensity (*dark*) is characteristic of water (e.g., CSF, *straight arrows*) and fast flowing blood (*vena cava*, aorta). Cortical bone has no signals (appears *black*) but marrow has low signal intensity. Roots and cord appear as intermediate signal intensity (*curved arrows*). Note the signal fall-off (darker mage) at greater distances from the posterior surface coil

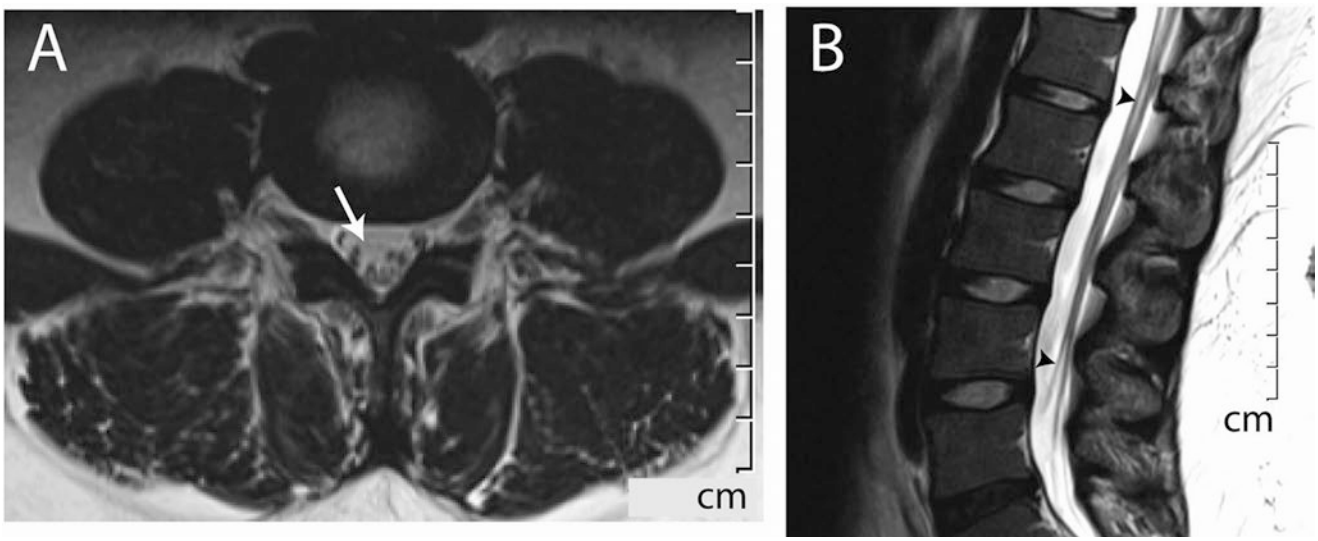

Fig. 7.14 Normal T2-weighted MRIs. (**a**) In the axial plane through a lumbar disc (*anterior up*). (**B**) In the midline sagittal plane of normal lumbar vertebrae (*anterior left*). CSF (*white arrows*) has a high signal intensity, especially where stationary, whereas fat is not as bright as in T1 images. Other tissues have intermediate signal intensity. Roots and cord (*black arrows*) are of intermediate signal intensity, so contrast with CSF. The disc nucleus is bright if it has not become desiccated from degenerative disease

pose potential dangers to patients and others in the scanning area. Patients with certain cardiac pacemakers, cochlear implants, neurostimulators, heart valves, and older aneurysm clips should not be examined by MRI as these devices may malfunction, be displaced by the magnetic field, or result in heating of the adjacent tissues. Additionally, rapidly changing magnetic fields in the scanner may lead to the generation of electric currents within a patient with implanted wires (usually related to cardiac pacemakers or nerve stimulators). If there is any question regarding the safety of an implanted object or device, radiologic consult is recommended. Since metallic objects such as oxygen tanks, wheelchairs, and other loose items such as scissors and jewelry are potential missiles when placed in the magnetic field, specially designed wheelchairs, oxygen tanks, and other items have been developed for use in proximity to strong magnetic fields.

Many types of orthopedic/spinal hardware, surgical wires, and surgical clips have been deemed MRI safe by the manu-

facturers. Although imaging with these in place is possible, many challenges arise in obtaining clinically useful images due to resultant alterations in the local magnetic field leading to image spatial distortion, signal loss, or failure of fat suppression. Methods exist for reducing artifact surrounding metal prosthesis. The most basic involve using pulse sequences with multiple repeating pulses to mitigate the magnetic field inhomogeneity. Additionally, obtaining images using a wide bandwidth and lower strength magnets (1.5 T) can decrease artifact but with a loss of signal to noise, and newer techniques are being developed, such as field mapping.

The radiofrequency pulse of an MRI scanner can generate several kilowatts of peak power that is partially deposited as heat in the body of the subject. While this has not been a practical limitation, special consideration is given to patients during pregnancy. Currently, there is no conclusive evidence to suggest that an embryo is adversely affected by magnetic or radiofrequency fields at the intensities used in clinical MRI scanners. However, given the uncertainty, many centers have developed specific policies regarding MRI during pregnancy. Anyone considering obtaining an MRI during pregnancy should consider the risk/benefit ratio associated with the exam, be familiar with the institutional policies, and consult with a radiologist regarding possible alternative imaging modalities.

Successful MRI generally requires a cooperative, near-motionless subject. Up to 10 % of the population experiences some degree of claustrophobia upon being placed in the magnet bore. Most of these patients will tolerate imaging with mild oral or intravenous sedation, although the severely claustrophobic may require general anesthesia.

For most clinical applications, the spatial resolution of MRI is slightly less than that of CT or plain radiography. However, contrast resolution is almost always superior. Limitations arise in situations that involve moving structures, specifically rapidly flowing blood and CSF. Because of the motion, the RF pulse sequence cannot be completed and these structures lack signal and appear black (flow void). Examples include CSF motion (termed CSF pulsation artifact) in the thoracic spine which cases dark CSF signal and may obscure subtle pathology. While rapidly flowing blood may appear as a signal void, slow-flowing blood tends to appear bright in T1-weighted images. The intravenous administration of gadolinium generally tends to increase the signal intensity of flowing blood.

Indications

MRI is an excellent method for imaging the spine. Multiple levels can be studied simultaneously and in virtually any desired plane with good soft tissue characterization and without radiation exposure. Soft tissue injuries including those of the peripheral nerves and contents of the spinal canal are better visualized with MRI than with any other current imaging modality. Epidural hematoma, syrinx, cord edema and swelling, and myelomalacia can be well demonstrated with MRI. Compression of the thecal sac and spinal cord by bone or soft tissue is easily recognized.

MRI is generally sensitive for focal collections of blood, whether acute, subacute, or chronic. Acute blood in the central nervous system is usually most apparent in gradient recalled echo (GRE) images and appears as an area of significantly decreased signal intensity. Subacute blood (1 week to 1 month) gradually becomes high in signal intensity in T1-weighted images. This always precedes the subsequent change from low to high signal intensity seen in T2-weighted images. In the spine, epidural hematomas may appear intermediate in signal intensity in both T1- and T2-weighted images and may mimic herniated disc material or other epidural soft tissue. Nonetheless, epidural blood and its resultant mass effect in the vertebral canal are generally well seen with MRI. Unlike an abscess, acute blood should not show enhancement following gadolinium administration. Hematomas in the soft tissues at the site of needle insertion will also be evident.

While CT can identify osseous changes related to degenerative disc disease, MRI is typically superior in evaluation of disc bulging or herniation, loss of disc height, loss of T2 signal (disc desiccation), and reactive marrow changes in the adjacent vertebral bodies. Additionally, hypertrophic, degenerative changes of the facet joints, synovial cysts, and thickening of the ligamentum flavum can also be evaluated with MRI, although small osteophytes, subchondral erosions of the facet joints, and ligamentous calcification are generally better demonstrated with CT. Defects of the pars interarticularis (spondylolysis) are often better appreciated with CT.

Postoperative scarring associated with discectomy will generally appear as epidural soft tissue of similar signal intensity to residual or recurrent disc material. Differentiation of fibrous tissue or scar from recurrent or residual disc material is made easier by intravenous administration of a gadolinium chelate. Fibrous tissue generally enhances uniformly, whereas disc material, with the possible exception of the periphery, generally does not enhance.

MRI has particular advantages for imaging infectious and inflammatory lesions. Osteomyelitis is generally readily apparent, and MRI is very sensitive for destructive or inflammatory process involving marrow or disc. Abscess adjacent to nerve plexuses or at other sites of needle insertion will be apparent by MRI. Any epidural or paraspinous soft tissue inflammation or mass effect is usually identifiable, and generally demonstrates enhancement with administration of intravenous paramagnetic contrast agent (Fig. 7.15). Arachnoiditis may reveal thickening and clumping together of nerve roots of the cauda equina (Fig. 7.16). Alternatively, the involved nerve roots may be adherent to the inner surface of the thecal sac and give the appearance of an empty sac. After intravenous paramagnetic contrast agent administration, there may be enhancement of nerve roots affected by arachnoiditis.

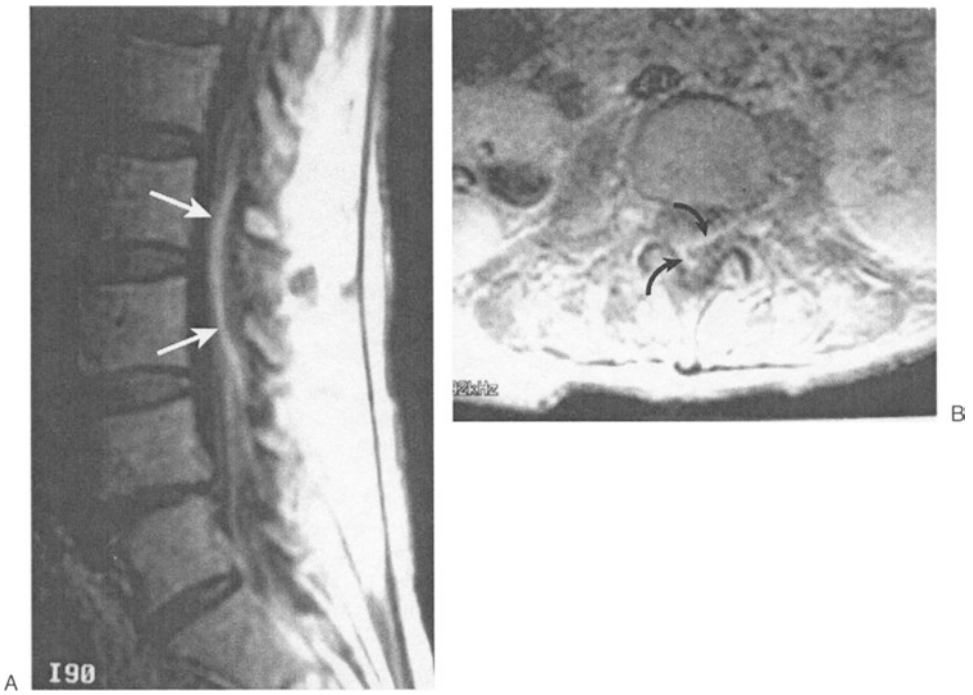

Fig. 7.15 T1-weighted magnetic resonance lumbar vertebral images after intravenous gadolinium injection, showing epidural abscess. The patient had tibial osteomyelitis treated with intravenous antibiotics and eventually amputation, leading to phantom limb pain treated by lumbar epidural catheter. Midline sagittal image (**a**) shows a lenticular mass (*arrows*) in the posterior vertebral canal of the second and third lumbar vertebrae. The anterior rim of the mass is bright because of gadolinium enhancement, whereas the area enclosed by this rim has lower signal intensity, probably indicative of purulent material. Axial image (**b**) shows dark CSF and the abnormal soft tissue posterior and to the left (patient's) of the dural sac. The rim of inflamed tissue enhances (becomes bright) with gadolinium, especially on the anterior and right aspects of the abscess (*arrows*)

MRI is the best imaging modality for evaluation of intramedullary masses, because the internal architecture and not merely the contour of the cord is demonstrated. Similarly, intradural extramedullary masses are well demonstrated, particularly with the use of intravenous paramagnetic contrast agent, although CSF pulsation artifact in the thoracic spine can occasionally obscure lesions in the spinal canal. The bone destruction and/or soft tissue mass associated with malignant epidural tumors are generally readily apparent with MRI. These lesions usually show decreased signal intensity in T1-weighted images and increased signal intensity in T2-weighted images relative to normal bone. Most such lesions show varying degrees of contrast enhancement.

Magnetic Resonance Neurography (MRN)

This is a technique used to optimize imaging of peripheral nerves [20, 21]. Traditionally imaging has played a marginal role in evaluation of peripheral nerves, while electromyography (EMG), history, and physical exam have played the central role in evaluation. However, MRN now provides direct imaging of peripheral nerves allowing for a more complete evaluation. Commonly imaged areas include the brachial plexus, the lumbosarcal plexus, and more peripheral nerves of the upper and lower extremities.

MRN technique typically uses both standard and thin slice acquisition techniques. 3 T magnets are preferred as they provide higher signal to noise. However, 1.5 T may sometimes be preferred to help reduce artifact from metallic prosthesis. Field of view should be kept as small as possible, necessitating close collaboration with referring physicians and integration of all available data to best localize pathology prior to imaging. Typically, 2D sequences include T1 and fat saturated (FS) fluid-sensitive sequences. In plane resolution should be about 0.4 mm with slice thickness of 4–5 mm proximally and 2–3 mm in the distal extremities. Fat is hyperintense on T1 sequences and thus is good for evaluation of perineural fat or muscular atrophy. Nerves typically appear isointense to muscle on T1 weight sequences. FS fluid-sensitive sequences are an important part of MRN. Normal nerves typically appear slightly hyperintense to skeletal muscle while most pathology appears bright on these sequences.

Similar to standard imaging, thin slice imaging is available with varying T1/T2 weighting and fat saturation. Thin slice acquisition is a powerful tool that allows for creation of multiplanar reformats as well as maximum intensity projection (MIP) reformats, which helps distinguish pathological

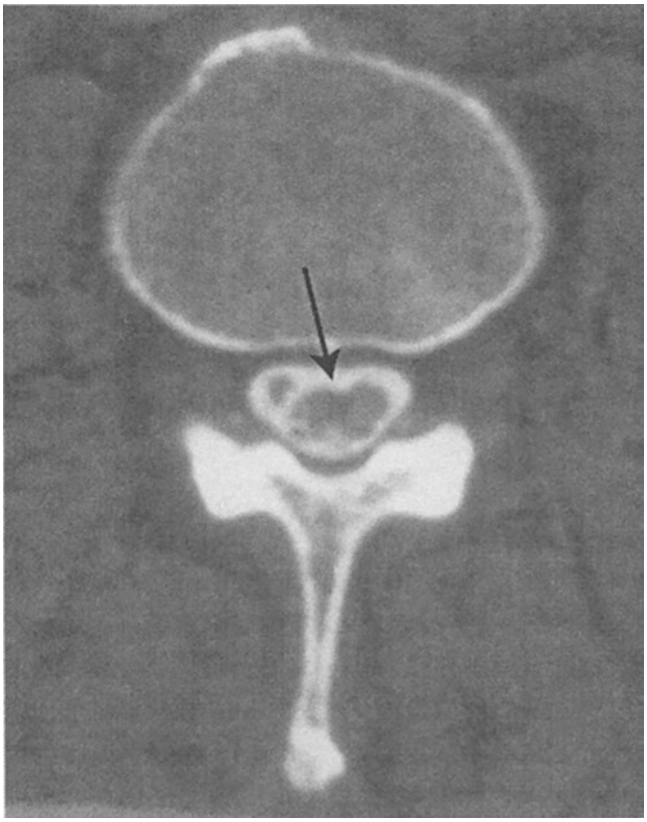

Fig. 7.16 CT image though the second lumbar vertebra after intrathecal contrast injection (CT myelogram), showing arachnoiditis. The nerve roots are thickened and clumped together in a mass (*arrow*)

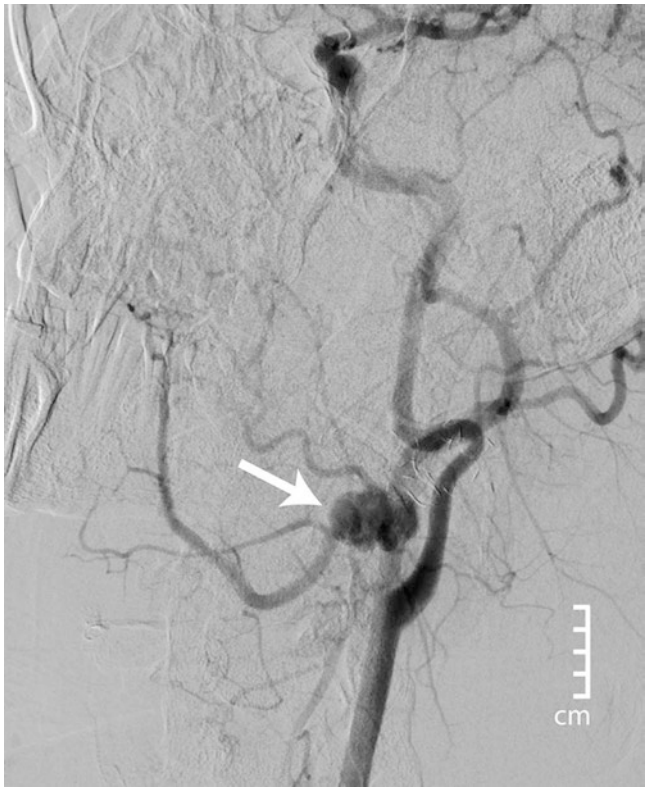

Fig. 7.17 Anterior–posterior projection image of a patient with a carotid pseudoaneurysm (*arrow*) after penetrating trauma using conventional angiography with digital subtraction technology

anatomy. Disadvantages include artifact produced by adjacent vascular structures.

Gadolinium-based contrasts are not routinely used in MRN as healthy nerves do not typically enhance due to the presence of a blood–nerve barrier. Even in the setting of trauma, contrast is of little value. Contrast is useful if there is concern for a neoplasm/mass, polyneuropathy, or infectious/inflammatory disorders. Since the blood–nerve barrier is damaged after nerve injury [22], gadolinium may possibly enhance injured nerve regions.

MRN has proven useful for evaluation of many different types of neuronal injury including focal injuries such as penetrating trauma, stretch injury, iatrogenic needle placement, and anesthetic injection, as well as injury from processes such as autoimmune disease, vasculitides, diabetes, or drug toxicity. With injury, nerves typically become hyperintense on fluid-weighted sequences and demonstrate focal enlargement compared to adjacent nerves. Additionally, the typical fascicular pattern becomes disrupted or irregular. After transection, a focal nerve discontinuity will be present. Enhancement is typically absent unless infectious or neoplastic etiologies are present. Secondary signs of nerve injury may be present due to Wallerian degeneration of the distal fiber segments, which results in edema and nerve swelling of the nerve, and edema may be identified in muscles denervated by the injury. Processes adjacent to the nerve that may contribute to injury are often included in the field of view, including hematomas, fractures, or degenerative changes. MRN allows for precise localization of injury but it can be limited by technical factors such as patient movement and field of view.

Conventional Angiography

Technology

State-of-the-art digital subtraction angiography systems use computerized image processing, resulting in superior contrast resolution. Vascular anatomy is delineated by intravenous injection of an iodine-containing contrast agent during simultaneous rapid sequence filming. It is generally regarded as the "gold standard" for blood vessel imaging (Fig. 7.17). Intravascular injection of contrast material requires placement of a catheter within the vascular tree of interest, generally via percutaneous puncture of the common femoral or brachial artery.

Limitations

Catheter angiography is an invasive procedure, and as such it carries with it a small but definite possibility of adverse events, including arterial injury, infection, renal or cardiac toxicity, infarction, bleeding, and idiopathic reaction to contrast media.

Indications

If transarterial needle placement for nerve block has resulted in symptomatic vascular damage, angiography is the optimal means of evaluating compromise of the lumen resulting from subintimal hematoma or creation of an arteriovenous fistula. Angiography of the spine may be necessary if other, less-invasive imaging modalities leave significant questions unanswered. Arteriovenous malformations of the spinal cord, for example, can be recognized with MRI, but the detailed anatomy can be best appreciated with angiography. Spinal dural arteriovenous fistulas or perimedullary arteriovenous fistulas are generally not well seen with MRI, because they typically occur in the thoracic region where CSF pulsation artifact is greatest. However, MRI may demonstrate accompanying signal change in the spinal cord secondary to ischemia from venous hypertension and stasis.

Noninvasive Angiography

Technology

While catheter (invasive) angiography remains the gold standard for evaluation of vascular structures, new options of noninvasive vascular evaluation are present [23]. Most commonly these include CT angiography (CTA) or MR angiography (MRA), both of which provide excellent evaluation of central and peripheral vessels (Fig. 7.18). CTA is performed using a conventional CT scanner with iodinated contrast administered intravenously while acquisition is performed in the phase when the contrast is most concentrated in the arterial structures, which optimizes evaluation of the lumen as well as the vessel wall [24]. A variety of techniques are available for using MR to evaluate vascular structures. Noncontrast MRA can be performed using "Time of Flight" (TOF) phenomena which relies movement of flowing blood to provide inflow enhancement to vascular structures. While this technique avoids the administration of contrast, it requires a small field of view and long imaging times, and image quality is limited. Therefore, contrast-enhanced MRA (CE-MRA) is preferred, in which a bolus of gadolinium-based contrast is administered intravenously. Sequences are obtained with T1 weighting.

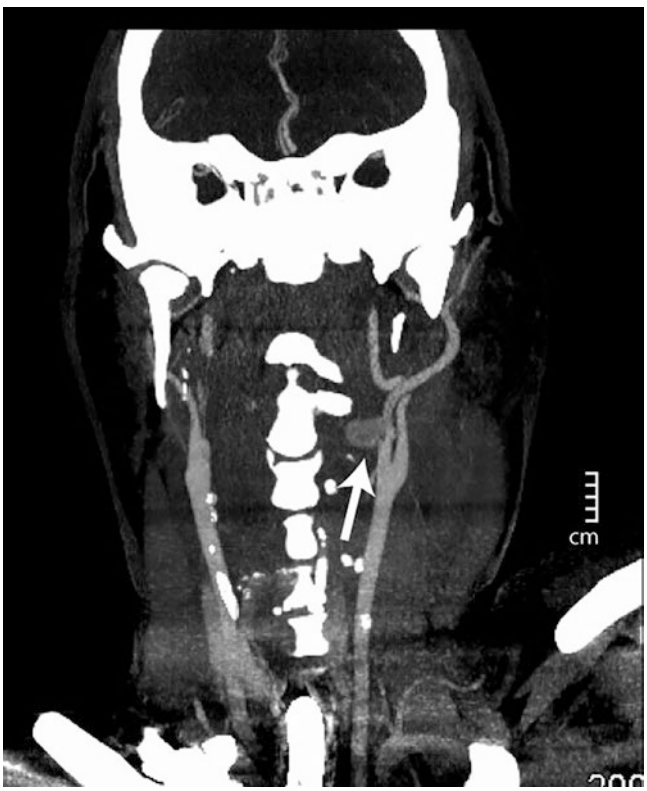

Fig. 7.18 Anterior–posterior projection image of a patient with a carotid pseudoaneurysm (*arrow*) after penetrating trauma using CT angiography (Same subject as Fig. 10.20)

Limitations

While CTA and MRA are both powerful tools for evaluating vascular pathology, they do have limitations when compared to invasive angiography, which provides better spatial resolution, and allows for intervention on an injured or occluded vessel if needed, and diagnostic criteria such as luminal pressure measurements can be obtained. Invasive angiography also has a higher temporal resolution, which allows for identification of an AV fistula.

Drawbacks of CTA include the use of iodinated contrast, radiation exposure, streak artifact, and poor bolus timing. With CTA, the angiographic phase may be missed by either imaging too early or too late, limiting evaluation of the arteries, and artifact associated with metallic implants can limit evaluation of adjacent vasculature. Drawbacks of MRA include the need for gadolinium-based contrast and patient motion. MRI is not as widely available as CT, and MRA exams are time consuming, limiting its use in critically ill or unstable patients. Exam length also requires patients to be motionless, which can be problematic with unstable or claustrophobic patients. Finally, multiple MRI artifacts can limit the diagnostic accuracy of MRA.

Indications

Indications for CTA and MRA are similar to those of conventional angiography. If there is concern for vascular injury during percutaneous needle placement, both CTA and MRA provide rapid evaluation and diagnosis. Various types of intrinsic vascular injury such as dissection, thrombosis, vasospasm, and pseudoaneurysm formation are all easily diagnosed. The presence of arteriovenous fistulas can be inferred if early venous drainage is present. Perivascular processes can be evaluated as well, such as a soft tissue hematoma.

Ultrasound

Ultrasound has several advantages over other imaging modalities including wide availability, portable equipment allowing for bedside exams, no known long-term side effects, and relatively low cost. Additionally, the spatial resolution of high frequency ultrasound probes exceeds all other cross sectional imaging modalities (CT and MRI). Another distinct advantage is the ability to obtain real-time temporally resolved images, which allows for observation of physiologic processes as they are occurring, such as turbulence and flow reversal.

Technology

The B mode (or brightness mode, also known as 2D mode), generates two-dimensional, gray scale, tomographic images. The M (Motion) mode is most commonly used in echocardiography. Color Doppler is used in the evaluation of blood vessels. Ultrasound probes use piezoelectric crystals that vibrate in response to a current and are capable of both sending and receiving sound waves. In the B mode, sound waves of a particular frequency are selected based on the depth of the structure of interest, typically ranging from 2 to 15 MHz. Higher frequency pulses are attenuated to a greater degree in the soft tissues and are generally selected for more superficial structures. Lower frequency pulses are capable of deeper penetration. Higher frequency probes have better spatial resolution. The spatial resolution of a 10 MHz probe will be 0.15 mm. In comparison, is the spatial resolution of CT is 0.3 mm, while the spatial resolution of MRI is about 1.0 mm, and digital radiography is about 0.17 mm. Penetration depth comes at the price of axial resolution. Thus, probe choice is generally based on the highest frequency that will penetrate the appropriate depth.

Whenever an emitted wave encounters a material with a differing density or acoustic impedance, a wave or echo is returned to the receiver. The acoustic impedance of a material is dependent upon its density and the velocity of wave propagation in the material. Air-containing organs such as lung have low acoustic impedance and very dense materials such as bone have high acoustic impedance. The greater the difference of the acoustic impedances of tissues the wave encounters, the larger the echo is and the brighter the structure appears on the image. Simply put, tissues through which sound waves pass easily, i.e., tissues that lack acoustic interfaces (typically fluids), do not result in echoes and therefore appear dark or hypoechoic. Tissues that have multiple interfaces and tend to reflect waves result in stronger echoes and appear bright or hyperechoic.

Temporal resolution is possible using M mode ultrasound. The time from one pulse to the next is termed the Pulse Repetition Period (PRP). Shorter pulse repetition periods (i.e., higher Pulse Repetition Frequencies) allow for increased temporal resolution. Finally, Doppler mode is very useful for vascular imaging. In Doppler mode, ultrasound pulses are reflected from moving targets, such as red blood cells. When an ultrasound wave encounters a moving target, its frequency changes based on the target's velocity. Therefore, the difference between the frequency of the transmitted pulse and the frequency of the received pulse allows calculation of the velocity of blood within the vessel.

Limitations

Sonographic waves are not able to penetrate bone, thus imaging of bony structures or organs deep to bone are not imaged well. For example, ultrasound is less useful in evaluating the adult central nervous system due to difficulties penetrating the ossified calvarium and spinal column. Additionally, ultrasound is not useful for evaluating structures deep to gas, thus limiting evaluation of the lung as well as organs located deep to gas-containing bowel, such as the pancreas. Large body habitus can also be a limiting factor, although this limits virtually all modalities to some degree. Ultrasound is also more operator dependent than other imaging modalities. Finally, retrospective review of images is more difficult in sonography because it can be difficult to determine the exact orientation in which scanning was performed.

Indications

Ultrasound guidance for blocks at the plexus and peripheral nerves levels has become routine. In these areas, evaluation of mass lesions from bleeding may be readily identified, although ultrasound has limited ability to distinguish hematoma from injected local anesthetic solution. Vascular injury may be evaluated by Doppler mode, although compared to invasive angiography and MR or CT angiography, ultrasound is less sensitive for subtle abnormalities such as dissection or subtle luminal irregularities. Ultrasound lacks adequate penetration for evaluation of the vertebral canal.

Imaging of Complications of Regional Anesthesia

Appropriate use of imaging techniques is an important aid in the evaluation of neural complications of nerve blocks. Imaging may not only confirm the presence of a mass such as abscess or hematoma but may also help in resolving more confusing diagnostic dilemmas. For instance, concurrent conditions such as spinal stenosis or herniated disc are readily apparent on CT and MRI. When possible, images from before the onset of neurologic complaints should be compared with postinjury images.

Although the optimal choice of the best imaging modality is ideally made through collaboration with a radiologist, we provide a generalized outline for how various imaging modalities might be used (Table 7.1). The best imaging modality will depend on the suspected condition. If peripheral nerve injury is suspected, MRN may demonstrate nerve

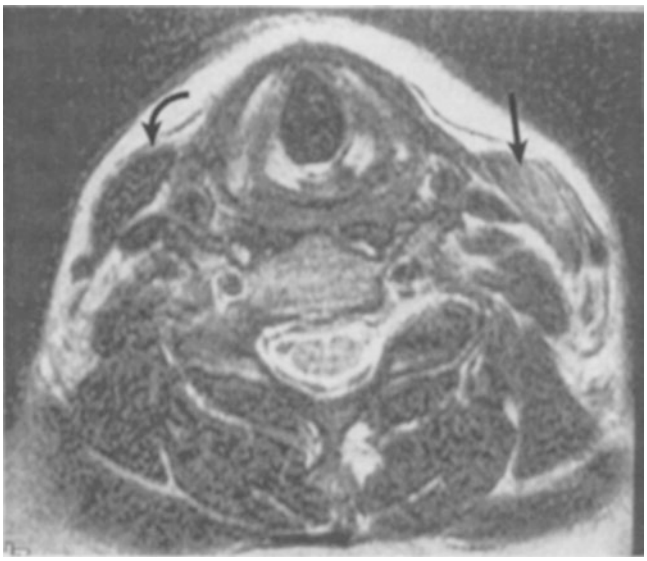

Fig. 7.19 T2-weighted axial image at the level of the sixth cervical vertebra, demonstrating local anesthetic myotoxicity. The patient had received intercostals bupivacaine 45 days before and complained of left neck pain. The left sternocleidomastoid muscle (*straight arrow*) is enlarged and shows uniformly increased signal intensity indicative of the elevated fluid content from edema

edema and/or nerve sheath expansion. MRI can also be used to evaluate for changes of muscle denervation which will appear as edema initially, atrophy in the chronic stages. If cord injection is suspected, MRI of the spine will evaluate for cord expansion or edema as well as the possibility of injection-related syrinx formation adjacent to injection. If cord infarct occurs, myelomalacia will be a chronic finding.

MRI is also useful for assessment of other spinal complications including suspected discitis, meningitis, and epidural abscess or hematoma. CSF leak can also be assessed with MRI, although CT myelogram may be more sensitive for identifying the site of the leak if contrast extravasation is visualized. Signs of arachnoiditis, which include clumping, peripheralization, and abnormal enhancement of the nerve roots, can be evaluated with MRI or CT myelogram.

Vascular injury can be assessed with ultrasound to look for hematoma or pseudoaneurysm. CTA and MRA allow for good depiction of the vessel lumen and can identify complications such as dissection and pseudoaneurysm. Imaging of suspected injury to other structures adjacent to an injection site is dependent on the site in question. MRI is good for looking for signs of muscle injury such as edema, expansion, myositis do to local anesthetic toxicity (Fig. 7.19) and compartment syndrome. Chest radiograph (upright, expiratory preferred) will evaluate for pneumothorax. Fluoroscopy (sniff test) can assess for diaphragmatic paralysis if phrenic nerve injury is suspected.

Cost may be a factor that limits the use of MRI, because CT is typically less expensive to perform. However, obtaining the correct information is almost always the predominating issue, and the cost of missing an important finding is high, so cost should rarely be an important factor in selecting the type of image. A factor favoring the use of MRI is the lack of ionizing radiation. Because the radiation dose for CT is low, this also should not be a consideration in choice of imaging.

Integration

The components of evaluation enumerated earlier need to be assembled into diagnostic and therapeutic decisions that can benefit the patient. Information gathered from these various sources is usually processed intuitively, and formulae or well-established decision pathways are not available for rare conditions such as neural injury from regional anesthesia. It is especially difficult to know when to consult other physicians or obtain elaborate tests and images. A general sequence for solving diagnostic problems begins with combining the set of positive observations into aggregate findings [25]. For example, lower extremity sensory loss and motor weakness with defective bowel and bladder control can be consolidated into the single aggregate finding of cauda equina injury. There may be a number of these aggregate findings (e.g., there might also be evidence of infection or bleeding), so the clinician must pick the most plausible condition as a hypothesis and seek confirmation of it. At this point, if the data are not persuasive or if there is more than one equally possible diagnosis, testing and consultation are considered. A final diagnosis can usually be validated by examining whether it can explain all the data.

A detailed history and physical examination are mandatory when a neural injury is discovered after regional anesthesia, which often results in a more reliable diagnosis. The decision of when to obtain consultation and diagnostic studies, however, is often unclear. Tests and consultations are only helpful if the information would change treatment, and the nature of the suspected diagnosis usually dictates whether studies should be obtained. Diagnoses with critical therapeutic implications should be pursued with the greatest intensity. A case in point is when the possibilities include epidural abscess or hematoma, which if not surgically relieved can lead to permanent and extensive neural injury and threaten life. Therefore, consultation and imaging are strongly recommended early in the workup if severe polyradiculopathy or myelopathy is evident. In contrast, identification of a mild neural injury to a peripheral nerve, or a mild monoradiculopathy following neuraxial injection, does not have as clear a therapeutic implication, so circumstances in which these are suspected might be pursued with less urgency, particularly with regard to intensive or invasive examination. If a neural defect is persistent or intense, studies may need to be pursued.

It is necessary to avoid focusing on only anesthetic causes of injury to the exclusion of alternative causes. If vascular occlusion is the cause of neural dysfunction but has been neglected

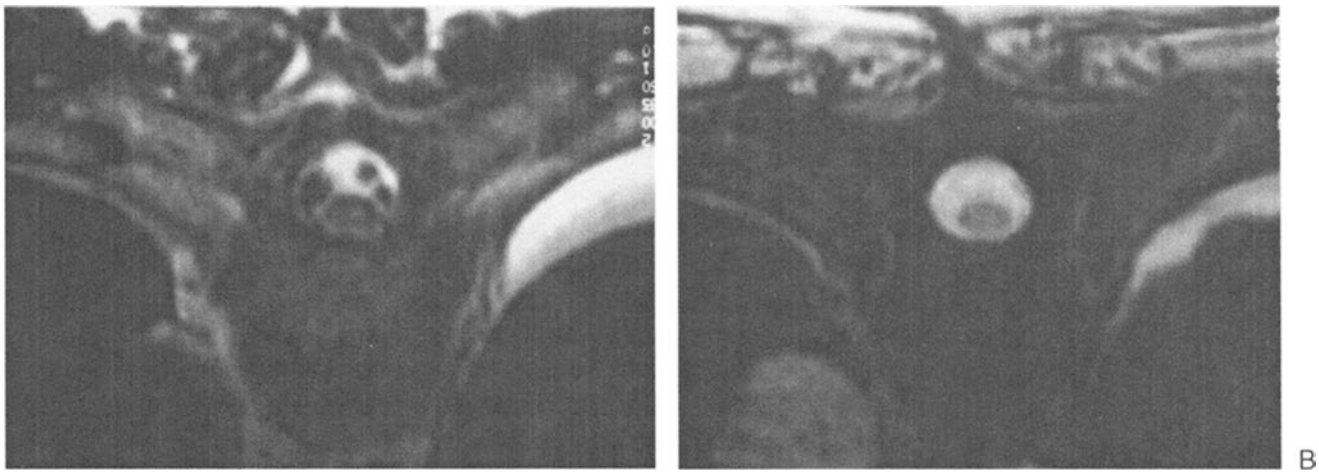

Fig. 7.20 (**a**) T2-weighted axial image through a thoracic vertebra, showing bright CSF and areas in the CSF of uncertain origin (see text). (**b**) Repeat image of same patient and level, using a different T2-weighted pulse sequence technique (gradient echo) less susceptible to flow artifact. The CSF is now uniform and without masses, and the cord appears normal

as an etiologic possibility, an opportunity for successful treatment may be missed. A sense of responsibility may ironically lead the anesthesiologist astray. Finally, there may be social reasons for obtaining diagnostic consultation or tests. The patient may only be satisfied by detailed workup, and legal considerations are an unavoidable fact of medical life.

Clarity and completeness of communication directly affects the quality of the information gained from consultation and tests. This usually requires discussion with the consultant (e.g., neurologist, neurosurgeon, neuroradiologist) because details may be incompletely available from the medical record, and few clinicians know how to interpret (or even find) anesthesia and recovery room notations. The key issue of accurate and complete communication is illustrated by a case:

An elderly man received epidural anesthesia as a component of his anesthetic for retropubic prostatectomy and node excision that lasted 7 h. The blockade, initiated before induction of general anesthesia, was uneventful, but dense and uniform sensory and motor dysfunction of the lower extremities persisted 12 h after the final 0.5 % bupivacaine injection. Fearing an epidural hematoma, MRI of the lumbar vertebral column was requested with the reason for imaging stated as "neurologic abnormality, rule out hematoma." The image (Fig. 7.20a) was interpreted as showing an abnormality, possibly hematoma or artifact. The epidural catheter was removed and surgical consultation pursued. Further imaging 3 h later (Fig. 7.20b) confirmed that the area of increased signal intensity was flow artifact by CSF motion; by this time, the block was beginning to recede.

Had the radiologist more completely understood the indication for imaging, it would have been clear that epidural bleeding was the suspected condition and that an intrathecal abnormality was only a remote diagnostic consideration. The images would have been interpreted as not supportive of hematoma as the etiology of the neurologic condition, and artifact would have been the more strongly suspected source of the abnormal image. Similarly, direct discussion between the anesthesiologist and radiologist after obtaining the initial images would have made clear the strong likelihood that the study was normal, avoiding consternation and disruption of care. The consultation should indicate what is being looked for, rather than simply specifying the test to be done. Finally, discussion can indicate the necessary degree of urgency, and because an iatrogenic condition is being sought, direct discussion may avoid injudicious wording of the written report.

There are adverse consequences from obtaining excessive diagnostic studies. Apart from the obvious considerations of complications from the procedures and cost, identification of more minor defects as resolution of tests is improved leads to the risk of overtreating insignificant conditions [26]. Additionally, false-positive results can lead to pursuit of an irrelevant diagnosis. Despite these concerns, imaging and neurophysiologic study are helpful in most cases when neurologic injury follows regional anesthesia.

Acknowledgement We thank Dr. Paul Barkhaus M.D. for his valuable input in writing this chapter.

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Regional Anesthesia and Anticoagulation

8

Robert B. Bolash and Richard W. Rosenquist

Key Points

- Bleeding complications following regional anesthesia are an uncommon but real concern, and are dependent on patient- and procedure-specific factors.
- A thorough patient history is necessary to identify any preexisting coagulopathy, use of anticoagulants or other agents which may exacerbate bleeding concomitant with regional anesthesia procedures.
- It is expected that regional anesthesiologists will increasingly encounter patients treated with popular anticoagulant drugs, including NSAIDs, warfarin, heparin, and ADP receptor blockers, as well as newer anticoagulants and other agents affecting coagulation (e.g., SSRIs/SNRIs), as more elderly individuals undergo surgery.
- Not only do we need to be very knowledgeable about newer developments in the ever changing world of anticoagulation, we also need to temper our enthusiasm for performing invasive procedures on patients who are at high risk for bleeding complications.

Abbreviations

ASRA	American Society of Regional Anesthesia and Pain Medicine
INR	International normalized ratio
PT	Prothrombin time
PTT	Partial thromboplastin time
SNRI	Serotonin norepinephrine reuptake inhibitors
SSRI	Selective serotonin reuptake inhibitors

R.B. Bolash, MD • R.W. Rosenquist, MD (✉)
Department of Pain Management, Cleveland Clinic,
9500 Euclid Ave/C25, Cleveland, OH 44195, USA
e-mail: bolashr@ccf.org; rosenqr@ccf.org

Introduction

There is a widespread conviction among anesthesiologists that regional anesthesia offers advantages over general anesthesia in select clinical settings. At the same time, the fear of bleeding complications attributed to performance of a neuraxial anesthetic or peripheral nerve block in a patient with a pathologic or pharmacologically induced coagulopathy is held with almost equal intensity. Despite a growing body of evidence describing bleeding complications associated with regional anesthetics, our understanding of the numerous factors leading to these complications remains limited. With the advent of newer pharmacologic agents that impair the physiologic coagulation cascade, both regional anesthesiologists and interventional pain physicians are required to maintain an understanding of the mechanism of action, half-life, cautions, and contraindications associated with the use of an ever-increasing number of anticoagulants.

Auroy et al. described the risk of complications related to regional anesthetics as lower than 5 in 10,000 patients in a series of patients who received spinal, epidural, and peripheral nerve blocks (2002) [1]. In the case of spinal or epidural hematoma, the relative risk has been quantified as 1:220,000 and 1:150,000, respectively, a rate that approaches the risk of general anesthesia [2]. However, the risk of neurologic complications after a neuraxial block is markedly elevated (1:1800) in patients with risk factors such as female sex, osteoporosis, or concomitant use of anticoagulants [3]. As efforts to reduce the risk of clinically relevant venous thromboembolism have increased, the consultant anesthesiologist or interventional pain physician has become increasingly involved in the clinical decision making, choice, and timing of the administration of neuraxial and regional anesthetics to mitigate the risk of bleeding complications.

Despite the relatively infrequent incidence of complications related to regional anesthesia, fear of bleeding complications exceeds the incidence of occurrence. With the advent of newer anticoagulants, increase in surgical volume, and aging of the

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_8

population, a growing familiarity with the risks associated with administering regional anesthetics or performing interventional pain procedures has become a vital part of the perioperative assessment. Anesthesiologists are becoming increasingly involved in providing a risk assessment to patients as well as other clinicians and are being called upon to collaborate on the timing and choice of anticoagulants alongside surgical and medical colleagues. While guidelines exist from the American Society of Regional Anesthesia and Pain Medicine (ASRA), the European Society of Regional Anesthesia and Pain Therapy (ESRA), the European Society of Anesthesiology (ESA), and the Scandinavian Society of Anesthesiology and Intensive Care Medicine, among others, such recommendations are based upon reported retrospective incidence or expert opinion rather than prospective data [4–7]. These statements serve as guidelines rather than a dictum for clinical decision making and, in most cases, omit patient- or surgical-related nuances underscoring the continued need for a comprehensive patient assessment and thoughtful physician judgment. The most recent guidelines addressing interventional pain procedures makes a specific attempt to tailor the guideline recommendations to specific interventional procedures and medication use [7].

Conversely, in the event of an adverse bleeding event, marked deviation from the standard of care or established guidelines positions the physician that performed the procedure unfavorably in medicolegal proceedings when documentation of the reason for a clinical decision is absent from the medical record.

Bleeding Complications

The potential risk of bleeding complications resulting from the performance of regional anesthesia is readily apparent given the near-universal association of nerve plexuses with vascular bundles containing both arterial and venous structures. Complications related to bleeding include minor oozing or bruising at the site of needle insertion to significant blood loss necessitating transfusion. The degree of concern for complications is directly related to the size of the needle, the number of times a vascular structure or tissue is punctured, the use of a catheter, the ability to compress the vessel, and any underlying coagulation abnormalities. Blood vessel trauma occurred in as many as 28 % of patients whose epidural space was accessed at L2–L3 using a 17G Tuohy needle, yet the incidence of a clinically relevant bleeding complication associated with this trauma occurs significantly less often [8]. Major bleeding related to the performance of regional anesthesia has resulted in persistent Horner's syndrome, peripheral nerve injury, hematoma formation, and blood loss requiring transfusion. The potential for clinically significant blood loss or hematoma-related complications are increased by the presence of inherent coagulation abnormalities or medically administered anticoagulants.

Ekatodramis et al. reported two cases of prolonged Horner's syndrome attributed to hematoma formation after a continuous interscalene block [9]. Several authors have reported peripheral nerve or brachial plexus injuries related to hematoma formation during axillary brachial plexus blocks [10–13]. In the case of lumbar plexus blocks, renal subcapsular hematoma, and psoas hematomas with and without neurologic complications, and with and without anticoagulants have been reported [14–18]. A case report by *Nielsen* describes bleeding after a series of intercostal nerve blocks performed for analgesia after cholecystectomy in an 80-year-old male receiving heparin [19]. After the fourth set of blocks, the patient's hematocrit decreased from 33–40 to 20 and eventually to 15 and transfusion of 8 units of packed red blood cells was needed to maintain a hematocrit above 30. The small hematoma that developed after the third set of injections expanded to cover a 30 × 65 cm area. Though the patient had no long-term sequelae, he developed pain in the right flank and hip for 4 weeks in the area of the hematoma. It is unknown if this complication could have been avoided if heparin was not being concomitantly administered.

Quantifying Risk

Prior to injection, it is vitally important that any history of coagulation abnormality be ascertained and that it be determined if medications or oral dietary supplements are being taken that can affect coagulation. Until recently, clinicians had adopted the ASRA guidelines broadly to direct perioperative and periprocedural administration of pharmacologic anticoagulation. Of late, guidelines have been expanded at the request of practicing regional anesthesiologists and interventional pain physicians to stratify anticoagulation risk based upon procedural subtype recognizing that large bore cannulation of the spinal neuraxis likely poses a risk greater than an intramuscular injection or peripheral nerve block in a readily compressible area with a small gauge needle [7]. Common pain procedures are now classified according to the potential risk for serious bleeding and determined to pose high, medium, or low risk (Table 8.1).

The guidelines writing committee recognized the additional risk attributable to advanced age, historical bleeding tendencies, advanced hepatic disease, and renal insufficiency. In the presence of one or more of these known risk factors, patients who would initially fall into a low-risk category should be advanced to an intermediate-risk category, and intermediate-risk patients should be advanced to the high-risk category [7]. Surgical history should also be considered in providing a risk assessment since fibrous adhe-

Table 8.1 Classification of pain procedures according to the potential risk for serious bleeding complications

High-risk procedures	Intermediate-risk procedures	Low-risk procedures
• Spinal cord stimulation trial and implant	• Interlaminar epidural steroid injections	• Peripheral nerve blocks
• Intrathecal catheter and pump implant	• Transforaminal epidural steroid injections	• Peripheral joint and musculoskeletal injections
• Vertebral augmentation (vertebroplasty and kyphoplasty)	• Facet medial branch nerve blocks and radiofrequency ablation	• Trigger point injections
• Epiduroscopy and epidural decompression	• Paravertebral blocks	• Piriformis muscle injections
	• Intradiscal procedures	• Sacroiliac joint injection and sacral lateral branch blocks
	• Sympathetic nerve blocks	
	• Peripheral nerve stimulation trials and implants	
	• Pocket revisions for IPG or ITP replacement	

Adapted from Narouze et al. [7]

sions can develop after spine surgery thereby distorting the anatomy of the epidural vessels, potentially increasing the likelihood of bleeding complications due to development of scar tissue that compromises the capacity of the epidural space [7]. For the sum of these variables, a comprehensive assessment of bleeding risk should account for both procedural and patient-specific variables, and necessitates physician judgment rather than rote categorization.

Pharmacologic Anticoagulation

Increases in population longevity, increased surgical volume, the broader indications for the use of anticoagulant therapies, the increased utilization of regional anesthesia and interventional pain procedures for the treatment of both acute and chronic pain conditions place regional anesthesiologists and interventional pain physicians into a consultant role for anticoagulated patients in the perioperative and periprocedural periods. Though there is no substitute for clinician judgment, a broad understanding of the indications, mechanism of action, half-life, and general recommendations about the use of anticoagulants is warranted for each agent.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) exert their analgesic effects by blunting prostaglandin production and inhibiting cyclooxygenase. Cyclooxygenase-1 (COX-1) is constitutively expressed while Cyclooxygenase-2 (COX-2) is induced in the presence of inflammation. Platelet function is affected when NSAIDs exert their effect on COX-1 preventing the formation of prostaglandin H_2. Commonly utilized NSAIDs include salicylates, cyclooxygenase nonspecific agents, and COX-2 selective NSAIDs.

Aspirin

Aspirin is taken by more than 50 million Americans for the prevention of cardiovascular events and utilized considerably less often for pain in light of the advent of an expanding pharmacopeia of alternative analgesic agents [20]. Aspirin has an irreversible affinity for COX-1 and blocks the production of thromboxane for the entire 7–10 day life span of a platelet [21]. Platelet aggregation and thrombosis is inhibited within hours of aspirin administration [22]. Support exists for the ongoing use of aspirin in patients to prevent recurrence of cardiovascular events, termed secondary prevention, and cessation of chronic salicylate use demonstrates an increased risk of cardiovascular events in these subjects [23–25]. This is attributed to a "rebound phenomenon" wherein thromboxane production increases and fibrinolysis decreases when chronic aspirin therapy is discontinued. Because 10 % of the platelet pool is replenished each day, complete restoration of platelet function does not occur until 10 days after cessation of aspirin therapy, though significant variability has been observed among clinical subsets. While low-dose aspirin was shown to increase the incidence of bleeding by a factor of 1.5, it did not lead to adverse clinical outcomes outside of intracranial surgery in a large review and meta-analysis [26]. Nonetheless, isolated case reports and case series implicate aspirin in the development of bleeding complications associated with spinal cord stimulator lead placement, removal, or spinal anesthetic injections [27–30].

Patient-related and procedural risk stratification should occur prior to modifying chronic salicylate therapy in light of the prothrombotic rebound phenomenon. Routine discontinuation of aspirin should be avoided for procedures characterized as low risk (Table 8.1). A shared assessment and risk stratification should occur for intermediate-risk procedures, especially when known vascular anomalies occur in close

proximity to the target, such as a variant course of the vertebral artery seen on cervical imaging prior to performing a stellate ganglion block. For intermediate-risk procedures in patients where aspirin is prescribed for secondary prevention, discontinuation of chronic salicylate therapy should represent the exception rather than the rule, and be supported by documentation indicating the reason for cessation of therapy. In high-risk procedures, an assessment of the indication for chronic salicylate therapy should be made; specifically, is the agent prescribed for primary or secondary cardiac prevention. Recognizing the importance of aspirin as a secondary preventive, a shared assessment and risk stratification should occur in conjunction with the managing physician and the proceduralist or consultant anesthesiologist. Among patient's prescribed chronic salicylate therapy for primary prevention undergoing a high-risk procedure (as classified in Table 8.1), chronic salicylate therapy should stop 6 days prior to performing the elective interventional procedure and can be resumed 24 h after conclusion of the procedure. In patient's prescribed chronic salicylate therapy for secondary prevention undergoing a high-risk procedure, chronic salicylate therapy should terminate only 4 days prior to performing an elective interventional procedure and can be resumed 24 h after conclusion of the procedure [7].

Nonaspirin NSAIDs

Nonaspirin NSAIDs reversibly inhibit cyclooxygenase, and the degree of inhibition of COX-1 parallels the increase of periprocedural bleeding risk. Because nonaspirin COX-1 NSAIDs inhibit platelet function reversibly, resumption of physiologic coagulation is dependent on the terminal half-life of the NSAID. NSAIDs such as meloxicam or etodolac have a stronger inhibitory effect on the COX-2 pathway and have a theoretical advantage of mitigating bleeding risk when compared to nonselective agents [31]. The COX-2 selective agent celecoxib does not inhibit platelet aggregation or hemostasis at therapeutic or supratherapeutic clinical doses and does not increase surgical blood loss [32–35]. Neither acetaminophen nor celecoxib requires dose modification prior to administering a regional anesthetic or performing an interventional pain procedure deemed high, medium, or low risk.

Because NSAIDs do not confer a cardiac or cerebrovascular protective advantage, these agents can be readily stopped without consideration of their effects on cardiac or cerebrovascular risk prevention. For procedures stratified as posing an intermediate or low risk of bleeding (as classified in Table 8.1), no modification of chronic NSAID therapy is indicated prior to, or following, performance of an interventional pain procedure or administering a regional anesthetic.

Table 8.2 Recommendations for the duration of cessation of chronic NSAID therapy in patients undergoing high-risk elective interventional pain procedures

NSAID	Approximate duration of five half-lives (days)
Diclofenac	1
Ketorolac	1
Ibuprofen	1
Etodolac	2
Naproxen	4
Meloxicam	4
Nabumetone	6

Adapted from Narouze et al. [7]

Nonaspirin NSAIDs should be discontinued prior to performing an elective high-risk interventional pain procedure based on the specific half-life of the agent. In general, a five half-life recommendation should be followed based upon the terminal pharmacokinetic elimination of agents at a steady state [7]. Table 8.2 provides an indication of the duration of NSAID cessation prior to performing a high-risk elective interventional pain procedure. NSAID therapy can be resumed 24 h following completion of the procedure.

Warfarin

Warfarin affects coagulation by inhibiting the gamma carboxylation of the Vitamin K-dependent coagulation Factors II, VII, IX, X, Protein C, and Protein S. Because Factor VII has the shortest half-life, the initial anticoagulant effects following a single dose of warfarin are attributable to depletion of Factor VII [36]. With ongoing use, all of the Vitamin K-dependent factors are inhibited once a steady-state drug concentration is reached. Response to warfarin dosing is heterogeneous and wide variations in therapeutic response are exhibited among treated patients, implicating warfarin as a notoriously challenging drug to initiate and maintain. This is compounded by the relatively narrow therapeutic index required for efficacy of this agent [37]. It is known that select patient subsets, including the elderly and women, require less warfarin to achieve a therapeutic INR, though significant variability still occurs among matched patients [38].

A spinal hematoma developed after a single dose of warfarin administered in advance of neuraxial anesthetic placement in at least one elderly female undergoing total knee arthroplasty, though other authors posit that safe levels of hemostasis are observed during the first 12–16 h following warfarin administration [36, 39]. When considering a change to therapeutic anticoagulation, a procedure-related bleeding risk assessment should be carried out as described in Table 8.1. For low-risk procedures, several authors believe that these injections can be performed in the pres-

Table 8.3 Commonly encountered anticoagulants and recommended period of abstinence for interventional procedures deemed high, intermediate, or low risk

Drug	Time interval to stop agent prior to procedure			Time to restart agent
	High bleeding-risk procedures[a]	Intermediate-risk procedures[a]	Low-risk procedures[a]	
Aspirin	Primary prophylaxis: 6 days	Shared risk assessment	No	24 h
	Secondary prophylaxis: shared risk assessment			
NSAIDs	See Table 8.2	No	No	24 h
Warfarin	5 days, normalized INR	5 days, normalized INR	Shared risk assessment	24 h
Subcutaneous heparin	8–10 h	8–10 h	8–10 h	2 h
Low-molecular-weight heparin: prophylactic dosing	12 h	12 h	12 h	12–24 h for medium-/high-risk procedures
				4 h for low-risk procedures
Low-molecular-weight heparin: therapeutic dosing	24 h	24 h	24 h	12–24 h for medium-/high-risk procedures
				4 h for low-risk procedures
Clopidogrel	7 days	7 days	No	12–24 h
Prasugrel	7–10 days	7–10 days	No	12–24 h
Apixaban	3–5 days	3–5 days	Shared risk assessment	24 h
Dabigatran	4–5 days +	4–5 days[**]	Shared risk assessment	24 h
Rivaroxaban	3 days	3 days		24 h
SSRI/SNRI	Shared risk assessment	No	No	

Adapted from Narouze et al. [7]
[**]6 days recommended in the presence of renal insufficiency
[a]Bleeding risk assessment as defined in Table 8.1

ence of a therapeutic INR <3.0, while others recommend a shared assessment be undertaken with the prescribing physician and the interventionalist [7, 40, 41]. A careful discussion of risk, benefits, and alternatives should be undertaken in all cases prior to performing intermediate- and high-risk procedures. Typically, warfarin should be stopped for 5 days prior to performance of an intermediate- or high-risk procedure, and an International Normalized Ratio should be quantified in advance of the injection. In patients who are at high risk for thrombus formation, consideration can be made for "bridge therapy": a technique wherein a short-acting low-molecular-weight heparin is initiated in the interim when warfarin levels are waning. By utilizing an agent with a short half-life, the abstinence period of therapeutic periprocedural anticoagulation is shortened. Following low-, intermediate-, or high-risk procedures, warfarin therapy can be restarted 24 h after completing the interventional procedure (Table 8.3).

Heparins

Clinically used heparins are available in an unfractionated or a low-molecular-weight form (enoxaparin, dalteparin) and can be administered subcutaneously or intravenously. Unfractionated heparin inactivates Factor IIa, Factor Xa, and Factor IXa and its anticoagulant effect can be reversed with the administration of protamine [6]. The incidence of spinal hematoma is increased when patients are heparinized within 1 h of dural puncture, are administered aspirin concomitantly, or experience a traumatic dural puncture [42]. ASRA recommends that intravenous heparin be stopped 2–4 h prior to a neuraxial intervention, and that heparin be avoided for at least 1 h after placement or removal of a neuraxial catheter [6, 43]. Regional anesthesiologists are more likely to encounter patients treated with intravenous heparin than their interventional pain physician counterparts given the typically elective nature of chronic pain procedures. Intravenous heparin should be stopped for 4 h prior to a low-, medium-, or high-risk procedure as defined in Table 8.1. Subsequently, intravenous heparin can be restarted as soon as 2 h following the procedure, or 24 h later if an intermediate- or high-risk procedure was performed and the neuraxial intervention was noted to be bloody [7]. Subcutaneous heparin at a dose of 5000 units 2–3 times a day inhibits coagulation via factor Xa. The anticoagulant effects of subcutaneous heparin are observed within 1 h of administration and dissipate 6 h later. In most subcutaneous heparin dosing regimens, the PTT remains within the normal range, and the ASRA guidelines do not dictate a contraindication to placement of neuraxial anesthetics on

patients receiving subcutaneous heparin [6, 44]. Despite this observation, at least two cases of spinal hematoma have been reported in patients receiving subcutaneous heparin [45, 46]. For this reason, in parallel with the elective nature of interventional pain procedures, the consensus committee broadly recommends an 8–10 h period of abstinence from subcutaneous heparin prior to an interventional procedure deemed low, medium, or high risk. Subsequently, subcutaneous heparin can be restarted 2 h following the injection (Table 8.3) [7].

Low-molecular-weight heparin has a more predictable bioavailability than standard heparin and demonstrates a dose-dependent antithrombotic effect mediated by the inhibition of Factor Xa. Rarely is laboratory monitoring of factor Xa activity required because of predictable bioavailability, making low-molecular-weight heparin comparatively easy to dose when compared to conventional unfractionated heparin. Low-molecular-weight heparins can be administered once daily or every 12 h for thromboembolic prophylaxis or therapeutic anticoagulation, respectively. A cumulative review of data demonstrates increased risk of bleeding complications in conjunction with low-molecular-weight heparins among females, the elderly, those with anomalies of the spinal cord or vertebral column, renal insufficiency, those with an indwelling catheter, or those in whom neuraxial cannulation was difficult or bloody [3, 47]. The ASRA guidelines recommend a 12 h interval after prophylactic low-molecular-weight heparin is administered before performing a neuraxial intervention or a 24 h period of abstinence if therapeutic anticoagulation doses are utilized. If blood is encountered during the placement of a neuraxial anesthetic, the guidelines recommend abstaining from a subsequent dose of low-molecular-weight heparin for an additional 24 h (Table 8.3). Should a neuraxial catheter be utilized, a minimum interval of 4 h should elapse before removing the neuraxial catheter based upon an FDA Safety Communication published since the 2010 ASRA guidelines [6, 48]. More conservatively, and supported by a multispecialty group, 12 h should elapse between dosing prophylactic low-molecular-weight heparin and the performance of procedures dictated as low, intermediate, or high risk. Similarly, an additional 12 h should elapse between resuming low-molecular-weight heparin. When therapeutic low-molecular-weight heparin dosing is utilized, a period of 24 h should elapse prior to, and following procedures characterized by low, intermediate, or high risk [7].

ADP Receptor Blockers

The active metabolites of clopidogrel and prasugrel irreversibly block ADP receptors on the platelet surface, thereby preventing activation of the GPIIb/IIIa receptor complex and reducing platelet aggregation. These agents are becoming increasingly adopted in the treatment of coronary vascular disease, cerebrovascular ischemia, and peripheral vascular disease. Because these agents offer cardiac and/or cerebrovascular protection, there remains risk with abrupt discontinuation of ADP receptor blockers, and an assessment of the bleeding risk posed by the interventional procedure should be quantified as dictated in Table 8.1. For low-risk procedures, no change to the dosing strategy is indicated prior to or following the injection. Prior to undertaking a medium- or high-risk procedure, consultation with the prescribing physician should provide a bleeding risk assessment and account for age, comorbidities, and concomitant antiplatelet agents administered in conjunction with the ADP receptor blocker [49]. Among most patients slated for a medium- or high-risk procedure (Table 8.3), a period of clopidogrel abstinence spanning 7 days should precede the injection. Among patients deemed high risk for thromboembolic event and undergoing a medium or high bleeding risk injection, a 5-day clopidogrel abstinence period should precede the administration of a regional anesthetic or interventional pain procedure. Following the injection, 12 h should elapse before resuming the usual daily dose of clopidogrel. Among patients undergoing medium- or high-risk procedures on prasugrel, the abstinence interval should span 7–10 days [7].

Newer Anticoagulants

A new generation of anticoagulants continues to enter the marketplace and carry the advantage that INR monitoring is not routinely required. These agents, including apixaban, dabigatran, and rivaroxaban, are not subject to fluctuating pharmacodynamics based upon dietary intake, and there are no specific antagonists to universally reverse the anticoagulant effects of these agents [50–52]. Like warfarin, these newer anticoagulants confer cardiac protection and may pose a risk of thrombosis during a period of abstinence (Table 8.3); hence a careful assessment in collaboration with the prescribing physician is indicated prior to performing an elective regional anesthetic or recommending changes to the chronic use of these agents. Because of the relatively recent introduction of these newer anticoagulants, a substantial body of clinical evidence demonstrating bleeding risk is absent from the literature, though this should not be misinterpreted as a demonstration of their long-term safety given that the incidence of spinal or epidural hematomas is infrequent, and an incident case may not have yet manifested. In the absence of a substantial body of data, the broad recommendation is to discontinue the agent for five half-lives prior to an injection carrying bleeding risk. The ideal time to resume these anticoagulant agents following a neuraxial injection is also unknown, though authors typically recommend a 24–48 h interval following the interventional procedure [50, 53, 54].

Apixaban is a Factor Xa inhibitor, which is rapidly absorbed and demonstrates a half-life of 12–15 h [55, 56]. PT and PTT are unchanged with apixaban therapy, and though a Factor Xa assay can indicate efficacy, it is not used in routine clinical practice. Apixaban therapy may prove superior to aspirin for the prevention of stroke or systemic embolism [57]. A conservative estimate of five half-lives of apixaban corresponds with a 3-day period of abstinence prior to performing an intermediate- or high-risk injection. A shared risk assessment is advocated for patients undergoing low-risk procedures. Among those deemed to pose significant thrombotic risk, the period of abstinence (Table 8.3) can be shortened to two half-lives. Twenty-four-hours should elapse between an interventional pain procedure and the resumption of apixaban.

Dabigatran is a direct thrombin inhibitor indicated for stroke prevention in patients with nonvalvular atrial fibrillation and is utilized as a preventative for venous thromboembolic disease in total joint arthroplasty [58–60]. Dabigatran demonstrates a half-life between 14 and 17 h and is cleared via renal elimination [61, 62]. PTT increases nonlinearly with Dabigatran, and thrombin time demonstrates only binary efficacy of the agent [63–65]. When quantification of clinical effect is required, ecarin clotting time measures thrombin activity and serves as a linear surrogate for the efficacy of dabigatran's effect [64]. A reversal agent for dabigatran has yet to come to market [66]. Recommendations for discontinuation of dabigatran prior to an intermediate- or high-risk interventional procedure, as defined in Table 8.1, correspond with five half-lives of the agent, or 4–5 days. When a low-risk procedure is being considered, authors recommend a shared assessment be undertaken with the prescribing physician and a two half-life interval elapse prior to administering a regional block. Dabigatran can be resumed at 24 h after performing the interventional pain procedure [7].

Rivaroxaban is also a direct factor Xa inhibitor with a rapid onset and a half-life ranging from 6 to 13 h [67–70]. Rivaroxaban is renally eliminated and indicated for the treatment of symptomatic venous thromboembolic disease and in the prevention of embolic stroke in patients suffering with atrial fibrillation [71, 72]. Though the agent possesses a black box warning against its use in patients with neuraxial anesthesia, no case reports of spinal or epidural hematoma have been reported in patients receiving rivaroxaban. Therapeutic efficacy is correlated with prothrombin time [63, 64]. Prior to performing neuraxial interventional pain procedures in patients treated with rivaroxaban, five half-lives, or 3 days should elapse. In those undergoing procedures deemed low risk, as indicated in Table 8.1, a shared discussion with the prescribing physician should be undertaken, and consideration of shortening of the period of abstinence to two half-lives may be considered in patients at significant thrombotic risk (Table 8.3). In all cases, 24 h should elapse before resuming rivaroxaban following an interventional procedure where the agent was stopped.

Additional Agents Effecting Coagulation

Therapeutics prescribed as adjunctive analgesics may also impart effects upon the coagulation cascade. Selective serotonin reuptake inhibitors (SSRI) and serotonin–norepinephrine reuptake inhibitors (SNRI) are widely used in select chronic pain conditions. These agents have been associated with an increase in bleeding risk that is not seen with tricyclic antidepressants [73]. The proposed mechanism of SSRI/SNRI-mediated bleeding is depletion of platelets' serotonin-mediated aggregation factors [74]. This observation has prompted a recommendation that interventionalists performing high bleeding risk procedures as outlined in Table 8.1, engage in a shared decision-making process with the prescribing physician or psychiatrist if the patient also has concomitant use of aspirin, NSAIDs, or other antiplatelet agents. Consideration for discontinuation should also quantify the risk of worsening depression or suicidality. Thus, the vast majority of patients undergoing interventional procedures, including high bleeding risk injections will require no change to their chronic SSRI/SNRI therapy. The abrupt discontinuation of SSRI/SNRIs can provoke a "discontinuation syndrome" which is manifested by flu-like symptoms, irritability, agitation, gastrointestinal upset, and sleep disturbance. When discontinuation of SSRI/SNRIs is indicated by collaborative discussions with the mental health provider and the interventionalist, a period of 1–2 weeks is required. The exception is fluoxetine which exhibits a longer terminal half-life and requires a washout period of 5 weeks [75–77].

Complementary and alternative medicines including herbal therapeutics are increasingly used with select compounds affecting coagulation. Patients often do not report the use of these agents due to the fear of stigmatization by allopathic physicians. The absence of standardized dosing of these agents and uncertain purity of these compounds leave the physician with even greater uncertainty. A recent consensus statement provided guidance on several agents with specific cautions noted for garlic, dong quai, danshen, gingko, and ginseng. Garlic inhibits platelet aggregation by reducing the formation of thromboxane and inhibiting phospholipase. The anticoagulant affect is dose dependent, though no studies quantify the impact of garlic's adverse effects on bleeding. Broadly, a platelet function test is recommended in those consuming greater than 1000 mg per day, or those who concomitantly use aspirin, NSAIDs, or SSRI/SNRIs [7]. Dong quai is a dried root utilized in Chinese medicine for menstrual cramps and premenstrual syndrome has gained the nickname "female ginseng." The anticoagulant effect of dong quai is attributable to its coumarin-like effect, and patients who concomitantly ingest dong quai with warfarin should have their INR quantified prior to proceeding with an interventional procedure [78]. Danshen is used as a positive inotrope, negative chronotrope, and coronary vasodilator that also inhibit platelet aggregation. Though the mechanism

of anticoagulation action exhibited by danshen is unknown, concomitant use with warfarin has demonstrated an increase in the INR prompting an assessment of INR in patient's concomitantly taking warfarin and danshen should be undertaken [7, 79]. Gingko is utilized as a treatment for memory impairment and vascular claudication. Gingko exerts its effect by inhibiting platelet activation factor [80]. A recent consensus guideline broadly recommends that platelet function be assessed when gingko is concomitantly administered with aspirin, NSAIDs, and SSRI/SNRIs [7].

Conclusions

Consultant anesthesiologists, regional anesthesiologists, and interventional pain physicians are likely to be confronted with a continually expanding pharmacopeia of anticoagulants and challenged with growing numbers of agents that possess anticoagulant effects. This evolution has broadened the interventionalist's scope of practice and now necessitates additional vigilance and familiarity with the broadening number of anticoagulants. As patients' life span increases, the diversity of pharmacotherapy expands and comorbidities compound in patients undergoing broader numbers of surgical procedures, familiarity with established and emerging anticoagulant therapies will become an increasing part of clinical practice. This places the proceduralist into a consultant role, necessitating careful consideration of the risks, benefits, and alternatives to both the choice of anesthetic or regional analgesic, and the decision to continue or alter chronic anticoagulation therapy.

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Infection in Association with Local and Regional Anesthesia

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Terese T. Horlocker, Denise J. Wedel, and Adam D. Niesen

Key Points

- Infections associated with regional anesthesia may be more prevalent than previously thought and are associated with various risk factors. In general, central neuraxial block should not be performed in patients with untreated systemic infection except in the most extraordinary circumstances.
- Strict adherence to aseptic technique, including masks and gloves, skin disinfection, and maintaining sterility of equipment, is critical to avoid infection and colonization of potentially harmful bacteria.
- Epidural abscess is most likely to occur in immunocompromised patients with prolonged durations of epidural catheterization, with the most common causative organism being *S. aureus*. In contrast, meningitis following neuraxial blockade occurs more frequently in healthy individuals who have undergone uneventful spinal anesthesia.
- In general, neuraxial blocks in patients with preexisting viral disease (herpes, HIV) or who are immunocompromised are safe; however, the usual precautions and safety measures are still recommended.
- The patient care team must be vigilant of any signs or symptoms of infection so that the source can be identified and treatment be initiated as early as possible.

Introduction

Infectious complications may occur after any regional anesthetic technique but are of greatest concern if the infection occurs around the spinal cord or within the spinal canal. Possible risk factors include underlying sepsis, diabetes, depressed immune status, steroid therapy, localized bacterial colonization or infection, and chronic catheter maintenance. Bacterial infection of the central neural axis may present as meningitis or cord compression secondary to abscess formation. The infectious source for meningitis and epidural abscess may result from distant colonization or localized infection with subsequent hematogenous spread and central nervous system (CNS) invasion. The anesthetist may also transmit microorganisms *directly* into the CNS by needle/catheter contamination through a break in aseptic technique or passage through a contiguous infection. An indwelling neuraxial catheter, though aseptically sited, may be colonized with skin flora and consequently serve as a source for ascending infection to the epidural or intrathecal space.

Historically, the frequency of serious CNS infections such as arachnoiditis, meningitis, and abscess following spinal or epidural anesthesia was considered to be extremely low—cases were reported as individual cases or small series [1–3]. However, epidemiologic series from Europe in the last decades demonstrate an increase in the frequency of infectious complications associated with neuraxial techniques [4, 5]. In a national study conducted from 1997 to 1998 in Denmark, Wang et al. [5] calculated the risk of *persisting* neurologic deficits to be 1:4343 following epidural analgesia. Moen et al. [4] reviewed the Swedish experience from 1990 to 1999 and reported a low incidence of epidural abscess but an alarming association of postspinal block meningitis with alpha-hemolytic streptococcal cultures, suggesting an iatrogenic origin of CNS contamination.

This chapter will discuss the clinical presentation of CNS infections, the laboratory and clinical studies evaluating the association between meningitis and dural puncture in bacteremic subjects, and the risk of infection during short term and chronic epidural catheterization in febrile and immunocompromised patients, including those with herpes simplex (HSV) and human immunodeficiency (HIV) virus. Finally, the importance and implications of aseptic techniques will be presented.

T.T. Horlocker, MD (✉) • D.J. Wedel, MD • A.D. Niesen, MD
Department of Anesthesiology, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA
e-mail: horlocker.terese@mayo.edu; wedel.denise@mayo.edu; niesen.adam@mayo.edu

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_9

Epidemiology of Meningitis and Epidural Abscess

Bacterial meningitis is the most common form of CNS infection, with an annual incidence in the United States of >2.5 cases/100,000 population. The epidemiology of bacterial meningitis changed significantly following the introduction and increasingly widespread use of vaccines for *H. influenzae* and *N. meningitidis*. Currently, *S. pneumoniae* accounts for nearly two-thirds of community acquired meningitis; causative organisms of nosocomial meningitis include gram-negative bacilli, *S. aureus*, and coagulase-negative staphylococci.

Most cases of spontaneous meningitis are associated with a recent infection (particularly otic or respiratory) or head trauma. Meningitis after spinal anesthesia has been rarely reported. In a study evaluating the frequency of meningitis in patients undergoing spinal anesthesia, Kilpatrick and Girgis retrospectively reviewed the records of all patients admitted to the meningitis ward in Cairo, Egypt [6]. During a 5-year period from 1975 to 1980, 17 of 1429 patients admitted with a diagnosis of meningitis had a history of recent spinal anesthesia. The patients developed meningeal symptoms 2–30 days (mean 9 days) after spinal anesthesia and were symptomatic for 1–83 days (mean 15 days) prior to hospital admission. Ten of the 17 had positive CSF cultures: 8 were *P. aeruginosa*, 1 was *S. aureus*, and 1 was *S. mitis*. These organisms were not cultured from patients who had not had spinal anesthesia. Two additional patients with a history of recent spinal anesthesia demonstrated evidence of tuberculous meningitis. The lack of positive CSF cultures was presumed to be a result of oral antibiotic therapy which was present in over half of patients at the time of admission. However, all patients, including those with negative CSF cultures, were treated with antibiotic therapy. Four of the 17 patients died. These results suggest that meningitis in patients with a history of recent spinal anesthesia may be due to unusual or nosocomial organisms and that aggressive bacteriologic evaluation and antibiotic coverage is warranted.

Most epidural abscesses are not related to the placement of indwelling catheters but are believed to be related to infections of the skin, soft tissue, spine, or hematogenous spread to the epidural space [7]. In a large retrospective review, epidural abscess accounted for 2–12 cases per 100,000 admissions to tertiary hospitals. The most commonly identified organisms were *S. aureus* (57 %), streptococci (18 %), and gram-negative bacilli (13 %). The source of infection was most often due to osteomyelitis (38 %), bacteremia (26 %), and postoperative infection (16 %). Only one of the 39 cases was related to an epidural catheter. In a more recent review, Ericsson et al. reported ten cases of epidural abscess. Four of these were associated with invasive spinal procedures including repeated lumbar punctures in the presence of meningitis (three cases), epidural catheter (one case), and a paravertebral anesthetic injection (one case) [1]. In a retrospective study, Danner and Hartman reported no spinal infections related to epidural anesthesia/analgesia [8]. These authors were able to characterize the clinical course of epidural abscess, as well as identify risk factors for neurologic recovery. Diagnosis was more difficult and often delayed in patients with chronic epidural abscesses, because these patients were less likely to be febrile or have an elevated leukocyte count compared to patients with acute abscesses. However, rapid neurologic deterioration could occur in either group. In addition, earlier diagnosis and treatment improved neurologic outcome. Steroid administration and increased neurologic impairment at the time of surgery adversely affected outcome.

Meningitis and Epidural Abscess After Neuraxial Anesthesia

Neuraxial anesthesia is a rare etiology of CNS infections (Table 9.1) [4, 5, 9–22]. In 1981, in the first combined series of more than 65,000 spinal anesthetics and approximately 50,000 epidural anesthetics, there were only three cases of meningitis and no epidural abscesses [19]. In 1997, a French multicenter prospective study by Auroy et al. that included 40,640 spinal and 30,413 epidural anesthetics reported no infectious complications [11]. Aromaa et al. reported eight cases of bacterial infections in patients undergoing 170,000 epidural and 550,000 spinal anesthetics (1.1:100,000 blocks) from a Finnish database [10]. More recent epidemiologic series are alarming. In a national study conducted from 1997 to 1998 in Denmark, Wang et al. reported the incidence of epidural abscess after epidural analgesia was 1:1930 catheters [5]. Patients with epidural abscess had an extended duration of epidural catheterization (median 6 days, range 3–31 days). In addition, the majority of the patients with epidural abscess were immunocompromised. Often the diagnosis was delayed; the time to first symptom to confirmation of the diagnosis was a median of 5 days. *S. aureus* was isolated in 67 % of patients. Patients without neurologic deficits were successfully treated with antibiotics, while those with deficits underwent surgical decompression (typically with only moderate neurologic recovery). It is difficult to determine why the frequency of symptomatic epidural abscess was so high in this series. Since perioperative antithrombotic therapy was involved in most cases, it is possible that the epidural abscesses were infected epidural hematomas, but this is not strongly supported by the diagnostic imaging studies and neurosurgical findings.

In a retrospective series from Sweden involving 1,260,000 spinal and 450,000 epidural anesthetics (including 200,000 placed for labor analgesia) performed over a decade, Moen et al. reported 42 serious infectious complications. Epidural

Table 9.1 Infectious complications following regional anesthesia

Author, year	Number of patients	Population	Regional techniques	Antibiotic prophylaxis	Duration of indwelling catheter	Complications
Kane [19]	115,000	Surgical and obstetric	65,000 spinal	Unknown	Unknown	3 meningitis (all after spinal anesthesia)
			50,000 epidural			
DuPen [16]	350	Cancer and AIDS patients	Permanent (tunneled) epidural analgesia	No	4–1460 days	30 insertion site infections, 19 deep-track or epidural space infections. Treated with antibiotics and epidural removal. Fifteen uneventfully replaced
Scott [21]	505,000	Obstetrics	Epidural	Unknown	Unknown	1 epidural abscess, partial recovery after laminectomy
Bader [12]	319	Parturients with chorioamnionitis	224 epidural 29 spinal 50 local anesthesia (26 general anesthesia)	Yes, in 13 %	Surgery only	None
Strafford [22]	1620	Pediatric surgical	Epidural analgesia	No	2.4 days median	3 positive epidural catheter tip cultures
						1 candida colonization of epidural space (also with necrotic tumor)
Goodman [17]	531	Parturients with chorioamnionitis	15 spinal	Yes, in 23 %	>24 h in 64 patients	None
			517 epidural anesthesia and analgesia			
Dahlgren [15]	18,000	All indications and ages	8768 spinal	Unknown	Unknown	None
			9232 epidural			
Kindler [20]	13,000	4000 obstetrics	Epidural	Unknown	Unknown	2 epidural abscess, both required laminectomy
		9000 surgical				
Auroy [11]	71,053	Surgical	40,640 spinal	Unknown	Unknown	None
			30,413 epidural			
Aromaa [10]	720,000	Surgical	170,000 epidural	Unknown	Unknown	4 meningitis
			550,000 spinal			2 epidural abscess
						2 discitis
						2 superficial skin infection
Wang [5]	17,372	Perioperative, cancer, and trauma pain	Epidural	Unknown	11 days mean	9 epidural abscesses
					6 days median	2 subcutaneous infections
Moen [4]	1,710,000	Pain, surgical, and parturients (200,000)	1,260,000 spinal	Unknown	2 days–5 weeks	29 meningitis
			450,000 epidural			13 epidural abscess
Cameron [13]	8210	Postoperative pain	Epidural	Unknown	2.8 days mean	6 epidural abscess, 1 required laminectomy; all recovered
						184 epidural insertion site infection
Christie [14]	8100	Postoperative pain	Epidural	Unknown	5.5 days median for epidural abscess	6 epidural abscess
					4 days median for meningitis	3 meningitis
The 3rd National Audit Project of The Royal College of Anesthetists, 2009 [9]	707,425	Perioperative, obstetric, chronic pain, and pediatric	324,950 spinal	Unknown		15 epidural abscess
			293,050 epidural			3 meningitis
			41,875 combined spinal-epidural			
			47,550 caudal			
Green [18]	9482	Obstetric	Epidural			2 epidural abscess
						2 paraspinal abscess

Adapted from: Horlocker TT, Wedel DJ. Regional anesthesia and infection [90]

abscess occurred in 13 patients; 9 (70 %) were considered immunocompromised as a result of diabetes, steroid therapy, cancer, or alcoholism [4]. Six patients underwent epidural block for analgesia following trauma. The time from placement of the epidural catheter to first symptoms ranged from 2 days to 5 weeks (median 5 days). Although prevailing symptoms were fever and severe backache, five developed neurologic deficits. All seven positive cultures isolated *S. aureus*. Overall neurologic recovery was complete in 7 of 12 patients. However, four of the five patients with neurologic symptoms did not recover.

Meningitis was reported in 29 patients for an overall incidence of 1:53,000. A documented perforation of the dura (intentional or accidental) occurred in 25 of 29 cases. Unlike the cases of epidural abscess, which tended to be reported in immunocompromised patients, the patients who developed meningitis following spinal anesthesia were reportedly healthy and undergoing minor surgical procedures. The time interval between neuraxial block and symptoms varied from 8 h to 8 days (median 24 h). Importantly, all patients complained of headache, but the classic symptoms of meningitis (fever, headache, and nuchal rigidity) were present in only 14 patients. In the 12 patients in whom positive cultures were obtained, alpha-hemolytic streptococci were isolated in 11 patients and *S. aureus* in 1. Meningitis results in residual neurologic deficits in six patients.

More recent data from multiple reports worldwide confirm the infrequent incidence of major infectious complications following neuraxial blockade, but echo this wide variability in frequency. In Australia, epidural abscesses were identified at a rate of 1:1368 in patients receiving epidural analgesia for acute postoperative pain [13], and 1:4742 in women who received an epidural for labor and delivery [23]. A United Kingdom (UK) 5-year retrospective review of epidural catheters placed for postoperative analgesia in a cohort of 8100 patients reported six cases of epidural abscess (1:1350) and three cases of meningitis (1:2700) [14]. A subsequent nationwide audit of major complications after epidural, subarachnoid, caudal, and combined spinal/epidural techniques in the UK was performed. Fifteen cases of epidural abscess and three cases of meningitis were identified in an estimated 707,425 procedures annually (1:39,301) [24]. Of note, epidural analgesia was found to have a significantly higher risk of infectious complications when compared to spinal anesthesia.

The obstetrical patient group is an interesting subset with epidural-related infections being extremely rare. Scott and Hibbard reported only a single epidural abscess in 505,000 epidurals for obstetrical analgesia and anesthesia over a 4-year period in the UK [21]. Moen et al. also noted a significantly lower incidence of infectious complications following epidural anesthesia in the obstetrical population (1:25,000) compared to the nonobstetrical population (1:3600) [4]. A more recent retrospective chart review of 9482 epidural placements in obstetric patients by Green and Paech from a major teaching hospital in Australia reported two epidural abscesses (1:4741) [18]. There was no comparison to nonobstetric epidural catheter placement in this study. Relatively short catheter durations and lack of immunocompromise in this generally healthy population are factors that may contribute to the apparently lower incidence of infectious complications.

Table 9.2 Factors associated with increased risk of neuraxial infection following neuraxial anesthesia

• Immunocompromised patient
• Chronically ill patient
• Bacteremia or viremia at the time of needle/catheter placement
• Breaks in aseptic technique
• Epidural catheterization (vs. single injection spinal/epidural)
• Prolonged catheterization
• Perioperative antibiotic administration

These large epidemiologic studies represent new and unexpected findings regarding the demographics, frequency, etiology, and prognosis of infectious complications following neuraxial anesthesia (Table 9.2). Epidural abscess is most likely to occur in immunocompromised patients with prolonged durations of epidural catheterization. The most common causative organism is *S. aureus*, which suggests the colonization and subsequent infection from normal skin flora as the pathogenesis. Delays in diagnosis and treatment result in poor neurologic recovery, despite surgical decompression. Conversely, patients who develop meningitis following neuraxial blockade typically are healthy and have undergone uneventful spinal anesthesia. Furthermore, the series by Moen et al. [4] validates the findings of individual case reports of meningitis after spinal anesthesia, in particular, the source of the pathogen is mostly likely to be the upper airway of the proceduralist [25–28]. While the frequency of serious infectious complications is much higher than reported previously, the results may be due to differences in reporting and/or clinical practice (asepsis, perioperative antibiotic therapy, duration of epidural catheterization) [4, 5]. Finally, although recent investigations have substantially illuminated the etiology, risk factors, and prognosis of infectious complications after neuraxial blockade, similar information for patients undergoing peripheral regional anesthetic techniques and invasive pain procedures is more limited and will be discussed separately [29–32].

Neuraxial Blockade in the Febrile or Infected Patient

Spinal or epidural anesthesia during bacteremia or viremia is a risk factor for infection of the central neural axis. Although the authors of previous studies did not report how many patients were febrile during administration of the spinal or epidural anesthetic, a significant number of the patients included in these studies underwent obstetric or urologic procedures, and it is likely that some patients had bacteremia after (and perhaps during) needle or catheter placement [4, 5, 15, 19]. Despite the apparent low risk of central nervous system infection following regional anesthesia, anesthesiologists have long considered sepsis to be a relative contraindication to the administration of spinal or epidural anesthesia. This impression is based largely on anecdotal reports and conflicting laboratory and clinical investigations.

Meningitis After Dural Puncture

Dural puncture has long been considered a risk factor in the pathogenesis of meningitis. Exactly how bacteria cross from the blood stream into the spinal fluid is unknown. The presumed mechanisms include introduction of blood into the intrathecal space during needle placement and disruption of the protection provided by the blood–brain barrier. However, lumbar puncture is often performed in patients with fever or infection of unknown origin. If dural puncture during bacteremia results in meningitis, definite clinical data should exist. In fact, clinical studies are few and are often antiquated.

Initial laboratory and clinical investigations were performed over 80 years ago (Table 9.3) [33–39]. In 1919, Weed et al. demonstrated that lumbar or cisternal puncture performed during septicemia (produced by lethal doses of an intravenously administered gram-negative bacillus) invariably resulted in a fatal meningitis [39]. In the same year,

Table 9.3 Meningitis after dural puncture

Author, year	Number of patients	Population	Microorganism(s)	Patients with spontaneous meningitis	Patients with dural puncture-induced meningitis	Comments
Wegeforth [38]	93	Military personnel	*Neisseria meningitidis* *Streptococcus pneumoniae*	38/93 (41 %)	5/93 (5.4 %), including 5 of 6 bacteremic patients	Lumbar punctures performed during meningitis epidemics
Pray [35]	416	Pediatric patients with bacteremia	*Streptococcus pneumoniae*	86/386 (22 %)	8/30 (27 %)	80 % of patients with meningitis were <2 years of age
Eng [34]	1089	Adults with bacteremia	*Atypical and typical bacteria*	30/919 (3.3 %)	3/170 (1.8 %)	Atypical organisms responsible for lumbar puncture-induced meningitis
Teele [37]	271	Pediatric patients with bacteremia	*Streptococcus pneumoniae* *Neisseria meningitidis* *Haemophilus influenzae*	2/31 (8.7 %)	7/46 (15 %)*	All cases of meningitis occurred in children <1 year of age; antibiotic therapy reduced risk
Smith [36]	11	Preterm infants with neonatal sepsis		0 %	0 %	
Centers for Disease Control and Prevention [33]	5	Parturients	*Streptococcus salivarius*	0 %	100 %	Anesthesiologist not wearing mask during spinal placement in 2 cases, visitors not wearing mask during spinal placement in 3 cases; 4 patients recovered, 1 died

Spontaneous meningitis = concurrent bacteremia and meningitis (without a preceding lumbar puncture). Lumbar puncture-induced meningitis = positive blood culture with sterile CSF on initial exam; subsequent positive CSF culture (same organism present in blood). From: Horlocker TT, Wedel DJ. Regional anesthesia and infection [90]

*Significant association ($p < 0.001$)

Wegeforth and Latham [38] reported their clinical observations on 93 patients suspected of having meningitis who received a diagnostic lumbar puncture. Blood cultures were taken simultaneously. The diagnosis was confirmed in 38 patients. The remaining 55 patients had normal cerebrospinal fluid (CSF). However, 6 of these 55 patients were bacteremic at the time of lumbar puncture. Five of the six bacteremic patients subsequently developed meningitis. It was implied, but not stated, that patients with both sterile blood and CSF cultures did not develop meningitis. Unfortunately, these lumbar punctures were performed during two epidemics of meningitis occurring at a military instillation, and it is possible that some (or all) of these patients may have developed meningitis without lumbar puncture. These two historical studies provided support for the claim that lumbar puncture during bacteremia was a possible risk factor for meningitis.

Subsequent clinical studies reported conflicting results. Pray [35] studied the incidence of pneumococcal meningitis in children who underwent a diagnostic lumbar puncture during pneumococcal sepsis. The incidence of meningitis was no greater among patients who were subjected to lumbar puncture, which produced normal CSF (8 of 30 patients, or 27 %), than among those who did not undergo diagnostic spinal tap (86 of 386 patients, or 22 %). Eng and Seligman retrospectively reviewed the records of 1089 bacteremic patients, including 200 patients who underwent lumbar puncture [34]. The authors reported that the incidence of meningitis after lumbar puncture did not significantly differ from the incidence of spontaneous meningitis and concluded: "*If lumbar puncture induced meningitis does occur, it is rare enough to be clinically insignificant.*"

However, not all studies have been as reassuring as those described earlier. In a review of meningitis associated with serial lumbar punctures to treat posthemorrhagic hydrocephalus in premature infants, Smith et al. attempted to identify risk factors [36]. Six of 22 (27 %) infants undergoing multiple (2–33) therapeutic dural punctures during a period of 2–63 days developed meningitis. Bacteremia, a risk factor for meningitis in this report, was associated with central venous or umbilical artery catheters. However, 11 septic infants who underwent dural puncture did not develop meningitis. The number of dural punctures, incidence of "difficult or traumatic" procedures and use of antibiotics did not differ between infants who developed meningitis and those who did not. A causal relationship between the dural puncture and onset of meningitis was not clear. Teele et al. retrospectively reviewed the records of 277 bacteremic children during a 10-year interval from 1971 to 1980 [37]. Meningitis occurred in 7 of 46 (15 %) children with normal CSF obtained during a bacteremia. However, only 2 of 231 (1 %) children who did not undergo lumbar puncture developed meningitis. These results were significantly different. In addition, children treated with antibiotics at the time of lumbar puncture were less likely to develop meningitis than children who were not treated until after lumbar puncture. The authors admitted that clinical judgment may have allowed the pediatricians to select the child in whom meningitis is developing before the CSF is diagnostic; these patients may appear more ill and thus suggest the performance of a lumbar puncture.

Prevention of lumbar puncture-induced meningitis with antibiotic therapy is supported by a more recent animal study. Carp and Bailey investigated the association between meningitis and dural puncture in bacteremic rats [40]. Twelve of 40 rats subjected to cisternal puncture with a 26-gauge needle during an *E. coli* bacteremia subsequently developed meningitis. Meningitis occurred only in animals with a blood culture result of ≥50 colony forming units/mL at the time of dural puncture, a circulating bacterial count observed in patients with infective endocarditis. In addition, bacteremic animals not undergoing dural puncture, as well as animals undergoing dural puncture in the absence of bacteremia did not develop meningitis. Treatment of a group of bacteremic rats with a single dose of gentamycin immediately prior to cisternal puncture eliminated the risk of meningitis; none of these animals developed infection.

This study demonstrates that dural puncture in the presence of bacteremia is associated with the development of meningitis in rats, and that antibiotic treatment before dural puncture reduces this risk. Unfortunately, this study did not include a group of animals that were treated with antibiotics *after* dural puncture. Since many surgeons defer antibiotic therapy until after cultures are obtained, the actual clinical scenario remains unstudied. There are several other limitations to this study. While *E. coli* is a common cause of bacteremia, it is an uncommon cause of meningitis. In addition, the authors knew the sensitivity to the bacteria injected, allowing for appropriate antibiotic coverage. The authors also performed a cisternal puncture (rather than lumbar puncture) and utilized a 26-gauge needle, producing a relatively large dural defect in the rat compared to humans and no local anesthetic was injected. Local anesthetic solutions are bacteriostatic, which may theoretically reduce the risk of meningitis in normal clinical settings. While these results may apply to the performance of spinal anesthesia in the bacteremic patient, they do not apply to administration of epidural anesthesia in the febrile patient, which is associated with a higher incidence of vascular injury and typically involves placement of an indwelling foreign body.

Meningitis After Spinal and Epidural Anesthesia

Even when meningitis occurs temporally after spinal anesthesia, it is often difficult to establish a cause-and-effect relationship. The following case report describes a probable case

of lumbar puncture-induced meningitis [41]. A 60-year-old man underwent kidney stone removal under general anesthesia. On postoperative day six, the patient remained afebrile, but was taken to the operating suite for transurethral clot evacuation. Spinal anesthesia was performed under aseptic technique. Cerebrospinal fluid was clear. Forty minutes later, shaking chills developed. Initial blood and urine cultures were negative. The following day, the patient became febrile and complained of headache and back pain and appeared confused. CSF examination revealed cloudy CSF with a leukocytosis (80 % polymorphonucleocytes), decreased glucose concentration consistent with bacterial infection, but no growth on culture. Three days later, a repeat lumbar puncture was performed with similar results. A third lumbar puncture was performed 2 days later; culture yielded group D streptococcus (enterococci). Group D enterococci are unusual sources of meningitis. In this case it is possible, though unlikely, that the patient was bacteremic prior to administration of the spinal anesthetic. It is more likely that the bacteria entered the blood stream during bladder irrigation (since bacteremia occurs in perhaps 60 % of urologic procedures), and traversed the dura at the puncture site, similar to the animals in the study by Carp and Bailey [40].

Bacterial meningitis can also present after epidural blockade with or without a localized epidural abscess [3, 42]. Ready and Helfer described two cases of meningitis following the use of epidural catheters in parturients [3]. In the first case, a healthy 28-year-old parturient underwent lumbar epidural catheter placement for elective cesarean section. The epidural analgesia was provided for 48 h postoperatively with an opioid. At the time of removal, a 4 cm erythematous indurated area, which was tender to palpation, was noted at the catheter entry site. Three days later, the patient complained of severe headache, nuchal rigidity, and photophobia. An area of cellulitis was present at the epidural insertion site. CSF examinations revealed an elevated protein (308 mg/dL), decreased glucose (27 mg/dL), and 3000 leukocytes/μL (73 % polymorphonucleocytes). Culture of the CSF was positive for *S. faecalis*. Urine and blood cultures were negative. There was no evidence of epidural abscess on MRI scan. Antibiotic therapy was initiated and the patient recovered completely.

In the second case, a lumbar epidural was placed in a healthy 25-year-old parturient. Delivery occurred uneventfully 50 min later, and the catheter was removed. No local inflammation was noted at the catheter insertion site. The patient reported a nonpositional headache and neck stiffness 24 h later. Lumbar puncture revealed elevated protein (356 mg/dL), decreased glucose (5 mg/dL), and 4721 leukocytes/μL (90 % polymorphonucleocytes). CSF cultured positive for *S. uberis* (a strain of α-hemolytic streptococcus). However, urine, blood, and vaginal cultures also grew the same organism. Antibiotic therapy was initiated, and recovery was complete. The short duration of the indwelling catheter; the lack of physical findings suggestive of infection at the catheter insertion site; and the presence of the organism in vaginal secretions, blood, and urine suggest that the source of the meningitis was most likely hematogenous spread of the infecting organism from the vagina. The case reported by Berman and Eisele [41] and the two cases by Ready and Helfer [3] demonstrate how a cause-and-effect relationship should not be assumed between the regional anesthetic and the CNS infection, but rather other possible sources should be investigated.

Epidural Abscess After Epidural Anesthesia

Several relevant studies have specifically examined the risk of epidural abscess in bacteremic patients receiving epidural anesthesia and/or analgesia. Few data exist regarding the placement and maintenance of epidural catheters in patients with an infection at a site distant from the neuraxis. Darchy et al. studied 75 patients in the intensive care unit receiving epidural analgesia (median 4 days), including 21 patients with a known localized concomitant infection [43]. Although five patients had catheter insertion site inflammation/erythema (with or without positive epidural catheter culture) the frequency was not increased by the presence of an infectious source distant to the epidural catheter site. However, the authors recommended a meticulous daily inspection of the catheter insertion site and immediate removal of the catheter if both erythema and local discharge are present, as these two signs of local inflammation are predictors of positive epidural catheter colonization/infection.

Jakobsen et al. examined the records of 69 patients with localized infections who had a total of 120 epidural catheters placed, undergoing on average 4 epidural anesthetics with catheters left in place for a mean of 9 days [44]. On 12 occasions the catheter was removed due to local infection, no specific therapy was instituted, and the infection resolved. There was one case of spondylitis, which was not apparently related to epidural catheterization. The retrospective nature of this study and the small number of patients limit the conclusions but suggest that placing an epidural catheter in a chronically infected patient may not be associated with a high risk of epidural infection.

Special Considerations in the Parturient

The obstetric patient presents a unique challenge, since the decision to not perform a neuraxial block may result in less than satisfactory analgesia and patient dissatisfaction. Despite these advantages, the anesthesiologist is frequently faced with the management of the parturient with suspected chorioamnionitis, approximately 8 % of whom are bacteremic. Bader et al. investigated the use of regional anesthesia in

women with chorioamnionitis [12]. Three hundred nineteen women were identified from a total of 10,047 deliveries. Of the 319 women, 100 had blood cultures taken on the day of delivery. Eight of these had blood cultures consistent with bacteremia. Two hundred ninety-three of the 319 patients received a regional anesthetic, in 43 patients antibiotics were administered prior to needle or catheter placement. No patient in the study, including those with documented bacteremias, had infectious complications. In addition, mean temperatures and leukocyte counts in patients who received blood cultures showed no significant differences between bacteremic and nonbacteremic groups. Goodman et al. also retrospectively reviewed the hospital records of 531 parturients who received epidural or spinal anesthesia and were subsequently diagnosed with chorioamnionitis [17]. Blood cultures were drawn in 146 patients; 13 were positive. Antibiotics were administered before the regional block was placed in only 123 patients, while nearly one-third of patients did not receive antibiotic therapy in the entire peripartum period. As with the study by Bader et al., leukocytosis, fever, abdominal tenderness, or foul smelling discharge was not predictors of positive blood cultures [12]. There were no infectious complications. These authors continue to administer spinal and epidural anesthesia in patients with suspected chorioamnionitis because the potential benefits of regional anesthesia outweigh the theoretical risk of infectious complications. However, the small number of patients with documented bacteremias in both studies defies a definitive statement regarding the risk of CNS infections in patients suspected of chorioamnionitis undergoing regional anesthetic techniques.

Herpes Simplex Virus

Herpes simplex virus type-2 (HSV-2) is an incurable, recurrent disease characterized by asymptomatic periods alternating at variable periods with recrudescence of the genital lesions. The primary infection is associated with viremia and can be accompanied by a variety of symptoms including fever, headache, lymphadenopathy, and, in rare cases, aseptic meningitis. In contrast, recurrent or secondary infections present as genital lesions without evidence of viremia. When obstetric patients present for delivery with evidence of active HSV-2 infection, cesarean section is usually recommended to avoid exposing the neonate to the virus during vaginal delivery. The use of central neuronal block has been considered controversial by some because of the theoretical concern of introducing the virus into the CNS. Although this issue is usually discussed in the context of obstetrical anesthesia, the incidence and prevalence of genital herpes has increased dramatically in the past two decades. Therefore, the theoretical risk of CNS contamination is present in the general surgical population as well.

Bader et al. reviewed management of 169 HSV-2 infected patients undergoing cesarean delivery. Five were classified as having primary infections with the remaining 164 being secondary [45]. General (59), spinal (75), and epidural (35) anesthetic techniques were used. One patient with primary HSV-2 developed transient unilateral leg weakness following bupivacaine spinal anesthesia. The problem resolved within 1 week. While this patient was classified by the obstetrician as having a primary infection, genital lesions had appeared 3 weeks prior to delivery and there was an active lesion at the time of delivery. The number of patients with primary HSV-2 infections was very small.

These recommendations are consistent with previous studies. Crosby et al. reviewed a 6-year experience with active HSV-2 infections in obstetrical patients in two institutions [46]. Cesarean section was performed on 89 affected parturients, all with recurrent herpes disease. There were no neurologic or infectious complications. In a similar retrospective review, Ramanathan et al. reported 43 epidural anesthetics in parturients with HSV-2 infection who had either active lesions (71 %) or had at least one recurrence during the pregnancy [47]. Again, no complications were noted in the parturient or neonate. One patient who was treated prenatally with steroids to promote fetal lung maturity developed a lesion in the postnatal period which resolved within 10 days. Neither of these studies included patients with primary infections.

Herpes simplex virus type-1 (HSV-1) the infectious agent for oral herpes rarely causes genital lesions. However, recurrent HSV-1 has been described in parturients receiving intrathecal and epidural morphine for pain management [48]. The postnatal association is controversial since several other factors such as emotional or physical stress, other infections, and parturition have been cited as causes of recurrent HSV infection. Valley et al. reported a case of thoracic and labial HSV-1 infection in a patient receiving epidural fentanyl [49]. While surgical stress may have been a factor, this patient had no other known risk factors, and lesions developed near the site of the epidural catheter.

Human Immunodeficiency Virus (HIV)

The risk of performing regional anesthesia procedures in HIV-infected patients is largely unknown. Hughes et al. reported the safe administration of central neuronal block in 18 HIV-infected parturients [50]. The patients studied showed no postpartum change in immune, infectious, or neurologic status. Avidan et al. and Bremerich et al. also reported a low complication rate for parturients with HIV infection on antiretroviral therapy that underwent spinal anesthesia. However, in all three series (with a combined total of 117 patients), the patients were relatively healthy and in the early

stage of their disease [51, 52]. The effects of anesthesia on patients with more advanced disease are unreported.

In a report on the use of epidural blood patch for postdural puncture headache in HIV-positive males, Tom et al. followed nine patients longitudinally for periods ranging from 6 to 24 months [53]. No complications were attributable to the epidural blood patch, although the authors noted the high incidence of neurologic manifestations in this population. Approximately 40 % of patients with the diagnosis of acquired immune deficiency syndrome (AIDS) have clinical signs of neurologic disease and at autopsy, patients with AIDS have a 70–80 % incidence of neuropathologic changes. While many of the neurologic symptoms are unrelated to complications associated with spinal or epidural anesthesia, some such as aseptic meningitis, chronic headaches, and polyneuropathy may be mistaken for problems related to needle placement. A clear understanding of the association of CNS symptoms with HIV infection is important in order to interpret postblock neurologic pathology.

Neuraxial Blockade in the Immunocompromised Patient

Large series have demonstrated that patients with altered immune status due to diabetes, neoplasm, immunosuppression following solid organ transplantation are at increased risk for infectious complications (Table 9.1) [4, 5]. These patients are susceptible to infection with opportunistic pathogens and, because antimicrobial therapy is less effective, experience increased morbidity and mortality compared to patients with normal immune function. Thus, a depressed immune state increases both frequency and severity of infection (Table 9.4).

Strafford et al. reviewed 1620 pediatric patients who received epidural analgesia for postoperative pain relief [22]. Epidural catheters were left indwelling for a median of 2 days (range, 0–8 days). No patient developed an epidural abscess. One patient with osteosarcoma metastatic to spine, chest wall, and lungs became febrile after 10 days of epidural catheterization. The catheter was removed, culture demonstrated candidal contamination. A second thoracic epidural catheter was placed 4 days later to provide superior analgesia. Two weeks later, she developed an acute sensory and motor block at T2. MRI showed an epidural fluid collection; an emergent laminectomy was performed. A large amount of necrotic tumor as well as fluid containing *C. tropicalis* was present in the epidural space. Her neurologic deficits resolved postoperatively. Three additional patients with chronic pain syndromes were evaluated for epidural infection, all were negative. The authors concluded that for terminally ill patients, the risk of infection with long-term epidural catheterization is acceptable, but recommended careful monitoring to avoid serious neurologic sequelae.

Chronic epidural catheterization in immunocompromised patients is also a potential risk for epidural infection. Du Pen et al. studied 350 cancer and HIV-infected patients in whom permanent (tunneled) epidural catheters were placed [16]. The authors examined three areas of the catheter track for evidence of infection: exit site, superficial catheter track, and epidural space. The rate of epidural and deep track catheter-related infections was one in every 1702 days of catheter use in the 19 patients who developed deep track (8) or epidural (15) infections (4 of the 19 patients had both deep track and epidural involvement). Bacteria cultured were most frequently skin flora. All 19 patients with deep infections were treated with catheter removal and antibiotics; none required surgical decompression or debridement. Catheters were replaced in 15 of the 19 patients who requested them after treatment with no recurrent infections. The authors state recommendations similar to Strafford et al., specifically long-term epidural catheterization is safe when patients are carefully monitored for signs of infection and receive prompt treatment when the diagnosis is established.

Injection of epidural steroids and underlying disease processes theoretically increase the risk of infection (Fig. 9.1) [54–56]. Strong described a 71-year-old man with a resolving herpes zoster infection involving the T5–T6 dermatome [56]. An epidural catheter was placed at the T6–T7 interspace, and 120 mg of methylprednisolone in 5 mL of 0.25 % bupivacaine were injected. Three additional doses of bupivacaine were administered, and the catheter was removed intact 26 h after placement. Four days later, a second epidural catheter was placed at the T5–T6 level. Oral antibiotic therapy

Table 9.4 Infectious complications following neuraxial anesthesia in the immunocompromised patient

• The attenuated inflammatory response within the immunocompromised patient may diminish the clinical signs and symptoms often associated with infection and result in a delay in diagnosis and treatment
• The range of microorganisms causing invasive infection in the immunocompromised host is much broader than that affecting the general population and includes atypical and opportunistic pathogens
• Initiation of early and effective therapy is paramount in optimizing neurologic outcome consultation with an infectious disease specialist is advised
• Prolonged antibiotic therapy (weeks–months) is often required because of persistent and immunologic deficiencies
• Since eradication of infection is difficult once established, prevention of infection is paramount in caring for immunocompromised patients

was initiated. Ten intermittent boluses of 0.25 % bupivacaine were made over a 3-day period, and the catheter was then removed. There was no evidence of infection at either catheter insertion site. The patient returned 3 weeks later with a fever, stiff neck, headache, and right-sided flank pain. No neurologic deficits were noted. A thoracic CT scan revealed an epidural abscess extending from T5 to T9. An emergency decompressive laminectomy was performed. Cultures at the surgical site were positive for *S. aureus*. The patient was treated with 21 days of intravenous antibiotics and was discharged without neurologic deficits. Factors contributing to this patient's epidural infection include an immunocompromised host (as suggested by the activation of a latent herpes infection), multiple catheter placement, and decreased immunologic response secondary to steroid administration.

Aseptic Technique

Most cases of meningitis associated with spinal anesthesia are reported as single cases or small case series. Older case reports often reported an association of meningitis with a break in sterilization techniques affecting patient preparation or the use of reusable equipment [57]. Disposable kits have reduced this risk, but nosocomial contamination is still a concern.

Hand Washing, Masks, and Gowns

Hand washing remains the most crucial component of asepsis; gloves should be regarded as a supplement to—not a replacement of—handwashing [58]. Conversely, the use of gowns and gloves does not further reduce the likelihood of cross contamination. Surgical masks, initially considered a barrier to protect the *proceduralist* from patient secretions and blood, may be appropriate due to the increasing number of cases of post spinal meningitis, many of which result from contamination of the epidural or intrathecal space with pathogens from the operator's buccal mucosa [4, 25–27]. Schneeberger et al. reported four cases of iatrogenic meningitis following spinal anesthesia occurring over a 4-year period [26]. The patients typically presented 24 h postoperatively with a severe headache (two received an epidural blood patch). All cases involved the same anesthesiologist, who had a history of recurrent pharyngitis and did not wear a mask during the procedure. Interestingly, similar reports have been noted among patients undergoing pain procedures [59]. In 2006, the American Society of Regional Anesthesia and Pain Medicine recommended surgical masks be worn during the performance of regional anesthesia and pain management procedures in an effort to reduce infectious complications [60]. The Centers for Disease Control and Prevention and American Society of Anesthesiologists subsequently made similar recommendations [61, 62].

Skin Disinfection

Chlorhexidine products have been shown to have a more effective, rapid, and longer lasting bactericidal effect than povidone iodine; the addition of isopropyl alcohol to chlorhexidine accelerates this effect [60, 63, 64]. Nearly all bacteria and nosocomial fungi are susceptible to chlorhexidine; resistance is exceedingly rare. Its efficacy is maintained even in the presence of organic compounds, such as blood. It is important to note that the United States Food and Drug Administration has not formally approved chlorhexidine for skin preparation prior to neuraxial preparation. This is due to a lack of animal studies studying the potential for neurotoxic effects of chlorhexidine, not due to any reported human cases of nerve injury. In fact, there are no confirmed cases of nerve injury with either chlorhexidine or isopropyl alcohol. Hence, alcohol-based chlorhexidine solutions are recommended by the American Society of Regional Anesthesia and Pain Medicine, American Society of Anesthesiologists, and Royal College of Anaesthetists as the skin antiseptic of choice prior to neuraxial and peripheral anesthetic procedures [24, 60, 61].

Breaches of aseptic technique continue to generate infections and case reports. In 2010, a series of *Klebsiella pneumoniae* and *Enterobacter aerogenes* bacteremia associated with an interventional pain clinic in New York City were reported by Wong and colleagues from the New York Department of Health and Mental Hygiene [65]. There were four laboratory-confirmed and five suspected cases of bacteremia in nine patients treated over a 3-day span. All nine patients underwent procedures at the same pain clinic, performed by the same physician and allied health assistant. Lapses in aseptic technique included lack of hand hygiene, not donning a surgical mask for interventional procedures, poor aseptic cleansing, and use of single-dose medication vials for more than one patient. It is difficult to pinpoint which of these breaks in aseptic technique was most responsible for the outbreak; it is likely that multiple factors acted synergistically to play a role. The plethora of case reports in the literature of neuraxial infections, some fatal, related to breaches in aseptic technique suggest that the reports from New York City were not isolated incidents [6, 25, 27, 41, 57, 66]. Thus, improving aseptic technique is something that every provider should consider in everyday practice (Table 9.5).

Table 9.5 Variables that may influence infectious complications

Site of catheter placement (thoracic vs. lumbar vs. caudal)
Choice of antiseptic and technique of application
Choice of barrier protection (masks, gloves, gowns)
Timing and selection of perioperative antibiotics
Duration of neuraxial catheterization
Use of bacterial filters
Dressing type(s) (transparent vs. dry gauze dressing; use of antiseptic dressings)

From: Hebl JR. The importance and implications of aseptic techniques during regional anesthesia [60]

Preparation of Injectate and Infusate

Preparation of an infusion in an inappropriate manner can lead to contamination and infection. In an effort to standardize and improve the practice of compounding sterile preparations, the United States Pharmacopeia (USP) and The National Formulary published Chapter 797 in 2004 [67]. USP Chapter 797 is the national standard for sterile compounding, including the preparation of local anesthetics. This regulation is enforceable by the Food and Drug Administration, the State Boards of Pharmacy, and the State Boards of Health. Importantly, full compliance with USP Chapter 797 became a requirement of the Joint Commission on Accreditation of Healthcare Organizations in 2008. Specifically, preparations (including local anesthetics) intended to be infused over several days are recommended to be prepared by pharmacy personnel in an International Standards Organization (ISO) Class 5 laminar flow workbench, within an ISO Class 7 buffer room [68]. When local anesthetic solutions are prepared according to these standards, infusions may remain microbiologically stable well beyond 72 h [69, 70]. The importance of meticulous compounding techniques was recently demonstrated in a 20 state outbreak of fungal meningitis. Contaminated injectable steroid solutions produced by a compounding pharmacy were the source of 751 cases of CNS or paraspinal infections and 64 deaths [2].

Transmission of life-threatening bacterial infections can also occur when healthcare providers do not adhere to Standard Precautions and instead use medication in containers labeled as single dose or single use for more than one patient. In July 2012, the Center for Disease Control and Prevention reported two outbreaks of invasive *Staphylococcus aureus* infection confirmed in ten patients being treated for pain in outpatient clinics [71]. In each outbreak, the use of single dose vials for more than one patient was associated with infection transmission. These outbreaks are a reminder of the serious consequences that can result when single-dose vials are used for more than one patient. Proper use of single-dose vials consists of (1) withdrawing contents into a new sterile syringe in an aseptic manner, (2) promptly using the contents for a single patient during a single procedure, and (3) disposing of the vial and any remaining contents. *Moreover, since 2007, the year that injection safety was included as part of Standard Precautions, 20 outbreaks associated with use of single-dose or single-use medications for more than one patient have been reported*. These series demonstrate that infection prevention practices are critical for patient safety.

Catheter Disconnects and Other Breaks in the Circuit

Breaks within the sterile circuit (e.g., solution bag changes, local anesthetic boluses, catheter-hub disconnects) may significantly increase the risk of contamination and subsequent localized or systemic infection [72]. Although the epidural catheter tip is frequently colonized, progression to epidural space infection rarely occurs [16, 43]. The low frequency of significant epidural infection (1–2 cases per 10,000 hospital admissions associated with epidural catheter placement) is especially notable when compared to the frequency of intravenous catheter-related septicemia, which approaches 1 %, or greater than 50,000 cases annually [2]. Several factors may contribute to the low incidence of epidural space infections, including meticulous attention to aseptic technique, careful monitoring of catheter insertion site, antibiotic prophylaxis, and use of bacterial filters. However, since these interventions are commonly initiated in patients with indwelling central venous catheters, additional factors unique to epidural anesthesia and analgesia, such as the bacteriostatic effect of local anesthetic solutions may also contribute.

Bupivacaine and lidocaine have been shown to inhibit the growth of a variety of microorganisms in culture [73]. Unfortunately, the bacteriostatic effect decreases significantly with concentrations of local anesthetic typically used to provide analgesia, while opioid solutions do not exhibit *any* ability to inhibit bacterial growth. In addition, growth of *S. aureus,* and coagulase-negative staphylococci, the most commonly identified pathogens in epidural infections, is inhibited only at higher concentrations of local anesthetic, such as solutions of 2 % lidocaine and 0.5 % bupivacaine. Therefore, although it appears that local anesthetic solutions are unlikely to prevent epidural infections in most patients receiving epidural analgesia, it is possible that in immunocompromised patients, local anesthetics may inhibit the growth of more fastidious organisms, even at low concentrations. Further clinical studies are needed to investigate the in vivo bacteriostatic effects of dilute local anesthetic solutions.

The catheter hub, catheter insertion site, and hematogenous spread are three major routes of entry for microorganisms into the epidural space, with the catheter hub accounting for nearly half of the sources [16, 74, 75]. A bacterial filter placed at the catheter hub acts as a physical barrier for bacteria present in the infusing solution and should theoretically reduce the incidence of epidural colonization. However, studies of epidural catheter tip cultures have reported mixed results, and cases of epidural infection following hub colonization despite the use of filters have been reported [16, 74, 76]. Possible explanations for hub-related epidural infections in patients with bacterial filters include a reduced antimicrobial effectiveness with prolonged use and direct contamination of the hub during filter-changing techniques. De Cicco et al. reported a positive trend between the number of filter changes and the rate of positive hub cultures [72]. These data suggest that continued attention to aseptic technique is warranted throughout the period of epidural catheterization, and that the use of bacteriologic filters is alone unlikely to be efficacious in preventing epidural colonization and infection [77].

Controversy exists regarding the conditions under which a disconnected epidural catheter can be safely reconnected. In an in vitro investigation, Langevin et al. [83] inoculated epidural catheters containing a 5 μg/mL fentanyl solution with *S. aureus, E. coli,* or *P. aeruginosa.* Eight hours after catheter contamination, providing the fluid in the catheter remained static, no bacteria were detected more than 20 cm from the contaminated catheter hub. Vertical or horizontal positioning of the catheter during incubation did not affect bacterial advancement along the catheter, as long as the fluid was displaced distally less than 20 cm. However, if the fentanyl solution was allowed to drain and advance 33 cm, bacteria were found at the epidural end of the catheter, 88 cm distally. The advancement of bacteria by fluid displacement is clinically significant; in more than two-thirds of patients, fluid will drain by gravity into the epidural space in less than 1 h after discontinuation of an epidural infusion. The authors concluded that the interior of a disconnected epidural catheter will remain sterile for at least 8 h if the fluid in the catheter remains static, and the catheter may be aseptically reconnected after removal of the contaminated section. In addition, the presence of a meniscus more than 20–25 cm from the free end of a disconnected catheter may indicate contamination of the catheter tip in the epidural space, and immediate catheter removal was recommended. Unfortunately, the authors did not evaluate the advancement of bacteria in epidural catheters filled with local anesthetic solutions or investigate the effect of a local anesthetic injected after the bacterial inoculation and incubation.

Anesthetic Management

These studies and epidemiologic data provide guidance in the administration of regional anesthesia and analgesia in the infected or immunocompromised patient (Table 9.6). However, as with all clinical judgments, the decision to perform a regional anesthetic technique must be made on an individual basis considering the anesthetic alternatives, the benefits of regional anesthesia, and the risk of CNS infection (which may theoretically occur in any bacteremic patient, not just those who undergo neuraxial blockade).

Numerous clinical and laboratory studies have suggested an association between dural puncture during bacteremia and meningitis. The data are not equivocal, however. The clinical studies are limited to pediatric patients who are historically at high risk for meningitis. Many of the original animal studies utilized bacterial counts that were far in excess of those noted in humans in early sepsis, making CNS contamination more likely [39, 78]. Despite these conflicting results, it is generally recommended that except in the most extraordinary circumstances, central neuronal block should not be performed in patients with untreated systemic infection.

Patients with evidence of systemic infection may safely undergo spinal anesthesia, provided appropriate antibiotic therapy is initiated prior to dural puncture, and the patient has demonstrated a response to therapy, such as a decrease in fever [40, 79]. Although few data exist on the administration of epidural anesthesia in the patient with a treated systemic or local (distant) infection, the studies by Bader et al., Goodman et al., and Darchy et al. are reassuring [12, 17, 43]. Placement of an indwelling epidural (or intrathecal) catheter in this group of patients remains controversial; patients should be carefully selected and monitored for evidence of epidural infection.

Spinal anesthesia may be safely performed in patients at risk for low-grade transient bacteremia after dural puncture. Once again, little information exists concerning the risk of epidural anesthesia in patients suspected of developing an intraoperative transient bacteremia (such as during a urologic procedure). However, short-term epidural catheterization is most likely safe, as suggested by large retrospective reviews which included a significant number of obstetric and urologic patients.

All patients with an established local or systemic infection should be considered at risk for developing infection of the CNS. Patients should be observed carefully for signs of

Table 9.6 Anesthetic management of the immunocompromised or infected patient

• Serious neuraxial infections such as arachnoiditis, meningitis, and abscess after spinal or epidural anesthesia are rare
• The decision to perform a regional anesthetic technique must be made on an individual basis considering the anesthetic alternatives, the benefits of regional anesthesia, and the risk of CNS infection (which may theoretically occur in any bacteremic patient)
• Despite conflicting results, many experts suggest that, except in the most extraordinary circumstances, neuraxial block should not be performed in patients with untreated systemic infection
• Available data suggest that patients with evidence of systemic infection may safely undergo spinal anesthesia, provided appropriate antibiotic therapy is initiated prior to dural puncture and the patient has demonstrated a response to therapy such as a decrease in fever (placement of an indwelling epidural, or intrathecal, catheter in this group of patients remains controversial)
• Available data suggest that spinal anesthesia may be safely performed in patients at risk for low-grade transient bacteremia after dural puncture
• Injection of epidural steroids and underlying disease processes resulting in immunocompromise theoretically increase the risk of infection
• A delay in diagnosis and treatment of major CNS infections of even a few hours significantly worsens neurologic outcome

infection when a continuous epidural catheter is left in place for prolonged periods. In addition, injection of local anesthetic or insertion of a catheter in an area at high risk for bacterial contamination such as the sacral hiatus may also increase the risk for abscess formation [80, 81].

Neuraxial block has been shown to be safe in patients with recurrent HSV infections, although exacerbations of HSV-1 have been reported in association with intrathecal and epidural opioids. There are inadequate data available regarding the safety of spinal and epidural anesthesia in the presence of primary HSV-2 infection; however, viremia, fever, and meningitis have been reported. These findings would suggest a conservative approach [45, 47, 48, 82]. Minimal data suggest that regional anesthesia can be performed safely in HIV-infected patients, although underlying neurologic pathology is common in these patients [49–53].

Diagnosis and Treatment of Neuraxial Infectious Complications

A delay in diagnosis and treatment of major CNS infections of even a few hours significantly worsens neurologic outcome. Bacterial meningitis is a medical emergency. Mortality is approximately 30 %, even with antibiotic therapy. Meningitis presents most often with fever, severe headache, altered level of consciousness, and meningismus. The diagnosis is confirmed with a lumbar puncture. Lumbar puncture should not be performed if epidural abscess is suspected, as contamination of the intrathecal space may result. CSF examination in the patient with meningitis reveals leukocytosis, a glucose level of <30 mg/dL, and a protein level >150 mg/dL. In addition, the anesthesiologist should consider atypical organisms in patients suspected of meningitis following spinal anesthesia.

Abscess formation following epidural or spinal anesthesia can be superficial, requiring limited surgical drainage and intravenous antibiotics. Superficial infections present with local tissue swelling, erythema, and drainage, often associated with fever, but rarely causing neurologic problems unless untreated. Epidural abscess formation usually presents days to weeks after neural blockade with clinical signs of severe back pain, local tenderness, and fever associated with leukocytosis (Table 9.7). The clinical course of epidural abscess progresses from spinal ache and root pain, to weakness (including bowel and bladder symptoms) and eventually paralysis [7, 8]. The initial back pain and radicular symptoms may remain stable for hours to weeks. However, the onset of weakness often progresses to complete paralysis within 24 h. Radiologic evidence of an epidural mass in the presence of variable neurologic deficit is diagnostic. Magnetic resonance imaging is advocated as the most sensitive modality for evaluation of the spine when infection is suspected [42, 83, 84]. A combination of antibiotics and surgical drainage remains the treatment of choice. As with spinal hematoma, neurologic recovery is dependent on the duration of the deficit and the severity of neurologic impairment before treatment [4, 5].

Infectious Complications of Peripheral Regional Techniques

The use of peripheral nerve blockade, including continuous peripheral nerve blockade, has expanded greatly in recent years. Despite increased clinical use, there are few investigations regarding the incidence of infectious complications with these techniques (Table 9.8) [30, 65, 85–88]. Of the investigations in the literature, none approach the sample

Table 9.7 Differential diagnosis of epidural abscess, epidural hemorrhage, and anterior spinal artery syndrome

	Epidural abscess	Epidural hemorrhage	Anterior spinal artery syndrome
Age of patient	Any age	50 % over 50 years	Elderly
Previous history	Infection or immunosuppression*	Anticoagulants	Arteriosclerosis/hypotension
Onset	1–3 days	Sudden	Sudden
Generalized symptoms	Fever, malaise, back pain	Sharp, transient back and leg pain	None
Sensory involvement	None or paresthesias	Variable, late	Minor, patchy
Motor involvement	Flaccid paralysis, later spastic	Flaccid paralysis	Flaccid paralysis
Segmental reflexes	Exacerbated*—later obtunded	Abolished	Abolished
Myelogram/CT scan	Signs of extradural compression	Signs of extradural compression	Normal
Cerebrospinal fluid	Increased white cell count	Normal	Normal

From: Horlocker TT, Wedel DJ. Regional anesthesia and infection [90]
*Infrequent findings

Table 9.8 Infectious complications after peripheral block

Author, year	Number of patients	Population	Regional techniques	Antibiotic prophylaxis	Duration of indwelling catheter	Complications
Bergman [85]	405	Surgical	Axillary catheter	Unknown	Mean 55 h	1 localized skin infection, treated with catheter removal and a course of antibiotics
Nseir [88]	1	Surgical	Axillary block, single injection	No	None	Fatal necrotizing fasciitis, provider did not wear mask during block
Capdevila [30]	1416	Surgical	256 interscalene, 126 axillary, 20 posterior lumbar plexus, 683 femoral, 94 fascia iliaca, 32 proximal sciatic, 167 popliteal, and 38 distal median and ulnar catheters	Yes, in some	Mean 56 h	28.7 % of catheters colonized 1 psoas abscess following femoral nerve block, treated with antibiotics
Neuburger [87]	2285	Surgical	600 axillary, 303 interscalene, 92 infraclavicular, 65 psoas compartment, 574 femoral, 296 sciatic and 355 popliteal catheters	97 % received perioperative single dose after catheter placement and before surgery	Median 4 days	96 local inflammation 73 local infection 20 infections requiring surgical drainage
Capdevila [86]	1	Surgical	Interscalene catheter	Yes	39 h	Acute neck cellulitis, interscalene and sternocleidomastoid abscess, mediastinitis requiring surgical debridement and prolonged antibiotic therapy
Wong [65]	9	Pain management	Sacroiliac joint steroid injection	No	None	4 laboratory confirmed and 5 suspected cases of *Klebsiella pneumoniae* and *Enterobacter aerogenes* bacteremia, provider did not adhere to multiple facets of aseptic technique

size of the large studies involving complications of neuraxial blockade. Auroy et al. reported no infectious complications in 21,278 single injection peripheral nerve blocks [11]. Furthermore, reports of infectious complications following single injection techniques are limited to a single case involving fatal necrotizing fasciitis following a single injection axillary block [88]. However, as this case demonstrates, the infections occurring following single injection techniques can nonetheless be devastating.

The more frequent placement of catheters for peripheral nerve blockade, often for prolonged periods, might be expected to increase the risk of infectious complications; however, few data are available to support this theoretical assumption. In the current literature, 23–57 % of peripheral nerve catheters may become colonized, with 0–3 % resulting in localized infection, and a proven systemic infection associated with the catheter occurring in 0–0.9 % [30]. Catheters are most frequently colonized with the most common skin microorganism *Staphylococcus epidermidis*. However, *Staphylococcus aureus* is the most commonly described organism in cases of localized infection and abscess formation [30, 87]. Colonization and infection during peripheral blockade likely occurs in a similar fashion as with neuraxial blockade. In particular, breaks in aseptic technique, localized infection at the skin puncture site, contamination of the local anesthetic solution, and tracking of organisms along the length of the catheter all are proposed mechanisms. For example, a patient developed acute neck cellulitis, interscalene and sternocleidomastoid abscesses, and mediastinitis following an infusion delivered via an elastomeric pump via an interscalene catheter [86]. The catheter was placed under strict aseptic conditions and dressed with a sterile dressing. However, the elastomeric pump was filled outside of the pharmacy by a member of the anesthesia team who did not wear sterile gloves and performed multiple manipulations of the infusion line. The patient required surgical debridement and prolonged intravenous antibiotics.

Two studies specifically evaluated the infectious risk in continuous peripheral nerve blocks. Capdevila et al. prospectively studied 1416 patients in 10 centers undergoing continuous peripheral nerve blocks for orthopedic procedures [30]. A total of 969 (68 %) of catheters were cultured when removed, and patients were actively monitored for signs of localized infection or sepsis. A positive bacterial colonization was

found in 278 (29 %) catheters, most commonly *S. epidermidis*. The incidence of local inflammation was present in 3 % of patients. In these patients 44 % of the catheters were colonized, whereas only 19 % of catheters were colonized in patients without inflammatory signs. There was no correlation between colonization and the presence of fever. Risk factors for local infection/inflammation were admission to an intensive care unit, male gender, catheter duration exceeding 48 h, and lack of antibiotic prophylaxis. A study by Cuvillon et al. investigated the incidence of infectious complications in 211 continuous femoral catheters [31]. Colonization of the 208 catheters examined after 48 h showed a rate of 57 % with the most common organism again being *Staphylococcus epidermidis* (71 %). Echography was performed in each instance of positive catheter colonization. No cellulitis or abscess was noted; however, three transitory bacteremias were attributed to the presence of the femoral catheters. There were no long-term sequelae due to infectious causes. Although the necessity of antibiotic prophylaxis during placement of permanent epidural catheters and implantable devices to treat chronic pain is well defined [32, 89], the importance of antibiotic prophylaxis during placement and maintenance of neuraxial or peripheral catheters is less clear. In a series of 405 axillary catheters, the single infectious complication occurred in a nonsurgical patient who did not receive the "usual" perioperative antibiotic prophylaxis [85].

Anesthetic Management

Strict adherence to aseptic technique is a cornerstone of preventing infectious complications in peripheral regional anesthesia. As with neuraxial techniques, the American Society of Regional Anesthesia and Pain Medicine recommends surgical masks be worn during the performance of peripheral blocks [60]. Donning a hat, removal of rings and wristwatches, performing hand hygiene prior to donning sterile gloves, and skin preparation with an alcohol-based chlorhexidine solution nerve catheters should be prepared by pharmacy personnel according to USP 797 guidelines [68]. Prophylactic antibiotics may be protective, but adequate data are not available to support this concept.

Diagnosis and Treatment of Peripheral Infectious Complications

Infections related to peripheral nerve blockade typically present as erythema and/or tenderness at the block site and can usually be diagnosed with history and physical examination. Occasionally, this may progress to cellulitis or abscess formation, and radiologic imaging with ultrasound, computed tomography, or magnetic resonance imaging may be required to define the extent of the abscess. Laboratory evaluation of the blood may reveal an elevated leukocyte count. Most localized infections can be treated with no more than catheter removal, with the occasional need for antibiotic therapy, and rarely surgical drainage.

Fig. 9.1**.** A thoracic epidural abscess is demonstrated by magnetic resonance image in a patient who underwent thoracic epidural placement for management of herpetic neuralgia. From: Horlocker TT, Wedel DJ. Regional anesthesia and infection. From: Finucane BT, ed. *Complications of Regional Anesthesia* [90]

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Continuous Peripheral Nerve Blocks Safe Practice and Management

10

Geert-Jan van Geffen and Jörgen Bruhn

Key Points

- Continuous peripheral nerve blocks can be used to provide effective and prolonged analgesia.
- A variety of needle/catheter assemblies exist, and perineural catheters can be installed using various guidance mechanisms, including nerve stimulation and ultrasound.
- Complications that may hinder the efficacy of a continuous regional block include inaccurate catheter tip location, catheter dislocation, infection at the catheter insertion site, and difficulty removing the catheter.
- Neurologic injury with continuous blocks is rare and related to multiple risk factors. Other complications that affect single-injection blocks, such as accidental vascular puncture and systemic local anesthetic toxicity, may also occur with continuous blocks.
- Complications associated closely with continuous blocks include increased risk of patient falls and problems with the infusion regimen or equipment.

Introduction

A continuous peripheral nerve block (CPNB) involves the percutaneous insertion of a catheter adjacent to a peripheral nerve, followed by local anesthetic administration through the catheter, providing analgesia for multiple days or weeks. This is in contrast to wound or intra-articular local anesthetic infusion in which catheters are inserted blindly into incision sites, fascia, intra-abdominally, or joints and in which the local anesthetic infusion is part of a multimodal pain treatment regimen for a limited period of time [1–3]. In 1946, the first application of a CPNB has been described [4]. In this case report, a needle was inserted near the supraclavicular brachial plexus and retained in place by a cork taped to the patient's chest, this allowed reinjection of local anesthetic when the surgical anesthesia wore off during prolonged surgery. Slight toxic effects were noted. Since then, CPNBs have evolved to an efficient safe analgesic technique for perioperative pain treatment [4, 5], and now numerous indications for CPNBs are described (Table 10.1) [6–17].

Compared with opioid analgesics CPNBs provide superior analgesia with a lower incidence of opioid-induced side effects such as nausea, vomiting, pruritus, and sedation and may offer an improved functional outcome after extremity surgery [18–24].

After ambulatory surgery, CPNBs for postoperative analgesia provided at home, improved not only analgesia, but also sleep quality and patient satisfaction, while decreasing supplemental opioid requirements and opioid-related side effects not only in adults but also in children (Table 10.2) [25–28].

Technique of CPNB Insertion

Patient Preparation

Sterility is of great importance for the performance of CPNBs. Antiseptic hand washing, wearing of sterile gloves, surgical mask and hat, and the use of alcohol-based chlorhexidine antiseptic solution is recommended. If ultrasound guidance is used, the ultrasound probe should be covered by a sterile ultrasound cover. The patient is draped and during the procedure sterility of the "anesthetic" field should be maintained (Table 10.3) [29–34].

G.-J. van Geffen, MD, PhD (✉) • J. Bruhn, MD, PhD
Radboud University Medical Centre, Nijmegen, Netherlands
e-mail: Geert-Jan.vanGeffen@Radboudumc.nl; Jorgen.Bruhn@radboudumc.nl

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_10

Table 10.1 Indications for CPNBs

Perioperative pain management [6]
Treatment of vasospasm induced by Raynaud disease [7]
Sympathectomy and vasodilatation for improvement of blood flow after microvascular surgery [8]
Limb salvage surgery [9]
Digit transfer or replantation surgery [10]
Treatment of intractable hiccups [11]
Treatment of peripheral embolism [12]
Chronic pain syndrome treatment [13]
Weever fish sting treatment [14]
Terminal cancer pain [15]
Phantom limb pain [16]
Battlefield pain relief [17]

Table 10.2 Advantages of continuous peripheral nerve blocks

Superior pain relief
Reduced opioid related side effects
Enhanced sleep quality
Faster rehabilitation
Reduced hospital costs
Improved patient satisfaction

Table 10.3 Strict guidelines of aseptic technique for continuous peripheral nerve blocks [29–31]

1. Remove watches and jewelry
2. Preprocedure hand washing with chlorhexidine gluconate in isopropyl alcohol
3.Wear surgical hat, mask, and grown
4. Skin disinfection with chlorhexidine gluconate in isopropyl alcohol
5. Sterile patient draping
6. Maintain sterility during procedure
7. Apply sterile dressing
8. Use bacterial filter during long-term catheterization
9. Minimize breaks within the sterile circuit such as solution bag changes, local anesthetic boluses, and/or catheter hub disconnections

Needle Choice

Regardless of which technique is used the classical "through-the-needle technique" or recently introduced "catheter-over-needle technique," the shape of the needle tip is important in order to avoid neural damage and atraumatic needles should be used. Despite the use of atraumatic needles, intraneural injection and catheterization may still occur [35].

Pencil point needles are considered less traumatic compared to beveled and Tuohy needles. However, the magnitude of nerve injury after needle nerve perforation is not related to one of the applied needle types. In order to obtain tactile feedback (a "pop") when fascias are pierced, blunt needles are recommended for the performance of continuous subfascial blocks such as fascia iliaca, transversus abdominis plane (TAP), or pectoral nerve (PEC) blocks [36, 37].

Mostly larger needles are used for the performance of CPNBs because a catheter needs to be threaded through the needle. Larger needles may make the procedure more painful; however, when the needle trajectory site is first anesthetized with local anesthetic then the procedure is only slightly painful.

Catheters

Catheters are made of polyamide, polyurethane, and Teflon. There is no universally ideal catheter. The material, design, and diameter of the continuous block catheters are chosen according to the specific requirements associated with the needle and catheter design. Overall the catheter should be tension resistant and must not break or shear. Kinking should be prevented. Therefore, some manufacturers reinforce the catheter with an integrated metal wire in the catheter wall. Others use metal stylets in the catheter which are withdrawn after catheter insertion. The metal wires may also serve as electrical conduits when nerve stimulation is used [38].

The catheters should have an ascending length indication so that the depth of catheter insertion and its position can be followed during advancement and surveillance thereafter.

Catheter tips for CPNBs should be relatively stiff in order to allow catheter advancement. Metallic coiled tips may ease ultrasonic visualization but may contribute to formation of adhesions at the tip of the catheter when there is no active infusion of local anesthetic or saline [39].

Due to multiple orifices on the end of the catheter, stiffness of the catheter tip is lost and these nonstimulating catheters are more difficult to thread, but there is no difference in quality of pain relief between catheters with an end hole, triple hole, or six-hole catheter tip [40].

Luyet developed a catheter with soft tip which rolls up and remains at the point where the cannula is positioned, three orifices allow free flow of local anesthetic [41]. For safety reasons catheters should be labeled, colored, and equipped with unique connectors for tubing with the syringe and line in order to avoid tube misconnection and prevent medication errors [42, 43].

Catheterization Kits

There are a number of different catheterization kits available. Catheterization equipment can be divided into: (1) catheter-through-needle devices, (2) cannula-over-needle-catheter-through-cannula devices, and more recently (3) catheter-over-needle devices, and finally, (4) preliminary suture/needle systems are available to anchor the catheters.

Needles with a specially designed tip, which facilitates placement along the nerve are now used. Facet tips ease catheter insertion parallel to the nerve; Tuohy tips are suitable for cases where it is necessary to introduce the catheter at an angle to the nerve. These needles are insulated and offer the possibility to be used with a peripheral nerve stimulator. The extension tube on the needle allows one to use an immobile needle technique.

1. *Catheter through needle*
   The catheter is introduced through the needle via a separate canal from where aspiration and injection occurs. This eliminates the need for equipment and disconnection and reduces the risk of needle displacement.

2. *Cannula-over-needle design*
   These assemblies include a cannula over a short beveled needle. The first commercially available equipment for CPNBs included this design. Later the possibility of electrical stimulation and connection tubing for aspiration and injection was added to the design. When the final needle tip position is reached, the needle is withdrawn and the cannula is left in place. Subsequently, the catheter is advanced 3 cm beyond the cannula tip.

3. *Catheter over needle*
   Two different designs exist. The first design consists of an outer 19 G catheter and flexible inner 25 G facet bevel needle. In order to puncture the skin and to navigate the catheter to its position, an adjustable movable grip is glided over the catheter. The grip can be moved so that the catheter and inner needle can be advanced. When the end point for the catheter and needle tip is obtained, a bolus is injected via the cannula. The catheter is held in place with the adjustable grip and the needle is withdrawn. Due to its flexibility, the catheter may bend away while advancing the catheter and needle, especially when deep blocks are performed.

   The other design relies on two components, an outer catheter sheath and flexible, kink resistant inner catheter. The needle is housed within the outer catheter and is used to position the distal catheter tip. If the final needle tip position is reached, the needle is withdrawn and the inner catheter, whose length is similar to that of the needle, is inserted into the outer catheter. Thus, the inner catheter replaces the needle [44, 45].

4. *Suture needle with catheter attached*
   With this recently developed system the catheter is attached to a large needle. The curved needle allows fine precise adjustment of the catheter in the vicinity of the nerve. Two holes through which local anesthetic exits the catheter, are sited at a junction in the catheter that is visible on ultrasound, so their position can be adjusted close to the nerve. Primary placement and subsequent repositioning are achieved by pulling either end of the through-and-through catheter, both of which can be secured to the skin. In a cadaver study, very successful and promising results were obtained with this system. Clinical studies in patients have not yet been performed [46].

   Catheter dislocation and leakage at the insertion site are significant concerns when traditional catheter-through-needle/cannula techniques are used. The diameter of the catheter is smaller than that of the needle used for skin puncture. Thus, the catheter is not held tightly by the skin leaving space for local anesthetic to leak upon infusion. With the catheter-over-needle technique the puncture hole is smaller than the catheter, creating a tight fit in the skin. So the catheter-over-needle design offers greater stability and less dislocation, compared with the traditional designs [47].

Nerve Localization Technique

Paresthesias and Tactile Feedback

The first CPNBs were performed using paresthesias or tactile feedback when the needle pierced the fascia and the fascial "pop" or "click" was felt [4, 5, 48, 49]. Decades ago Moore suggested that the most reliable way to guarantee successful blockade when performing peripheral nerve blockade was to first elicit a paresthesia. He used the term: "no paresthesia, no anesthesia" and it soon became doctrine [48]. Successful nerve blockade demanded proximity to the nerve as evidenced by the occurrence of mechanical paresthesias. Although the safety of this method has been questioned [50], and the sensitivity of eliciting paresthesias as an endpoint for needle to nerve contact, is only 38 % [51], no definitive evidence is available linking this technique (eliciting paresthesias) with neurological damage [52]. This dictum first proposed by Moore more than 50 years ago is still being used as a nerve localization technique in daily practice [53]. The loss of resistance technique is simple, safe, and effective and can be applied with minimal resources; however, only limited indications for these exist when performing continuous peripheral nerve blocks (Table 10.4).

Electrical Nerve Stimulation

Since 1962 when Greenblatt and Denson constructed a neurostimulator [59], peripheral nerve stimulation has been used to localize nerves. Despite the advent of ultrasound-guided

Table 10.4 Continuous (loss of resistance) nerve blocks

Continuous block	Fascia to be recognized	Indication
Transversus Abdominis Plane (TAP block) [54]	Internal oblique fascia	Abdominal wall surgery
		Cesarean section
Ilioinguinal/iliohypogastric block [55]	External and internal oblique aponeurosis	Herniorrhaphy
		Orchidopexy
		Bone crest grafting
Fascia Iliaca compartment block (FIC block) [56]	Fascia lata and fascia iliaca	Femur surgery
		Knee surgery
		Proximal femur fracture
		Analgesia
Axillary block [57]	Neurovascular sheath	Arm and hand surgery
Rectus sheath block [58]	Anterior and posterior wall of the rectus sheath	Umbilical or incisional hernia repair

peripheral nerve blockade, nerve stimulation remains a popular technique used alone or in combination with ultrasound guidance [53].

The success of nerve stimulation-guided regional anesthesia relies on the reproducible observation that, as the needle moves closer to the nerve, less current is needed to evoke a motor response. When a motor response can be elicited by using less than a minimum current, the needle is sufficiently close to the nerve to predictably block the selected target with injection of local anesthetic [60].

An elicited motor response at or below 0.5 mA is considered a common end point for successful final needle placement adjacent to a peripheral nerve and this is usually followed by local anesthetic injection and catheter insertion. Because catheters are usually inserted blindly and some distance beyond the needle tip to avoid inadvertent dislocation, verifying a correct catheter tip position is not possible. There is no guarantee that the introduced catheter tip is close enough to the target nerve and that subsequent infusion through the catheter with diluted local anesthetic will provide analgesia. Therefore, most anesthesiologists choose to administer a loading dose through the needle before inserting the catheter. An incorrectly placed catheter only becomes apparent after the effect of the loading dose has worn off [61].

This secondary block failure occurs in up to 26 % of patients [62, 63].

In order to avoid secondary (continuous) block failure, the catheter may be directly inserted through the needle as soon as the optimal needle position is reached, followed by injection of local anesthetic through the catheter. Lack of anesthesia indicates an improperly positioned catheter and the needle insertion procedure and catheter insertion should be repeated. However, electrical nerve stimulation may no longer be used for nerve localization. Moreover, the first bolus injection precludes that an equal dose of local anesthetic is injected, which may influence the effectiveness of second attempt.

Catheter Advancement and Tip Localization Using Electrical Stimulation

Catheters follow an unpredictable course when threaded through a needle [64–66].

Stimulating catheters can be inserted while electrical current is applied on the tip of the catheter. During catheter advancement, this may provide real-time information that the catheter tip is still in close proximity to the target nerve as long as the required muscular contractions are observed during catheter advancement [38, 67, 68]. If the motor response decreases or disappears then either the needle or the catheter is redirected until the motor response reappears. Threading of the catheter may be eased by distending the perineural space, by injecting dextrose 5 % (D5W) [69–71].

Manufacturers construct noninsulated tips of the needles and the bare tips of the stimulating catheters in the same way, in order to ensure that the muscle twitches will be similar for needle and catheter if these two are at equal distances to the nerve. However, stimulating catheters have a conducting area with size and geometry that are different from the ones described for needles and the sensitivity of motor response to electrical stimulation is different. When needle nerve contact is made muscular contractions are observed between 0.01 and 2.0 mA [72–74]. Generally, a minimal output between 0.2 and 0.5 mA has been advocated as the optimal current intensity correlating with a short distance between nerve and needle, while avoiding intrafascicular positioning of the latter, but no strict minimal numerical thresholds for stimulating catheters are recommended [75]. Although no correlation between minimal electrical charge at the tip of the stimulating catheter and the efficacy of the peripheral nerve block can be demonstrated [76].

Improved analgesia has been shown in stimulating vs. nonstimulating catheters. The reduction regarding the need for analgesic rescue treatment was between 8 % and 56 % [77–83]. However, for continuous femoral nerve blocks for knee surgery, this difference has not been shown. It is likely that any catheter tip placed under the fascia iliaca fascial plane will

provide effective analgesia, especially if a sufficient volume of local anesthetic is infused. Moreover, nociceptive areas from the knee are also innervated by the sciatic nerve and the posterior division of the obturator nerve [72, 84–87].

Ultrasound Guidance for Catheter Insertion

The introduction of real-time ultrasound guidance has been a major advancement in the practice of regional anesthesia. Compared with the previous described nerve localization techniques, US allows faster block performance, fewer needle passes, a reduced incidence of vascular puncture, faster block onset, and greater block success. For these outcomes, the recommendation that US guidance is superior to other nerve localization techniques can be made [88].

Unfortunately, this conclusion cannot be automatically inferred to perineural catheter placement, because in single-injection blocks it is always possible to reposition the needle in order to obtain optimal spread of local anesthetic around the nerve. This real-time positioning is not possible with a flexible catheter and the catheter insertion is therefore comparable to a single-point injection [89]. Moreover unlike needles, flexible perineural catheters rarely remain within the 2-dimensional 1 mm ultrasound (slice) view, making it difficult to observe catheter tip placement relative to the target nerve. Lastly, compared to single-injection blocks the angle between the long axis of the placement needle and target nerve is important if a catheter-through-needle technique is used for perineural catheter insertion. When a catheter is threaded through a needle with a position perpendicular to the nerve, then it may traverse the nerve [80].

For ultrasound-guided perineural catheter insertion, three approaches exist. The needle in plane, nerve in short-axis approach; the needle out of plane, nerve in short-axis approach; and the needle in-plane, nerve in long-axis approach [90].

Needle In-plane, Nerve in Short-Axis Approach

For visualization of the nerve and surrounding structures, most often a short-axis view (SAX) is used. The cross-sectional view allows easy visualization of the anatomical structures involved and dynamic assessment and verification of circumferential distribution of local anesthetic upon injection is possible. Finally if the transducer moves slightly, the image is still workable [91].

If the needle is inserted parallel to the ultrasound beam (in-plane) then a direct visualization of complete needle and tip relative to the nerve is possible. When the catheter is advanced through the needle, the emergence of the catheter through the needle may be visualized and the tip followed during catheter advancement. Because of the perpendicular orientation of the block needle and target nerve, it is important to advance the catheter only a small distance beyond the needle tip in order to avoid bypassing the target nerve. However, there is a risk that also the catheter is displaced when the needle is withdrawn over the catheter.

Although no objective evidence exists, some anesthesiologists suspect that with a more rigid catheter the risk of overshooting the target nerve is increased. Therefore, they suggest to use flexible catheters [92]. By using flexible catheters, Ilfeld et al. could not demonstrate any difference in effectiveness of continuous popliteal-sciatic nerve blocks when the catheter was inserted only a minimum distance (< 1 cm beyond the needle tip) compared to a more traditional distance (5–6 cm). Nor did any catheter dislodgement occur during Tuohy needle withdrawal [93]. Caution is warranted with extrapolating these results to other catheter designs, ultrasound approaches, or anatomical locations.

Self-coiling catheters are developed and coil up as soon as they are advanced beyond the needle tip. This allows the catheter tip to remain close to the initial needle-tip position, even when a perpendicular approach to the nerve has been chosen [41]. However, these results should be interpreted with caution because no clinical studies in patients have been described. The position of the catheter tip relative to the target nerve is less important than the analgesia provided by the perineural infusion.

It is irrelevant to patients where the tip appears to be relative to the target nerve. The end point of interest is analgesia provided by the perineural infusion. Therefore, an alternative is to advance the catheter 3 cm beyond the needle tip and then after needle removal the catheter is retracted while incremental doses of local anesthetic are injected. When an optimal spread of local anesthetic is obtained, catheter withdrawal is stopped and the catheter is anchored in place [94].

A benefit of short-axis needle in-plane approach is that the same US technique for single-injection peripheral nerve block and continuous peripheral nerve blocks can be used. Moreover, this approach can be applied in all anatomic catheter locations, and some speculate that the relatively low rate of dislocation for continuous interscalene and supraclavicular blocks is explained by choosing an in-plane approach with positioning of the catheter from posterior to the upper trunk to lie under the investing fascia [95].

A disadvantage of the nerve in short-axis needle in-plane approach is that new needle entry sites have to be chosen and the needle trajectory to the target nerve is longer compared with more traditional nerve stimulation techniques. Especially with deep blocks, long needles, which may bend, have to be used [96]. This, in combination with the depth of the target nerve, makes needle shaft and tip visualization a demanding task. Then the disadvantage of this needle approach outweighs the advantages and another needle approach is advised [97].

Needle Out-of-Plane, Nerve in Short-Axis Approach

A benefit of this approach is that a similar needle approach to the nerve can be used and no modification of the standard practice for an electrical nerve stimulation-guided block is

necessary, including the site of puncture, needle direction, and tactile feedback during needle progression. Using the shortest needle trajectory to the nerve, the needle is guided tangentially to the target in order to avoid nerve injury and to guarantee catheter placement parallel to the nerve.

Theoretically, the catheter remains nearer to the nerve, even when threaded more than a centimeter past the needle tip. The main disadvantage of this technique is the inability to visualize the needle tip [91]. Hydro localization, injecting small amounts of local anesthetic, while advancing the needle is a technique used to systematically trace the needle tip during its advancement thereby reducing complications [98].

The longitudinal orientation of the needle with the nerve makes precise visualization of the catheter tip less crucial, because it is supposed that the catheter tip remains in close proximity to the nerve while advanced. Marhofer et al. used an out-of-plane needle approach for interscalene and femoral nerve blocks and advanced the catheter 3 cm beyond the tip of the cannula and retracted the catheter during permanent slow saline administration and US guidance until the spread of the fluid was confirmed as optimal relative to the target nerves. All catheters were successfully placed [99].

Needle In-plane and Nerve in Long-Axis Approach

The long-axis visualization of peripheral nerves and in-plane insertion of both the needle and the catheter may allow real-time visual control of catheter advancement in superficial locations. Using to-and-fro movements and slight rotation of the bevel of the needle, the catheter may be visualized in the ultrasound beam, which facilitates correct positioning [100].

Keeping the needle, catheter, and needle in the ultrasound beam width of 1 mm is a very demanding and time-consuming task. Ten percent of the femoral catheters cannot be placed using this approach within 30 min. Moreover, mild withdrawal of the catheter was sometimes necessary in order to assess the catheter's deviation from plane [101]. This imposes the risk of catheter shearing [102]. Other limitations of this nerve and catheter visualization technique are that the nerve must have a relatively straight course. The needle in-plane, nerve in long-axis technique is the most challenging of the three needle and catheter approaches discussed [90].

Ultrasonographic Catheter Tip Localization

Theoretically, ultrasound has the potential to confirm catheter tip location. However in practice, identifying the tip is often challenging because flexible catheters do not remain within the ultrasound plane of view. Therefore, additional means for tip identification are used such as observation of the location of fluid [92]. Injecting agitated microbubbles, which appear as a hyperechoic injectate within the anechoic local anesthetic fluid [103, 104], or the use of color Doppler in which the injectate appears as a mix of colors superimposed on the grayscale background, or simply inject air through the catheter [105]. The air test improves the assessment of catheter tip location compared to chance, but there is no difference compared to direct visualization of the catheter without air injection. The relationship of the hyperechoic artifact with the target nerve may aid in judging the catheter tip location and subsequent distribution of the local anesthetic injectate. The disadvantage of this air test is the introduction of an artifact near the target nerve that may blur the image and hinder catheter replacement. Therefore, it is recommended to keep the volume of injected air to a minimum (< 1 ml) to limit artifactual interference. Moreover, the detrimental effects caused by an accidental intravascular catheter placement with subsequent intravascular air injection are avoided when this minimal amount of air is used [106].

Complications of Continuous Peripheral Nerve Blocks

Serious complications of regional anesthesia and analgesia are rare. Many of the complications that might occur during placement of the continuous peripheral nerve blocks result from needle placement and injection through the needle and are identical to complications of single-injection peripheral nerve blocks [107].

All blocks carry with them the inherent risk of regional anesthesia: failure, nerve damage, local anesthetic systemic toxicity, bleeding, infection, and damage to surrounding structures. Scrupulous attention to detail in the performance of the block and catheterization, and careful postoperative management of the catheter infusion will allow the provision of excellent analgesia at an acceptable small, but never zero incidence of serious complications [108].

Inaccurate Catheter Tip Placement

CPNB-specific complications during catheter insertion include inaccurate catheter tip placement. Catheter placement too far from the target nerve results in block failure. Secondary block (infusion) failure has an incidence varying between 10 % and 40 %.

A higher BMI and long indwelling time are likely to predispose to higher failure rates [109]. This is only a minor complication compared to epidural, intrathecal, intravascular, interpleural, and intraneural catheter placement all of which may result in poor outcomes [35, 110–118].

One common denominator in these reported complications is catheter threading. Most catheters are threaded more

than 3 cm from the catheter tip. Therefore, in order to prevent complications do not thread the catheter more than 3 cm past the tip of the needle. Threading more than that is not necessary, it only increases the risk of complications and jeopardizes the success of the block.

These reports also prove that both single blocks and the first injection through the catheter (or the start of an infusion) should only be performed in an environment that allows the ready identification and prompt management of any resulting complications.

Catheter Dislocation

Catheter dislocation and leakage at the insertion site are complications arising during local anesthetic infusion. The diameter of the catheter is smaller than that of the needle used for skin puncture and creating space for local anesthetic to leak upon infusion when a catheter-through-the-needle catheter technique is used. The transparent dressing disconnects from the skin and the catheter gets dislocated. The incidence of catheter dislocation varies between 1 and 25 % [99, 119, 120]. Movement and time are considerable factors for perineural catheter tip displacement. For preventing accidental catheter removal, different strategies are used. Combining different methods of catheter fixation may reduce the incidence of accidental catheter removal to 1 % [120–122]. Other methods used are subcutaneous tunneling [123, 124]; however, tunneling and suturing are not without risks. The tunneling needle may inadvertently cut the catheter [125]. Catheter anchoring devices may be helpful in securing catheters for regional anesthesia [126–128].

Also sealing the insertion site with 2-Octyl cyanoacrylate (Dermabond®) has been used to secure catheters [129]. Even shortly after application of the glue, catheter removal is still possible [130, 131]. The application of glue not only provides fixation but also a barrier to the entry of gram-positive skin flora along the catheter exit tract and this may prevent catheter-related infections [132]. Mostly transparent dressings, which allow inspection of the catheter insertion site are used, but chlorhexidine gluconate impregnated dressings may reduce bacterial colonization rates in regional anesthesia catheters [133].

Infectious Complications of CPNBs

Bacterial colonization of CPBNs occurs easily and the incidence varies between 27 % and 57 % depending on the location of the catheter and criteria used for the definition of colonization [134]. The highest microbial density is found in the axilla and groin region in men. This is not surprising when one considers the high density of sebaceous glands and humidity of these skin sites [135]. Skin disinfection is less efficient in areas with a high density of sebaceous glands [32]. So both factors contribute to the high incidence of colonization of femoral and axillary catheters. The most frequently identified organisms are *Staphylococcus epidermidis* (71 %), enterococcus (10 %), and klebsiella (4 %) [136]. Although colonization of the catheter may occur, this does not automatically lead to infection. Forty-four percent of the catheters are colonized if signs of local inflammation are present versus only 19 % when no evidence of inflammation exists. This suggests that catheters also become contaminated during removal despite aseptic conditions [119]. Tunneling of catheters seems to offer some protection against colonization [123, 137]. The incidence may decrease to 6 %, whether this will influence the infection rate should be examined [138].

In regional anesthesia, antimicrobial continuous peripheral nerve catheters have not yet been introduced, even though the effectiveness of antimicrobial central venous catheters has been confirmed [139]. CPNB infection is a rare event with an incidence between 0.02 % and 3 % [134, 136, 140, 141]. Serious case reports have been described such as psoas abscess complicating femoral nerve block [142], thigh abscess after continuous popliteal sciatic nerve block [143], acute neck cellulitis and mediastinitis complicating continuous interscalene block [144]. The German society for Anesthesia and Intensive Care has published clear definitions (Table 10.5) for an infectious complication after regional anesthesia [145].

Neuburger et al. examined 3491 CNPB catheters and used the definition (Table 10.5) in relation to infection occurring after CPNBs. A small infection occurred in 4.2 %, a mild in 2.4 %, and severe infection in 0.8 % of the patients who had a perineural infusion. The surgical intervention for severe infection consisted mostly of a simple superficial incision but in 58 % deep surgical drainage was necessary. All infections were successfully treated without sequela.

Table 10.5 Definition of infectious complication after regional anesthesia

Severity	Symptoms
Small infection	Redness, swelling, or pain upon palpation (two or more criteria should be present)
Mild infection	Pus on the needle or catheter insertion site, fever, leukocytosis, treatment with antibiotics
Severe infection	Surgical intervention (superficial and/or deep surgical drainage)

It is interesting to note that patients experienced pain upon pressure at the catheter insertion site, regardless of the severity of the infection. This sign seems to be an important predictor for a pending infection. So during follow-up in these cases the catheter insertion site should not only be visually inspected but also palpated. Pain upon palpation, redness, and pus on the catheter insertion site are reasons to remove the catheter [141].

Risk factors for infection include male sex, absence of perioperative prophylaxis, admission to an intensive care unit, the experience of the anesthesiologist, and the duration of catheterization [119]. Diabetic patients have a 2.4 times higher risk for catheter-associated infections compared with nondiabetic patients [146]. It is unknown whether the site of catheter insertion increases the risk of infection. Some report a higher incidence of infection with axillary and femoral catheters [119, 147], while others report the highest incidence of infection with the interscalene catheter insertion site [141].

No guidelines exist regarding whether regional anesthesia can be safely performed in immune compromised patients or in patients with systemic infections. On an individual basis the risks and benefits of regional anesthesia should be considered. The general consensus suggests not to perform regional anesthesia if an active infection exists at the presumed needle insertion point. If an active infection exists and the decision is made to perform a CPNB, then the distance between the active infection site and needle and catheter insertion site should be as far away as possible. Ideally, catheter insertion should not be performed if there is any evidence of active infection and only if active antibiotic treatment has already been started. The use of immunosuppressive drugs is not associated with a higher risk of infectious complications after regional anesthesia. The opposite is true of patients with diabetes mellitus and malignant diseases. Prophylactic use of antibiotics may be considered in these patients [134].

Strict adherence to aseptic technique is a cornerstone of preventing infectious complications in regional anesthesia. It is recommend to wear a hat, surgical mask, and sterile gloves. Skin preparation should be performed with an alcohol-based chlorhexidine solution [32].

It is interesting to note that EMLA cream (an eutectic mixture of lidocaine 2.5 % and prilocaine 2.5 %) has a similar bactericidal effect to Skinsept Pur (alcohol-based preoperative skin disinfectant) and has a longer bacteriostatic effect. This difference was significant after 4 h and lasted 12 h. Whether this finding has clinical relevance in terms of reducing nosocomial infection needs further studies [148].

Close surveillance of bacterial infections of CPNBs makes a veritable detection of adverse events possible and the effects of changes in clinical procedures can be followed. Reisig et al. revised an existing hygiene regime for CPNBs based on the results of a close surveillance system. A major change occurred when the skin disinfection (spray-and-scrub) combined procedure, lasted 10 min. The effect was a decrease in infection rate by almost 75 % [33]. For further discussion on this topic, please refer to Chap. 6.

Complications of Catheter Removal

Removal of indwelling catheters should be easy and painless. Nerve catheter entrapment can occur from a variety of mechanisms, including, looping, knotting, and kinking [149–151]. The incidence of knotting is 0.13 %. In all cases the catheter was inserted more than 8 cm from the needle tip and could have been prevented by not advancing the catheter more than 3 cm [152]. Knotting may result in difficult or impossible catheter removal.

In order to prevent kinking and breaking upon withdrawal, manufacturers reinforce the catheters with a stainless steel coil or wire. These flexometallic catheters can be stretched to more than 300 % of their original length without breaking, which is 10 times greater than other types of catheters [153]. The risk of this catheter design is that the polyurethane covering and inner stainless steel coil separate. This may occur during attempted removal of a catheter. In these cases, if the entire needle catheter system is not withdrawn as a single unit, but only the catheter is withdrawn through the needle the catheter will be severed and the metal wire retained and the polyurethane covering withdrawn [154]. Instructions in catheter kits now include not to remove the needle before the guidewire is withdrawn [155].

Coiled catheter tips can withstand 13.7 N of force prior to unraveling. When catheters are cut this property is lost and only a little traction is necessary before disengagement occurs. The unraveling increases the distance between coils at the catheter tip which allows tissue entrainment and makes catheter entrapment more likely [156]. Stimulating catheters require more force to remove than other type of catheters and it is suggested that the catheter design with exposed metal coils may contribute to the adhesion of catheter tips after prolonged use, especially when there is no active infusion of local anesthetic or saline [39]. In practice, retained catheters show no signs of adhesions once they were removed, although they may have been destroyed during removal [157].

In order to avoid catheter infection and dislodgement, CPNB catheters are tunneled. Tunneling of catheters lead to a significant increase in the force required to cause dislodgement but also more force is required for removal of the catheter [158]. Recommendations for the management of entrapped peripheral nerve catheters are mostly derived from the management of entrapped epidural catheters [159–161]. When a catheter is difficult to remove it is important to preserve the integrity of the catheter and avoid shearing and breakage of the catheter. Keep the catheter connected to the

pump and continue the infusion with saline. Prior to manipulating the catheter, the catheter tip may be localized by CT or MRI. Most catheters are MRI compliant and can be left in place during 1.5-T MRI scans. Although the MRI scanner's applied fields induce currents, the electrically conducting wire within the polyurethane catheter does not heat more than 3 ° and injuries are therefore unlikely. However, it is strongly advised to follow the manufacturer's recommendation regarding the MRI compatibility of the catheter [162]. Before continuing to manipulate the catheter the patient is examined to ensure that sensory function has been restored. Gentle traction on the catheter should not elicit pain or paresthesias. If this happens caution is warranted. The catheter may have adhered to neural structures and the pulling and tugging may cause nerve damage. Surgical removal of the catheter should then be considered. Changing body position and bolusing 30–50 ml of saline through the catheter may aid in removal of retained catheters [163, 164].

An entrapped peripheral nerve catheter may also be removed with the aid of an interventional radiologist under fluoroscopic guidance. During this procedure, a guidewire is inserted into the catheter in an attempt to unwind the knot. Dilating sheaths of increasing size are subsequently placed over the catheter and distal tension is applied to pull the knot against the dilator. These maneuvers will reduce the size of the knot until it retracts into the dilator and is subsequently removed intact. This technique has been proved to be very successful [152]. Surgical intervention is the ultimate therapy if other means and continuous traction were not successful.

Neurological Complications

Serious permanent complications after continuous peripheral nerve blockade are uncommon. The origin of neurologic symptoms and signs in the perioperative period are most likely unrelated to the blocks. New, all-cause neurological symptoms were reported in 8.2 % at day 10, 3.7 % at 1 month, and 1.3 % at 6 months, but after careful examination of these patients it was shown that few complications were block related [140, 165].

For peripheral regional anesthesia, in general, the incidence of transient adverse neurologic symptoms purely associated with CPNBs is 0 % to 0.2 % [119, 141, 166–169]. Introducing a catheter in the close vicinity of a nerve does not increase the risk of neurological complications. This suggests that if neurological damage occurs after CPNBs, it is most likely caused by the needle during the initial block insertion.

Based on the estimated rate of occurrence of nerve injury after single-injection peripheral nerve block, almost twice as many nerve injuries are seen in proximal brachial plexus (interscalene) blocks compared with distal brachial plexus (axillary blocks) [170].

The observed differences in risk of nerve injury between proximal and distal parts of the brachial and lumbosacral plexus may be explained by the observed differences in the ratio of neural to nonneural tissue [171].

Unintended catheterization of nerves might be much more common than usually thought and may be influenced by the needle and catheter tip, but this does not invariably lead to neural injury [35].

It is suggested that stiff catheter tips more easily penetrate the outer epineurium and become embedded in the loose epineurium. Intrafascicular penetration is prevented by the strong sheath of the perineurium which is different from the loose tissue framework of the interfascicular epineurium. Intraepineural injection through the catheter will separate the fascicles upon injection [172, 173]. High injection pressures during injection should be prevented and might indicate intrafascicular injection [174].

When the catheter is placed under ultrasound guidance it is common to inject a small amount of fluid to confirm correct placement of the needle tip. Subepineural, parafascicular injections are characterized by low injection pressures and when ultrasound is used, expansion of the cross-sectional surface area with a change in echogenicity during injection is noted [175]. Discrimination of subepineural and extraneural tip position based on an injection of 0.5 ml is possible. The first injection of local anesthetic through the catheter should preferentially be performed under ultrasound guidance.

It is important to avoid late secondary neurological damage due to an insensate limb. Theoretically, patients with blocked extremities are more predisposed to limb injury and pressure neuropathy because of the lack of protective pain reflexes and reduced proprioception. Some anesthesiologists consider discharge of patients with a motor block controversial, but withholding the analgesic benefits of long-acting local anesthetics and CPNBs in ambulatory patients is unjustified. Klein et al. found an infrequent incidence of neurologic complications and injuries despite discharge with an insensate extremity [63]. When patients are discharged, they should be provided with instructions, to wear a sling, not to bear weight and to protect the anesthetized limb in order to avoid damage.

In conclusion, neurologic injury after peripheral nerve blocks is multifactorial and involves anatomy, site of needle and catheter insertion, bevel and catheter tip type, nerve–needle tip interaction, pressure of the needle tip, and underlying patient factors.

Accidental Vascular Puncture and Hematoma Formation

During CPNB placement, the incidence of vascular puncture is 5.7 % and 6.6 % for femoral and sciatic nerve catheters, respectively [176]. Ultrasound-guided PNB is associated with a reduced incidence of inadvertent vascular puncture [166, 177]. Serious hemorrhagic complications have been rarely described in CPNBs. Significant blood loss is more worrisome than neural damage. Hematoma formation may lead to nerve injury due to pressure ischemia, either as perineural hematoma or by occupying and pressurizing an anatomic compartment [169, 178]. Moreover, hematoma formation may be a risk factor for bacterial infection.

Bleeding complications of peripheral nerve blocks are less serious than those caused by central neuraxial blocks and the risks remain undefined. Information regarding the safety of CPNBs in patients treated with low-molecular-weight heparin (LMWH) or oral anticoagulants is scarce. A few studies have been performed involving the risk of hemorrhagic complications. Chelly et al. removed lumbar plexus catheters in patients with an INR between 1.5 and 3.9 and no serious complications occurred [179]. In another study, they demonstrated that continuous and single peripheral nerve blocks can be safely performed before the initiation of thromboprophylaxis and aspirin on the day of surgery and that perineural catheters can be safely removed when the patient is receiving thromboprophylaxis using low-molecular-weight heparin, warfarin, and aspirin [180]. Buckenmaier applied CPNB catheters for the management of pain in combat wounded patients who are anticoagulated with LMWHs. They used a liberal policy regarding LMWH and CPNBs and demonstrated that no catheter-related bleeding complications occurred [181]. Idestrup et al. showed that the concurrent administration of a continuous femoral nerve block and once-daily administration of the anticoagulant rivaroxaban (orally administered Xa inhibitor) and the timed removal (20 h) of the femoral catheter were not associated with severe hematoma formation. Ecchymoses were observed in 12 % of patients following total knee arthroplasty. No patients required removal of hematoma or decompression at the femoral catheter site [182]. Visoiu and Yang placed bilateral continuous nerve blocks in a child with coagulopathy undergoing laparotomy. The final decision to perform this technique was based on normal thromboelastogram (TEG) but abnormal PT and PTT. They suggested to evaluate the validity of TEG in the prediction of bleeding risk and the safety of regional anesthesia in coagulopathic patients [28].

Recommendations from the American Society of Regional Anesthesia differ from the European Society of Anesthesiology and state that for patients undergoing deep plexus or peripheral nerve block the same recommendations suggested for neuraxial techniques, should be followed. This conflicts with the European recommendation which state that single-injection axillary, femoral, or distal sciatic nerve block may be performed in the presence of aspirin or anticoagulants use. However, these should be stopped when deep blocks, where access is difficult and arterial trauma is a risk, are performed such as interscalene, supraclavicular, infraclavicular, and lumbar plexus blocks. Whenever lumbar plexus, paravertebral blocks with or without catheters, are inserted or withdrawn, the same guidelines that apply to neuraxial blocks should be followed [183].

The Dutch Society of Anesthesia states that a simple difference between superficial and deep blocks does not exist and proposed an alternative strategy. A block classification based on the negative consequence of bleeding complication was made (Table 10.6). Blocks in the category "limited consequences in case of bleeding " can be performed without stopping the use of anticoagulants. When blocks in the category " intermediate negative consequences of bleeding complication" are performed, then low-molecular-weight heparins prophylaxis, aspirin, NSAIDs, clopidogrel, prasugrel, ticagrelor, dabigatran, rivaroxaban may be continued. In these cases the INR should be lower than 2. If LMWHs or dabigatran or rivaroxaban is prescribed for therapeutic use then they should be stopped for at least 24 h. When continuous lumbar plexus or cervical paravertebral blocks are performed then the recommendations that apply for neuraxial blocks should be followed. For some additional discussion on this topic, please refer to Chap. 7.

Local Anesthetic Toxicity

Local anesthetic systemic toxicity (LAST) is a rare complication of PNBs. The incidence is 0.87 per 1000 PNBs. Most cases are the consequence of direct intravascular injection or secondary plasma absorption of large volume of LA. The incidence of LAST in CPNBs is not known. In Wiegel's study no patient showed signs of LAST [169], but 1 of 405 patients treated with continuous axillary nerve blocks developed preseizure signs of LAST. Despite low rates of infusion, LAST is a rare but possible complication of CPNBs [140].

Ultrasound guidance has improved safety. The risk of LAST has been reduced by 65 % with ultrasound guidance; it occurs only rarely in the contemporary practice of PNBs [184]. Ultrasound guidance minimizes inadvertent vascular puncture and even if inadvertent vascular puncture with intravascular injection of LA occurs, the lack of injectate spread around the neural target is an alarm sign and the injection is discontinued. Other mechanisms whereby ultrasound guidance reduces the risk of LAST are the reduced dose of LA which may be used. Furthermore in US-guided blocks, frequent needle adjustments are performed in order to obtain the maximum spread around the nerve. Therefore, LA is

Table 10.6 Peripheral nerve blocks divided in negative consequences of bleeding complication

Limited consequences	Intermediate consequences	Severe consequences
Superficial blocks	*Paravertebral blocks*	*Paravertebral blocks*
Distal nerves arm	Thoracic paravertebral	Cervical paravertebral
Saphenous nerve		Lumbar plexus
Sural nerve		Psoas compartment
Tibial nerve		
Ilioinguinal nerve		
Fascial blocks		
TAP		
Fascia iliaca		
Superficial perivascular	*Deep perivascular*	
Interscalene brachial plexus	Infraclavicular brachial plexus	
Supraclavicular brachial plexus	Proximal sciatic nerve	
Axillary brachial plexus		
Femoral nerve		
Obturator nerve		
Midfemoral sciatic nerve		
Distal sciatic nerve		

injected in incremental doses and in multiple locations around the nerve, and this reduces the maximum local anesthetic blood levels following PNB and the risk of LAST [185, 186].

Besides the nerve localization technique, other important risk factors for LAST includes site of injection, local anesthetic type, dosage, and weight. Paravertebral and upper limb blocks have an increased risk of LAST compared with lower limb and trunk blocks [184]. This is in contrast to the findings of Auroy et al. They demonstrated that lumbar plexus block was associated with a higher risk of LAST than other blocks [187]. Whether continuous lumbar plexus blocks also pose a greater risk of LAST than other types of continuous perineural infusions is unknown. One study showed an incidence of 0.9 % of LAST in continuous lumbar blocks which is certainly higher than for other CPNBs [140, 188]. Therefore, caution is warranted and it is advised to extensively monitor for signs of LAST during the application of continuous lumbar plexus block because the local anesthetic is deposited in or near a highly vascularized psoas muscle compartment. Continuous infusion will not result in sudden onset of toxicity, but if only bolus injections are employed then patients are at risk of LAST if catheter migration occurs. For further discussion of this topic, please refer to Chap. 3

Other Complications

CPNB's and Acute Compartment Syndrome

Pain relief with a CPNB carries the risk that the diagnosis of an acute compartment syndrome (ACS) is delayed. In ACS, swelling and increased pressure within the muscle compartments occur. This compromises the capillary perfusion pressure which can cause cellular ischemia, neurological deficit, necrosis of the muscles, and rhabdomyolysis with subsequent renal failure. The only way to avoid these complications is early recognition and attendant decompression with fasciotomy. The diagnosis requires a high index of suspicion and is challenging [189]. The cardinal symptom of compartment syndrome is pain and there is concern that this may be masked by the effective pain relief of regional anesthesia [190, 191].

After a systematic review of the literature, no case report suggested that CPNBs delayed the diagnosis of ACS. In many case reports, pain was present but ACS not considered for a period of time. Increasing demands for analgesia should trigger clinical review [192, 193].

Dense peripheral nerve blocks can interfere with the assessment of pain. Dilute concentrations of local anesthetics reduce the intensity of motor block and dense sensory block. Ischemic pain primarily mediates through the thicker A-Beta fibers, while surgical pain is mediated through the thin unmyelinated C-fibers. Smaller nerve fibers are blocked before the larger fibers and myelinated fibers are blocked before unmyelinated fibers. By using analgesics in dilute concentration, it is possible to obtain sufficient postoperative pain relief without excluding the possibility of ischemic pain being felt by the patient. This strategy was effective in preventing devastating complications of ACS [194, 195]. An alternative approach is not to use a continuous infusion of local anesthetic but to use bolus injections. This allows a window of observation when the bolus wears off. The disadvantage of this approach is uneven pain relief and a lower level of patient comfort.

There is insufficient evidence to either endorse or prohibit the use of CPNBS and other regional anesthetic techniques in patients at risk for ACS. A high index of suspicion, careful postoperative monitoring with special attention directed toward analgesic consumption, and a focused physical examination is the best diagnostic tool for ACS. It is a disservice to our discipline and unethical to deny the majority of trauma patients a good quality analgesic experience simply because regional anesthesia has been made the scapegoat in the literature for inadequate clinical assessment of ACS. Vigilance and awareness remain keys to early detection and prevention of ACS [195, 196].

Phrenic Nerve Palsy

A side effect of interscalene brachial plexus blocks is concomitant block of the phrenic nerve with subsequent hemidiaphragmatic paresis [197]. During normal inspiration, as the diaphragm contracts, the lower part of the rib cage along with the abdomen moves outward. In patients with unilateral diaphragm paresis, this does not occur and the expansion and ventilation of the lower lung is reduced. This results in a decrease in forced vital capacity and forced expiratory volume by more than 25 % [198].

One may try to avoid phrenic nerve block by injecting a low dose of local anesthetic and avoiding spread of local anesthetic toward the anterior scalene muscle and phrenic nerve [199]. However when a continuous interscalene brachial plexus block is started, the phrenic nerve cannot be spared by local anesthetic anymore [200–203].

Tsui et al. noticed that shortness of breath typically occurs on the second day after the continuous infusion has been running. This supports the hypothesis that the anterior scalene muscle and phrenic nerve are flooded with excess local anesthetic [204]. They also reported that a bolus of normal saline (10–30 ml) via the catheter may "wash off" local anesthetic after a block. The underlying mechanism and best regimen for block reversal is unclear, several mechanisms have been suggested; a dilutional effect by saline, a reduction in local pH, alteration of local sodium content, or even a placebo effect [205].

Excessively lengthy phrenic nerve block and diaphragm paresis may result in lower lobe collapse, atelectasis, and pleural effusion of the lung [206, 207]. Patients should be informed and understand that untoward events may be experienced during continuous interscalene brachial plexus block. They should report any side effect to the anesthetic team, because physicians from other specialties may be unaware of these effects or complications [208]. Unilateral diaphragm paresis is only symptomatic in 45 % of patients, but after cessation of the infusion of local anesthetic the diaphragm function should be restored and the symptoms disappear.

Falls

Falls are an important cause of morbidity in hospitalized patients and occur in 1.6 % of patients after surgery. Preoperative variables that predict falls include older age, functional dependence in any basic activity of daily living, and an ASA score of 3 or greater. Intraoperative variables that predicted postoperative fall are longer surgical times and blood transfusion requirement [209]. Falls occur after orthopedic surgery regardless of the presence of peripheral nerve block, female sex, patient age greater than 65, prolonged admission, and primary or revision knee arthroplasty, are all significant risk factors for a postoperative fall [210].

Risk factors identified for hospitalized falls included gait instability, lower limb weakness, urinary frequency or incontinence, history of previous falls, and the prescription of sedatives and hypnotics [211]. CPNBs of the femoral nerve affect the quadriceps function required for ambulation after surgery and therefore the use of continuous femoral blocks increases the risk of falls in patients undergoing orthopedic surgery [212–214]. Patients undergoing total knee replacement have a threefold higher risk of falling than patients undergoing hip replacement [215].

In considering the risk of falls, it is important to take into consideration the concentration and rate of infusion of local anesthetic but also the surgical procedure. Quadriceps strength is decreased by 60 % after knee surgery, regardless of whether or not peripheral nerve blocks are used for postoperative pain relief [216]. Falling after surgery causes substantial additional morbidity for the patient. Therefore, many hospitals have implemented fall prevention strategies [217–219]. Having implemented a preoperative patient education program on the prevention of falls after total knee arthroplasty, no in-hospital falls were recorded. Therefore, this education program was made mandatory for all patients undergoing orthopedic surgery [220].

Optimal Infusion Regimen for Perineural Infusions

The optimal infusion regimen for perineural infusions is not known. Many variables including: nerve localization technique (blind, nerve stimulation-guided, ultrasound-guided) nerve location (upper vs. lower extremity and distal vs. proximal), catheter type (end hole, multihole), catheter tip position (perineural vs. subepineural vs. epineural) postoperative pain intensity, affect the efficacy of the perineural infusion. Infusions of ropivacaine, bupivacaine, or L-bupivacaine in various concentrations, are most commonly used. Low local anesthetic concentrations are used in order to minimize muscle weakness during CFNB and to allow mobilization. However, for continuous posterior lumbar plexus catheters,

continuous femoral nerve blocks, and continuous popliteal-sciatic nerve blocks, it has been demonstrated that local anesthetic concentration and volume do not influence block characteristics as long as the total dose remains constant [221–223]. Thus, these results suggest that lowering the concentration of local anesthetic is not effective in minimizing the undesired motor weakness during CPNBs. Reducing the concentration at a given infusion rate will decrease muscle weakness but at the expense of reduced analgesia [224]. On the contrary, lowering the infusion rate with a concurrent increase in concentration will not compromise analgesia and is an effective strategy in lowering the infusion rate per hour. This practice may have great advantages. The use of a lower local anesthetic volume may result in fewer changes of the medication syringes or bags. Besides economical benefits this regimen may reduce infectious complications [225]. Any break within the integrity of pump and catheter infusion system, such as solution bag changes and or catheter-hub disconnections may increase the risk of contamination and the possibility of developing a subsequent localized or systemic infection [226]. For continuous interscalene and infraclavicular blocks, the relationship between volume and concentration is different. A lower concentration of local anesthetic at a higher basal rate provides superior analgesia. This is opposite to the lower extremities and shows that the interaction is complex and varies with catheter location [227, 228].

At this moment the information is insufficient to provide an evidence-based local anesthetic infusion regimen with optimal basal rate, bolus volume, and lockout. A basal infusion of local anesthetic reduces breakthrough pain and improves sleep quality. The possibility to top up this infusion by the patient, or a nurse, further improves analgesia. Ilfeld described extensively different local anesthetic delivery regimens for different locations. Most published investigations report a basal infusion rate of 4–10 ml/h (with lower rates for catheters of the lower extremity and higher rates for the upper extremity), a bolus volume of 2–10 ml, and a bolus lockout period of 20–60 min [21]. The maximum recommended hourly total dose of local anesthetic for CPNBs is also unknown, but a wide safety margin seems to exist [229].

Summary

Enormous strides have been made in the use of CPNBs in the past decade or two. For years continuous epidural anesthesia was the gold standard for effective postoperative pain control using regional anesthesia. In recent years, the use of CPNBs for the control of postoperative pain has increased and now competes with continuous neuraxial blockade for efficacy and safety. Ultrasound guidance and nerve stimulation, alone and together, have led to the enthusiastic use of both single and CPNBs. The other major advance we have experienced in recent years is a great improvement in the quality of Catheter/Needle assemblies available to the anesthesiologist. Through-the-needle and over-the-needle/catheter assemblies each have their proponents, advantages, and disadvantages. All of these changes have led to a better and safer experience for patients. With these improvement come additional risks, but on analysis, the benefits of CPNBs outweigh the risks but we must continue to find ways to reduce those risks.

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Part III

Specific Regional Blocks: Safe Practice and Management of Adverse Events

Complications of Regional Anesthesia: Upper and Lower Extremity Blockade

11

Stephen Choi, Patrick B.Y. Wong, Kristen Gadbois, and Colin J.L. McCartney

Key Points

- Nerve injury after peripheral nerve blocks can be due to needle trauma, chemical neurotoxicity, ischemia, or compression.
- Intraneural needle placement can cause significant injury, either from direct needle trauma or pressure-related ischemia after injection. Although this probably occurred without sequelae prior to the advent of ultrasound-guided regional anesthesia, there is no evidence to support deliberate intraneural injection. On the contrary, current guidelines recommend utmost care should be taken to avoid accidental intraneural needle placement.
- The hypothesis that performing peripheral nerve blocks under ultrasound guidance can prevent direct needle injury has not been proven. However, there is evidence to suggest that ultrasound use may decrease the incidence of local anesthetic systemic toxicity (LAST) for peripheral nerve blocks.
- Local anesthetics have been shown to have neurotoxic effects during in vitro studies. Although the dose and concentration used in clinical practice is generally safe, it is prudent to use the lowest concentration possible to achieve the desired effect.
- After peripheral nerve block temporary neurologic deficits may occur in 3 % of patients with most symptoms resolving within days or weeks of surgery. Permanent injury is rare, occurring on average 2.4 instances per 10,000 blocks.
- Practitioners must be familiar with the potential complications specific to each nerve block prior to performance.

S. Choi, MD, FRCPC, MSc (✉)
Department of Anesthesia, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada
e-mail: Stephen.Choi@sunnybrook.ca

P.B.Y. Wong, MD, FRCPC • K. Gadbois, MD, FRCPC
C.J.L. McCartney, MBChB, PhD, FRCA, FRCPC
Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, ON, Canada
e-mail: pawong@toh.ca; kgadbois@toh.ca; cjlmccartney@gmail.com

Regional techniques have the potential to provide many benefits for patients including reduced use of anesthetic agents enabling quicker recovery, enhanced analgesia, reduced morbidity, and potentially better functional outcomes. The advent of ultrasound guidance has greatly increased the number of practitioners providing safe, effective, regional anesthesia. A continued barrier to its wider use is the fear of neurological injury despite the rarity of its occurrence. Adverse events can occur after any medical intervention, but nerve injury after regional anesthesia is so rare that it is very difficult to study. Its true incidence is difficult to ascertain due to the rarity of the event and/or negative reporting bias although estimates have been made (Tables 11.1 and 11.2). However, when these complications occur, they can be devastating for all stakeholders: the patient, the anesthesiologist, and the practice of regional anesthesia. Early reports of severe spinal cord damage after spinal anesthesia [2, 3] resulted in regional methods being almost abandoned in the United Kingdom. Subsequently, others soon demonstrated that spinal anesthesia could be used safely with proper attention to detail [4]; however, the reports of injury are required reading because they highlight the need for appropriate vigilance and attention to detail and the catastrophic outcomes if ignored.

Because of their severity, these problems require close scrutiny to determine etiology, establish principles of management to minimize disability and prevent future occurrences. The focus of this chapter is to identify how peripheral nerves may be damaged during upper and lower extremity regional anesthesia procedures. This includes direct trauma from the block needle, but also complications due to incorrect placement of the block needle (pneumothorax, intravascular injection, block of unwanted neural elements).

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_11

Table 11.1 Incidence of neurological complications after neuraxial blocks [1]

Technique	Complication	Incidence (per 10,000 blocks)
Spinal anesthesia	Radiculopathy/neuropathy	3.78
	Cauda equina syndrome	0.11
	Intracranial event	0.03
	Paraplegia	0.06
Epidural analgesia	Radiculopathy/neuropathy	2.19
	Cauda equina syndrome	0.23
	Intracranial event	0.07
	Paraplegia	0.09

Table 11.2 Incidence of temporary neuropathy after peripheral nerve block [1]

Block technique	Estimated rate of occurrence (%)
Interscalene	1.84
Supraclavicular	0.03
Axillary	1.48
Midhumeral	0.02
Lumbar plexus	0.19
Femoral nerve	0.34
Sciatic nerve	0.41
Popliteal nerve block	0.24

The investigation of an individual patient should recognize that other factors are often frequent causes of postoperative nerve injury. In the last decade, knowledge of contributing factors of postoperative nerve injury has advanced significantly. The etiology, incidence, diagnosis, management, and prevention of neurological complications of peripheral block will be discussed. However, prevention has to be the guiding principle because of the very limited capacity of the nervous system for either repair or recovery.

Peripheral Nerve Injury

Injury to peripheral nerves is not quite as catastrophic as to the neuraxis, but can still result in considerable patient morbidity. Peripheral nerves can be injured by direct trauma, chemical neurotoxicity, ischemia, compression, infection, and by stretching. Many of these may affect the surgical patient without involving regional techniques, but the greatest concerns here are direct needle trauma and intraneural injection.

Direct Trauma

Three layers of tissue closely invest peripheral nerves: the epineurium, perineurium, and endoneurium. Although needle placement or injection within any of these layers is undesirable, recent evidence suggests that it is injection within the perineurium that is most likely to cause significant injury [5]. The epineurium is an external enveloping layer surrounding the fascicles and connective tissue within the nerve. The perineurium is a multilayered epithelial sheath that surrounds individual or groups of fascicles. Needle placement within the fascicle can cause injury directly or through pressure-related ischemia after injection [5].

Short bevel needles are purportedly less likely to injure nerves than long bevel needles [6]; however, there is little epidemiological evidence to support this assertion. What is more certain is that the injury is less severe if the needle is inserted with the bevel "parallel" to the line of the axons, rather than at right angles when fascicles will be transected rather than split longitudinally [7]. Neurotmesis, complete disruption of axon and myelin sheath, is far more likely to cause permanent injury than neuropraxis due to compression or stretch because the myelin sheath is preserved.

The use of ultrasound guidance should, theoretically, reduce the risk of direct needle trauma to the nerve. However, because of the relatively low incidence of complications from peripheral nerve blocks, studies have not been able to establish a benefit of ultrasound guidance compared to nerve stimulation alone in terms of nerve injury [8, 9].

Chemical Neurotoxicity

The peripheral nerves are reasonably well protected from chemical injury, but solutions containing preservatives and their accidental contamination are best avoided. There is no evidence to suggest that local anesthetics, in clinically used concentrations, have any more adverse effect on peripheral nerves than they do on the neuraxis. However, occasional laboratory studies, such as the observation that local anesthetics have toxic effects on cell cultures [10], do raise questions. Such "toxicity" is related to both concentration and duration of exposure, but the implications of these findings to man are unclear given the large numbers of patients who receive the drugs annually. However, it would seem prudent to use the lowest concentration of drug possible to achieve the desired effect, especially when an infusion technique is used [11].

Local anesthetic adjuvants (other than epinephrine) are used to prolong the duration of single injection techniques. Multiple agents have been studied including clonidine, dexmedetomidine, midazolam, neostigmine, and dexamethasone. Electron micrography of isolated rat nerves demonstrates histologic evidence of damage associated with some additives when used alone or in combination [12]. Further, most have limited prolonging effects at the expense of unwanted side effects such as excessive sedation, hypotension, and bradycardia with clonidine [13]. Dexamethasone alone (667 μg/mL) combined with ropivacaine (0.25 %) appears to have minimal issues with neurotoxicity in rats [12], and minimal side effects with the greatest effect on pro-

longing block duration in human trials [14]. Combining multiple perineural adjuvants enhances toxicity in rat neuronal cell cultures [12]. Other important factors to consider include the preparation of the adjuvant. Specifically, multidose preparations often contain preservatives that can be neurotoxic. While sodium bisulfite appears to be fairly neutral, benzyl alcohol is a potent neurotoxin. Furthermore, use of perineural adjuvants is "off-label" and practitioners should carefully weigh the risks and benefits of their use. Finally, specifically regarding dexamethasone and dexmedetomidine, there is emerging evidence suggesting that intravenous administration of these drugs may also prolong analgesic duration, without the safety concerns of perineural injections [15, 16].

Other Factors

Most local anesthetic drugs have a vasoconstrictor effect at low concentrations, but there are no data to suggest that this contributes to injury, even when a solution containing clinical concentrations of epinephrine is used. Many upper and lower limb blocks will be performed in patients whose surgery will be performed under tourniquet and they can have a much more profound effect especially if poorly applied, so that there is mechanical distortion or excessive pressure. Compression due to hematoma or abscess is possible, these lesions having the same risk factors as after central blocks, but they tend to spread more readily through the peripheral tissues, so high pressures are not generated.

It has been argued, in the context of nerve entrapment syndromes [17], that patients with a pre-existing neurological problem are more likely to suffer injury if a second, more distant insult occurs: the "double crush" phenomenon. However, the relevance of this to the risk of a patient with peripheral nerve disease (e.g., diabetic neuropathy) suffering injury from a peripheral block is unclear. Peripheral nerve injury requires disruption of the perineurium and, in practice, this is very difficult to accomplish; recent experience with ultrasound indicates that nerves are difficult to impale, tending to move away from approaching needles. Even if a nerve is pierced, it is difficult to maintain the needle within the nerve, most of the solution leaking out of the epineurium after a small volume has been injected [18].

Incidence

Temporary sensory or motor impairment may occur in nearly 3% of patients after a peripheral nerve block, but most symptoms resolve within days or weeks of surgery [1]. Permanent injury is more rare; Auroy and colleagues reported this in an average of only 2.4 instances per 10,000 blocks [19]. There is quite marked variation in the incidence of both temporary and permanent syndromes, with popliteal block having the greatest incidence of permanent injury (31.5 per 10,000 patients). Risk factors can be related to patient, surgical, and anesthetic factors. Patient factors include pre-existing neurological disorder, diabetes mellitus, extremes of obesity, male gender, and extremes of age. Surgical factors include direct surgical trauma, compressive dressings, tourniquet pressure and/or time, compression by hematoma or abscess, and poor patient positioning [20].

Diagnosis and Management

Symptoms suggestive of postoperative neuropathy (persisting sensory or motor symptoms beyond 48 h after last dose of local anesthetic) should prompt a full history to identify any predisposing risk factor or causative element in the anesthetic or surgical technique, plus a detailed neurological examination to define the problem precisely. As noted above, most injuries have an excellent prognosis, but the symptoms of even a minor deficit can be distressing, so considerable patient reassurance may be required. More severe deficits, or those which fail to resolve within 2–3 weeks, should be referred to a neurologist or neurosurgeon for further investigation and management. However, it is important that the anesthetist is fully involved in this process because surgical colleagues (and patients) can, quite correctly, become irritated if the anesthetist fails to follow up such problems. Conversely, the anesthetist (or department) taking this seriously will build a relationship between colleagues that will, in turn, facilitate the practice of regional anesthesia and future referral if necessary.

Having made that point it is important that the evaluation of any postoperative neurological deficit includes a search for factors unrelated to anesthesia technique. The incidence of nerve injury arising during surgery is several orders of magnitude greater than during regional anesthesia, so this must be considered before assigning responsibility to any one technique or practitioner. For example, the risk of nerve injury during total hip arthroplasty is as high as 1–2 % [21], and similar estimates are quoted for other orthopedic procedures. Surgery may predispose to nerve injury through direct trauma or stretching, tourniquet pressure, compressive dressings, hematoma or abscess formation, and improper patient positioning during surgery. However, some of these are considered to be the joint responsibility of surgeon and anesthetist.

Prevention

As with central blocks, thorough preoperative assessment and careful attention to the detail of block technique are essential in the prevention of neurological injury after peripheral blocks. It also seems advisable to use the lowest concentration of local anesthetic possible, particularly when infusions are used for postoperative analgesia.

Table 11.3 Factors which may indicate intraneural needle placement, and actions to reduce the risk of subsequent peripheral nerve injury

Symptom/sign	Action
Pain on needle placement or injection	Withdraw needle, stop injection, and redirect needle
High injection pressure	Withdraw needle until pressure to inject decreases [5]
Current threshold <0.4 mA	Withdraw needle until threshold >0.4 mA [18]
Sonographic visualization of nerve expansion	Stop injecting. Redirect needle [18]
High electrical impedance	Withdraw needle until impedance decreases [26]

More specifically, evidence suggests that a major factor predisposing to peripheral nerve injury is intraneural (or more accurately intrafascicular) needle placement or injection. Traditional teaching states that both of these produce severe pain and should therefore be easily detectable, so that needle position can be corrected if it occurs. However, recent studies suggest that neither intraneural needle placement nor injection is always painful, with ultrasound suggesting that they have been performed in an unrecognized manner for many years. Robards and colleagues [22] found that when typical final currents (0.2–0.4 mA) were achieved for popliteal nerve block the needle tip was intraneural in 100 % of cases. Similarly, Macaire and colleagues [23], using nerve stimulation for median nerve block at the wrist, identified that the needle tip was intraneural on several occasions, with this placement explaining the faster block onset seen in their nerve stimulation group.

Such observations may have led to the suggestion that intentional intraneural injection might optimize success without invariably leading to injury [24]. However, a paucity of evidence remains, even with from animal models, to support deliberate intraneural injection [25]. Further, it is difficult to avoid the conclusion that the high incidence of neuropathy after popliteal block [1] is directly related to the ease with which intraneural needle placement occurs during this technique [22]. Until there is much evidence to the contrary, intraneural needle placement and solution injection are practices to be avoided. Recent evidence suggests that several factors, apart from a gentle technique and inserting the needle with the bevel parallel to the nerve, may reduce the likelihood of severe injury, all of them aimed at preventing accidental intraneural injection (Table 11.3).

Many of the warning symptoms of direct nerve contact outlined above require a conscious, or only mildly sedated, patient to report them, and this would suggest that blocks should not be performed after administration of heavy sedation or anesthesia. However, this is a matter of some controversy.

Local Anesthetic Toxicity

A rare complication but nonetheless possible across all peripheral nerve blocks is the potential for local anesthetic systemic toxicity (LAST). Barrington et al. found an incidence of LAST of 0.98 per 1000 blocks [8]. This was similar to the incidence reported by Auroy of 0.8 per 1000 blocks [19]. The use of ultrasound guidance further reduces this risk. Orebaugh et al. reported no incidences of LAST in 2146 ultrasound-guided blocks, compared to 5 incidences of LAST in 3290 nerve stimulator (non-ultrasound guided) nerve blocks (1.5 per 1000 blocks) [9]. Similarly, Sites et al. reported an incidence of 0.08 per 1000 of LAST in ultrasound-guided peripheral nerve blocks [27] and, when Barrington et al. analyzed complications based on nerve localization technique, they found the incidence of LAST when ultrasound guidance was used was only 0.8 per 1000 blocks compared to 1.2 per 1000 blocks with nerve stimulator localization [8].

There are multiple causative factors including rapid uptake from highly vascularized tissues, to excessive dosing, to inadvertent intravascular injection. If block needles traverse veins, unknown to the practitioner due to compression, larger conduits for local anesthetic absorption or direct intravascular injection may result. Practitioners should take care to intermittently release pressure on the probe and scan for venous structures, inject in incremental doses, and observe local anesthetic expansion. Many practitioners commonly add epinephrine to local anesthetic solutions to provide an earlier signal (from increasing heart rate) of intravascular injection.

Upper Extremity Block Procedures

Block Site Specific Complications

Interscalene

Interscalene brachial plexus block (ISB) targets the nerve roots of the brachial plexus and is appropriate for shoulder/proximal arm procedures. Most complications are of a self-limited/benign nature lasting the duration of the local anesthetic. These include: (1) Hoarseness due to ipsilateral recurrent laryngeal nerve block and (2) Horner's syndrome due to ipsilateral stellate ganglion block.

Anesthesiologists should be aware of the possibility of injury to the spinal accessory nerve, long thoracic, or dorsal scapular when performing ISB by the posterior approach as these nerves course through the middle scalene muscle. Case reports of permanent injury due to inadvertent transection en-route to the brachial plexus have been described [28].

Potentially more severe is block of the ipsilateral phrenic nerve that can compromise pulmonary function by approxi-

mately 25 %. ISB should therefore be avoided in patients who would not tolerate such a decrease. Volumes greater than 10 ml result in 100 % ipsilateral phrenic nerve block [29], while volumes as low as 5 ml, still producing reliable analgesia, reduce the incidence of phrenic nerve block by about 50 % [30, 31].

There are other rare case reports of more devastating complications including epidural or intrathecal spread of local anesthetic causing significant harm. These were due to injection of excessive local anesthetic volume and migration of an in situ continuous catheter, respectively.

Equally rare is CNS toxicity from injection into the vertebral artery and pneumothorax. However due to their rarity ultrasound guidance may not decrease the incidence of these complications.

Supraclavicular

Supraclavicular brachial plexus block (SCB) targets the brachial plexus at the level of the trunks. It had fallen out of favor due to risks of pneumothorax with landmark/nerve stimulation guided techniques, but has experienced a recent resurgence since the advent of ultrasound. While the theoretical risks of phrenic nerve block (~50 %), Horner's syndrome, and intravascular injection persist, large case series demonstrate an incidence of <1 % [32]. Despite ultrasound guidance, pneumothorax still remains a potential complication causing significant morbidity [33, 34].

Infraclavicular

Infraclavicular brachial plexus block (ICB) targets the brachial plexus at the level of the cords. There is minimal risk of phrenic nerve palsy and pneumothorax. The risk of intravascular injection is present as the inferior cord is often in close proximity to the axillary vein. However, previous case series have demonstrated a very low complication rate (<1 %) [35].

Axillary

Complications associated with axillary brachial plexus block (AXB), except for LAST, are fairly minor and self-limited. The potential for cephalad spread to block unwanted neural elements is exceedingly low. More common are hematoma due to the close proximity of nerves to the axillary artery and vein.

Lower Extremity Block Procedures

Block Site Specific Complications

Lumbar Plexus/Psoas Compartment

The lumbar plexus consists of T12–L4 spinal nerves. Soon after exiting their respective intervertebral foraminas, these spinal nerves form the lumbar plexus within the psoas muscle, anterior to the transverse processes. Due to its location, lumbar plexus block is often referred to as psoas compartment block. Terminal branches arising from the lumbar plexus (ilioinguinal, iliohypogastric, genitofemoral, lateral femoral cutaneous, femoral, obturator) have major contributions to the sensory and motor functions in the groin, hip, and thigh. Because injection of local anesthetic at this single location can block multiple branches supplying the lower limb, lumbar plexus block is the preferred peripheral nerve block for some practitioners as their first choice for lower limb analgesia. However, due to the deep location of the lumbar plexus and its close proximity to other important structures, there is more potential for adverse events compared to other peripheral nerve blocks (Table 11.4).

In the large survey from France by Auroy et al., lumbar plexus blocks were the only peripheral nerve block technique linked to cardiac and respiratory arrests out of more than 50,000 procedures [19]. The only death reported in the peripheral nerve block group was after a lumbar plexus block. Overall the authors estimated the incidence of serious complications after lumbar plexus block at 80/10,000 [19]. In all these reported cases of serious complications, high dermatomal level and bilateral mydriasis were observed, suggesting intrathecal spread of local anesthetic. Other cases of intrathecal local anesthetic injection during lumbar plexus block have subsequently been reported [36]. Epidural spread of local anesthetic from lumbar plexus block can also cause significant complications. In a prospective, multicenter case series, Capdevila et al. [37] reported three cases of severe hypotension out of 20 lumbar plexus blocks. The authors attributed the hemodynamic instability to unintended epidural anesthesia [38].

Misplacement of needle during lumbar plexus block can cause other complications such as renal injury/hematoma and intraperitoneal injections [39]. Similar to other peripheral nerve blocks, the lumbar plexus block is not immune to post-block neurologic symptoms and seizures resulting from intravascular injections. There are also case reports in the literature of psoas abscesses after lumbar plexus blocks [40].

Table 11.4 Reported complications from lumbar plexus block in the literature

Infection/psoas abscess
Intraperitoneal injection
Retroperitoneal hemorrhage/hematoma
Trauma to kidney
Neurologic symptoms
Seizure
Epidural/spinal spread of local anesthetic
Respiratory arrest
Severe hypotension
Cardiac arrest

Bleeding after lumbar plexus block is a bigger concern than other peripheral nerve blocks due to the deep needle penetration required and the vascularity in the area. Retroperitoneal hematoma has been reported for a patient receiving lumbar plexus block less than 24 h after low molecular weight heparin [41]. The American Society of Regional Anesthesia and Pain Medicine has subsequently published guidelines for regional anesthesia and anticoagulation [42]. The guidelines distinguished lumbar plexus block from more superficial peripheral nerve blocks in that bleeding for this "deep" block carries more significant morbidity. As such it was suggested that the same precaution for anticoagulation and neuraxial blocks should apply to lumbar plexus blocks as well. However, evidence suggests that avoiding anticoagulation at the time of needle insertion is not enough to eliminate retroperitoneal bleeding after lumbar plexus block [43].

Femoral

Femoral nerve block targets the femoral nerve at the level of the femoral crease as it exits below the inguinal ligament, lateral to the femoral artery. The proximity of the nerve to major vessels increases the risk of vascular puncture and local anesthetic toxicity. However occurrence is exceptionally rare, in particular with the use of ultrasound guidance [9, 27].

There have, however, been some case reports of bleeding and major hematoma formation with the use of femoral nerve catheters in patients on prophylactic low molecular weight heparin therapy [44]. The location of femoral nerve blockade also renders continuous catheters prone to bacterial colonization (28.7–57 %); however, the incidence of bacterial complications remains small (0.01–0.07 %) [39, 45].

The incidence of postoperative neurologic deficit with femoral nerve block is in keeping with upper extremity nerve blocks at ~0.2–0.4 % [39, 45].

Of greater concern with femoral nerve blockade is the ensuing quadriceps weakness that may contribute to postoperative falls and, in some cases, results in wound dehiscence and or peri-prosthetic fractures [46, 47]. Of note, a 60–62 % reduction in quadriceps muscle strength has been shown following total knee arthroplasty in the absence of any regional block [48, 49]. Memtsoudis et al. found an overall incidence of inpatient falls after total knee arthroplasty to be 1.6 % [50]. The use of a peripheral nerve block was not found to increase the risk of fall (1.58 % with block vs. 1.62 % without block, OR 0.85) [50].

Saphenous (Adductor Canal)

The saphenous nerve is the terminal sensory nerve of the femoral nerve and is typically blocked within the adductor canal where it is bordered by the sartorius muscle anteriorly, the vastus medialis laterally, and the adductor muscles medially (adductor longus or magnus depending on distance down leg). As with femoral nerve blocks, there remains a risk, albeit low, of vascular puncture and local anesthetic toxicity given that this block is performed as a perivascular injection.

While the saphenous nerve is a sensory nerve, there have been reports of associated quadriceps weakness attributed to the possibility of retrograde local anesthetic spread towards the motor fibers of the femoral nerve [51, 52]. While quadriceps weakness has been demonstrated, it has been shown to be much less than with a femoral nerve block—a reduction in strength of 4.9–8 % from baseline compared to 49–88.9 % with femoral nerve block [53, 54]. As previously mentioned, a 60–62 % reduction of quadriceps strength has been shown following TKA in the absence of a peripheral nerve block [48, 49]. There has also been demonstration of local anesthetic spread to the popliteal sciatic area with injection within the adductor canal. This, however, was not associated with any motor weakness within the distribution of the sciatic nerve [55].

Proximal Sciatic

The sciatic nerve arises from the lumbosacral plexus (L4-S3). It exits the pelvis via the greater sciatic notch beneath the piriformis muscle. It then travels along the posterior thigh to the popliteal fossa, where it divides into the tibial and common peroneal nerves. The sciatic nerve can be blocked anywhere along this path; however, most commonly sciatic nerve block is done proximally at the gluteal or subgluteal region, or near the popliteal fossa.

The incidence of neurologic symptoms after proximal sciatic nerve block appears to be in line with other lower limb nerve blocks [1, 19]. However, care in attributing cause is required when neurologic symptoms arise as the sciatic nerve is a common site of injury secondary to certain surgical procedures (e.g., 1–2 % for hip arthroplasty) [21], and surgical positioning (e.g., lithotomy or frog leg) [56]. There are also concerns of nerve injury secondary to ischemia due to tourniquet use during surgery, the addition of epinephrine to local anesthetic, or a combination of both. The use of tourniquet in itself might be less of an issue compared to the tourniquet pressure—one large case series concluded that tourniquet pressure >400 mmHg is associated with neurological symptoms after femoral-sciatic nerve blocks [57]. The fear of epinephrine compromising blood supply to the nerve has some authors proposing omission of epinephrine for proximal sciatic nerve block [58]. However, a review from Neal concluded that low-dose epinephrine (at 1:400,000 concentration) mixed with local anesthetic can in fact transiently increase blood flow to the peripheral nerves, and avoidance of epinephrine in nerve block due to fear of nerve ischemia is unfounded.

Popliteal Sciatic

The popliteal sciatic block targets the sciatic nerve at the level of the popliteal fossa. At this level the sciatic nerve is composed of 72–75 % connective tissue, which is thought to potentially confer protection against inadvertent nerve fiber damage during in the case of intraneural injection [59, 60]. However, Auroy et al. found a higher incidence of peripheral neuropathy following sciatic blocks at the popliteal level compared to the sciatic blocks done at higher levels (31.5 in 10,000 blocks vs. 2.4 in 10,000 respectively) [19]. One must also be aware of the potential for ischemic damage secondary to a combination of local anesthetic volume and the common use of tourniquets in lower extremity surgery.

The use of nerve catheters at the popliteal sciatic level is associated with a lower incidence of bacterial colonization than with high sciatic and femoral nerve techniques (18.9 % vs. 30.4 % vs. 28.4 %, respectively) [39]. There have been reports of bleeding and hematoma formation with popliteal sciatic nerve catheters in patients on prophylactic low molecular weight heparin [44].

Intravenous Regional Anesthesia

Intravenous regional anesthesia (IVRA) was first described over a century ago by Bier [61]. Rather than targeting specific nerves, IVRA provides anesthesia by isolating the circulation of a limb with a high-pressure tourniquet, and subsequent injection of local anesthetic into a vein within that limb. IVRA of upper limb has been proven over the years as a safe, simple, and reliable method to provide surgical anesthesia, whereas lower extremity use of IVRA has been shown to have high failure rate (36.8 % in one study) [62].

A well-functioning pneumatic tourniquet is paramount in IVRA as it prevents venous outflow and isolates the injected medication to the limb, thus minimizing systemic side effects from these drugs. Malfunction or incorrect use of the pneumatic tourniquet (e.g., too low an inflation pressure) can lead to serious local anesthetic complications and should be avoided at all cost. A double-tourniquet may be useful for managing tourniquet-related pain (see later) and to increase the margin of safety if one cuff fails. It is recommended that tourniquets be inflated 50–100 mmHg higher than the patients' blood pressure, or to 250 mmHg for upper extremities and 300 mmHg for lower extremities [63]. However even with appropriate use of pneumatic tourniquet, severe LAST events such as seizure and cardiac arrest have been reported during the tourniquet inflation period [64].

Local anesthetic can enter systemic circulation despite a functioning tourniquet via intraosseous circulation (tourniquet cannot compress vessels within bone) and during fracture manipulation [65]. Alternatively increase in venous pressure above the inflation pressure can also cause local anesthetic leakage. This can occur when large volume of fluid is injected intravenously in a rapid fashion [66]. The location of the tourniquet also plays a role with detectable leakage of local anesthetic in 100 % of IVRA of the lower limb compared to only 25 % with IVRA of the upper limb [67].

Once there is significant circulatory communication between the limb and systemic circulation, the adverse effects will be based on the medication(s) injected for IVRA. LAST is the most feared and for this reason the use of local anesthetics with less potential for cardiovascular toxicity such as lidocaine [68], or prilocaine [69], is preferred. Other side effects such as nausea and sedation from opioid [70, 71], or hypotension from clonidine [72], have been reported. Despite the theoretical risk of muscle weakness or paralysis when muscle relaxant is used as an adjunct in IVRA, there have been no reports of serious complications from this class of medications.

Ultimately, to minimize the potential complications of the medications used for IVRA, one should: (1) ensure proper functioning of tourniquet prior to the block, (2) adequately exsanguinate the limb prior to tourniquet inflation [73], (3) slowly inject the lowest dose of local anesthetic possible [74], as far distal from tourniquet as possible [75], (4) keep tourniquet inflated for at least 20 [63] to 30 min [76], after local anesthetic injection, (5) consider sequential deflation and reinflation if tourniquet time is less than 40 min [77], and (6) consider using a forearm instead of upper arm tourniquet if possible, with emerging evidence suggesting that forearm tourniquet use can lead to decrease in total time of inflation [78], local anesthetic dose, and symptoms of LAST [79].

The pneumatic tourniquet also prevents arterial inflow to the limb. This confers multiple benefits: (1) decreases blood loss, (2) provides good surgical conditions, (3) prevents vascular congestion in the limb and the subsequent increase in venous pressure. However, decrease in arterial blood supply can lead to ischemic injury to the limb. The high pressure exerted from the tourniquet can also cause crush injury tissues directly underneath [80]. Tourniquet pain is a common complication of IVRA and may result in progressive hypertension. Treatment options include the use of IV sedation, alternately deflating and reinflating one of the cuffs on a double-cuffs tourniquet, or use of a rescue forearm tourniquet [81].

Overview

Complications occur rarely after regional anesthesia, but can be devastating to all involved. Careful patient selection and gentle block performance reduce risks considerably, and recent advances such as ultrasound guidance may allow new strategies to further reduce risk. If symptoms of injury do develop, prompt and thorough clinical assessment, investiga-

tion, treatment, and follow-up are vital to minimize the final degree of disability.

With respect to non-neurologic complications, slow, incremental injection with intermittent aspiration reduces the likelihood of LAST. Additionally, careful, vigilant technique with appropriate visualization of nerves, needle tip, and proximal relevant anatomy is necessary to avoid significant morbidity.

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Complications of Thoracic Wall Regional Anesthesia and Analgesia

12

Christine Lee and F. Michael Ferrante

Key Points

- There are a multitude of approaches to anesthesia and analgesia of the torso, each with their own advantages and risks. The gold standard is thoracic epidural anesthesia, while recent approaches aim to refine the anesthetized area, increasing safety and comfort.
- Thoracic epidurals cover the largest area and offer significant pain control following procedures of the chest wall. While incidences of direct damage to the spinal cord are rare, hemodynamic changes, specifically hypotension, are a major potential complication.
- Paravertebral blocks have the advantage of anesthetizing specific dermatomes while sparing inferior regions that would be blocked by an epidural. Paravertebral blocks are also amenable to ultrasound guidance and continuous catheter infusion. The risk of epidural, subdural, subarachnoid, intravascular, and pleural puncture is present and can be avoided by good anatomical knowledge and attention to technique.
- Intercostal blocks are another alternative to thoracic epidural analgesia and can be performed under ultrasound guidance. Complications are rare but may include pneumothorax, hematoma, and intravascular injection.

Introduction

Thoracic epidurals and regional techniques such as paravertebral blocks, intercostal nerve blocks, and interpleural analgesia are mainstays to provide intermittent, temporary, or continuous anesthesia or analgesia in the thoracic and abdominal regions. The regional techniques listed earlier may be appropriate alternatives to the gold standard: thoracic epidural analgesia (TEA) for providing analgesia of the chest wall for selected groups of patients. In addition, these techniques could be used in the treatment of the chronic pain patient. These analgesic techniques have been used to treat pain related to thoracotomy [1, 2], rib fractures [3–5], trauma [6], and chronic pain [7]. In recent years, utilization of these has been extended to include breast surgery [8, 9], shoulder surgery [10, 11], laparoscopic cholecystectomy [12], and inguinal hernia repair [13]. These procedures have been known to have a very low-risk profile. However, there are still complications the operator must be aware of for each procedure.

More recently, with the use of ultrasound, there are new techniques for thoracic wall blocks including the Pecs I and II blocks and serratus plane block [14]. In addition, ultrasound can be used for more traditional techniques including epidurals, paravertebral blockade, intercostal nerve blocks, and interpleural analgesia. Of note, interpleural analgesia is less commonly utilized due to more effective, less invasive approaches and potential complications. The advantages of paravertebral, intercostal nerve blocks, and chest wall planar blocks over thoracic epidural analgesia are related to the unilateral nature of these blocks, a less extensive sympathetic block, and therefore an attendant decrease in overall physiologic trespass (e.g., lack of hypotension) [15, 16]. When compared to intravenous opioid analgesia, these regional analgesic techniques provide excellent pain relief without interfering with respiratory drive [3, 17, 18].

When appropriately used and performed, there is substantive evidence that thoracic epidural, paravertebral, intercostal nerve blocks, and interpleural analgesia provide excellent perioperative pain relief. In deciding which block will be appropriate for a particular case, it is important to consider the type of anesthesia and/or analgesia necessary. There are many different approaches to these techniques and there are numerous potential complications. We will first describe the background and utility of each analgesic technique. We will then discuss the pertinent anatomy, how to perform each technique, and discuss potential complications.

C. Lee, MD (✉) • F.M. Ferrante, MD, FABPM
Department of Anesthesiology, David Geffen School of Medicine at UCLA, Santa Monica, CA 90404, USA
e-mail: CLee@mednet.ucla.edu; MFerrante@mednet.ucla.edu

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_12

Thoracic Epidural

Thoracic epidural analgesia is utilized for a variety of thoracic and abdominal surgeries for postoperative analgesia. It has been shown to improve outcomes in patients after lung transplantation and has become the most widely used interventional technique to provide pain control in this patient population [19, 20]. Careful attention to detail and technique make this a safe procedure to perform. A continuous catheter technique with a combination of local anesthetic and opioid is commonly used in the postoperative period to provide a longer duration of pain relief. The potential disadvantages involve the physiologic changes that occur with sympathetic blockade, most importantly, resultant hypotension.

In the pain management population, thoracic interlaminar epidural steroid injections are indicated more commonly for radiculopathy caused by a disc protrusion or by stenosis of central canal, in the intervertebral foramen or lateral recess. They are less commonly used for treatment of radiculopathy from degenerative disc disease, compression fractures, herpes zoster, and postherpetic neuralgia [21].

Thoracic Spine Anatomy

Knowledge of the differences between thoracic and lumbar anatomy is required for a successful thoracic epidural block. The thoracic spine is kyphotic. The anterior aspect of the neural arch is formed by two vertebral bodies along with the posterior longitudinal ligament. The anterolateral border is formed by the pedicles and the posterolateral border by laminae and ligamentum flavum. The spinous processes are aligned steeply in the high- to mid-thoracic regions, but become less acutely inclined in the low-thoracic region. In contrast to the lumbar epidural space, the thoracic epidural space contains less fat, and the dura is less adherent to the surrounding bony canal. As a result, the ligamentum flava are less likely to meet the midline. The anterior thoracic epidural space is filled predominantly with valveless veins, which connect to the basivertebral venous plexus and azygos vein [22].

Neural Blockade

Thoracic interlaminar epidural injections are typically performed with use of a paramedian approach to avoid the steep and oblique angulation of overlapping spinous processes encountered by using a median or midline technique.

Classical Technique

Most percutaneous approaches to the thoracic epidural space are conducted by the usage of surface anatomic landmarks. The prominent C7 spinous process, the scapular spine (T3), and the inferior border of the scapula (T7) are useful landmarks used to approximate the puncture site to the intended segment. Counting up from the iliac crest can improve accuracy for lower thoracic (T10–T12) epidural placement. In spite of these landmarks, the exact vertebral interspace can be misplaced by one or two segments [23]. Fluoroscopy can be used to guide placement using bony structures and to verify appropriate catheter position after injection of contrast media. There is currently no evidence that using fluoroscopy for thoracic epidural placement improves safety or decreases adverse events. The use of ultrasound to facilitate epidural catheter placement is developing.

The block is commonly performed by placing the patient in the sitting position with the neck flexed and resting on a head rest. The targeted thoracic segments are identified. The area is prepped and draped and sterile technique should be utilized. The skin and subcutaneous tissues are anesthetized with local anesthetic using a 1.5-cm 25 gauge needle approximately 1 cm lateral to the inferior aspect of the targeted spinous process. The needle should contact the ipsilateral lamina or transverse process and anesthetize the periosteum. The needle should be directed medial and cephalad to anesthetize the eventual tract of the Tuohy (or Husted) needle. The epidural needle is inserted perpendicular to the skin surface with the bevel cephalad. It is advanced until the ipsilateral lamina or transverse process is contacted. If lamina is not contacted, there is risk of entering the paravertebral space if the needle is directed in a lateral direction. The needle depth to the lamina should be noted and then the needle withdrawn back to the skin and subsequently advanced in a slightly medial direction. This process is repeated until the needle contacts bone at a slightly more superficial depth than the original laminar depth. This position suggests the needle tip at the junction of the lamina and spinous process in the midline. The needle is withdrawn and advanced with the same medial angle in small steps in a cephalad direction to the same depth. At this point either bone or ligamentum flavum will be reached. If bone is contacted, the needle is then redirected cephalad and then advanced. When bone is no longer contacted, and the depth exceeds the previous depth, the epidural stylet is then removed. The Luer lock loss-of-resistance syringe is then attached to assess loss of resistance. Once loss of resistance is obtained, the epidural needle is stabilized and catheter threaded. The catheter is secured using a sterile locking

device and dressings. For thoracotomies or thoracoscopies, it is advisable to avoid placing dressings on the same side as the surgery [24].

In some cases, patients may not be able to be placed in a sitting position for thoracic epidural placement. This situation can be encountered in ventilated intensive care unit patients and those in the recovery room immediately after surgery. The same technique can be used in patients in a lateral decubitus position. Briefly, the patients are placed on the lateral edge of the bed or cart. In the lateral decubitus position, the approach of the needle can be from the floor toward the midline. Subsequent steps identifying midline and cephalad angulation are repeated [24].

Ultrasound Guidance

Ultrasound guided thoracic epidural can be performed by placing the patient in sitting position with head resting on a headrest. When performing ultrasound-guided epidural blockade in upper or lower thoracic levels, the technique involves using a transverse interlaminar ultrasound view. This view is easily obtained for the upper or lower thoracic levels. When the thoracic epidural block is performed in the mid-thoracic spine, it can be difficult to obtain an interlaminar view because of the more sharply angled spinous processes. In this case, a parasagittal oblique view is employed.

The ultrasound-guided thoracic epidural block is performed in a three-step process. The first step is to obtain a paramedian sagittal transverse process view. Start by placing the low frequency curvilinear probe on the longitudinal plane 3–4 cm lateral to the right or left of the middle of the spinous processes at the level to be blocked depending on the handedness of the clinician. The ultrasound probe is moved lateral and medial to identify successive transverse processes. After the transverse processes are identified in this view, the ultrasound transducer is slowly moved toward the midline until the superior and inferior articular facets are seen. In longitudinal paramedian ultrasound articular process view, the superior and inferior articular facets appear as hyperechoic hills and valleys in succession, with each hill representing a facet joint.

The last step is obtaining the paramedian sagittal oblique view. After identifying the articular processes using the paramedian sagittal articular process view, the longitudinally oriented transducer is tilted to angle the ultrasound beam in a lateral to medial trajectory toward the midline. The lamina of each thoracic vertebrae will appear as a series of hyperechoic curvilinear lines with an acoustic shadow beneath each one. The interlaminar space will appear as gaps between successive vertebra providing an acoustic window to visualize the ligamentum flavum, epidural space, and posterior dura.

After the interlaminar space is identified, the skin is prepped with antiseptic solution, and a 22 gauge 3 ½ in. needle suitable for epidural use is inserted through the skin at the middle of the lateral aspect of the longitudinally placed ultrasound transducer utilizing an out-of-plane approach. While an assistant holds and adjusts the ultrasound transducer, the clinician advances the needle under real-time ultrasound guidance in an oblique lateral to medial trajectory using a loss of resistance technique until the needle tip rests in the epidural space [25].

Complications/Treatment

Risks of thoracic epidural analgesia include neuraxial hematoma, infection, hypotension due to local anesthetic effects and sympathetic blockade, urinary retention, and side effects associated with use of neuraxial opioids. Risks associated with epidural placement, such as inadvertent dural puncture, intravascular injection, and catheter migration also occur. A perceived hazard of thoracic epidurals vs. lumbar epidurals is the risk of neurologic injury to the spinal cord. However, complications associated are relatively rare. In 4185 patients undergoing thoracic epidural analgesia, the overall incidence of complications was 3.1 %. This included unsuccessful catheter placement (1.1 %), dural puncture (0.7 %), postoperative radicular pain (0.2 %), and peripheral nerve lesions (0.2 %). Unintentional dural perforation was observed more often during lower thoracic (3.4 %) than during mid (0.9 %) or upper (0.4 %) thoracic spine placements. No epidural hematomas or abscesses were identified [26]. An additional retrospective study involving 2837 patients receiving thoracic epidural analgesia for cardiac surgery reported no epidural hematomas or abscesses and only two superficial skin infections at the site of insertion (0.07 %) [27]. An additional prospective study in 1071 patients scheduled for thoracic epidural catheterization for postoperative analgesia for abdominal procedures showed a lack of neurologic sequelae associated with the procedure [28].

A rare, but devastating complication of thoracic epidural anesthesia is neurologic injury from direct trauma to the spinal cord with needle placement. Thoracic epidural needle placement or catheterisation may also lead to epidural hematoma or infection. The incidence of epidural hematoma appears to be less than 1 in 150,000 patients and usually occurs in the presence of impaired coagulation. Consensus statements for the administration of neuraxial techniques in the presence of anticoagulants have been published by the American Society of Regional Anesthesia [29]. The most

traumatic event likely to cause bleeding is epidural catheter placement, followed by catheter removal, needle placement, and daily catheter management [30]. Incidence of epidural abscess overall is low. The risk of infection is related to a number of factors including antibiotic usage and duration of use. A catheter left in place longer term has a higher probability of infection. The risk of infection appears to increase after the second day of epidural catheterization [31]. Because of this patients should be monitored frequently in the early postoperative course for signs of epidural hematoma and abscess. The need for thoracic epidural analgesia should be evaluated each postoperative day and the risks and benefits of an indwelling catheter should be assessed especially after catheter day four [29]. Vigilance and a high level of suspicion may prevent neurologic sequelae. Early imaging, neurosurgical consultation, and emergent decompression are imperatives to avoiding permanent neurological injury.

A common complication of neuraxial local anesthesia is hypotension. The cardiovascular responses to epidural anesthesia result from autonomic blockade with its effects on both the vascular beds and function. Venous and arterial dilatation occur, but as a result of the large amount of blood in the venous system, venodilatation effects predominate. Compensatory vasoconstriction of capacitance vessels will occur in the remaining unblocked areas. Hemodynamic changes relate to extent of involvement of groups of nerves supplying the peripheral vessels, the splanchnic bed (T5-L3), and the heart (T1–4) [32]. Upper thoracic spinal anesthesia can decrease MAP, which equals a reduction in coronary blood flow [33]. This is of particular concern in cardiac surgery, where hypotension is common with using local anesthetics via thoracic epidural analgesia during these procedures. Volume expansion and alpha agonist administration are necessary in patients with severe hypotension. Of note, low-level thoracic epidural-induced sympathectomy can create changes in sympathetic–parasympathetic equilibrium, producing coronary artery spasm [34]. In patients undergoing lung resection or transplantation, where volume is used sparingly, ionotropes may be necessary to address severe hypotension.

Complications associated with neuraxial opioid usage include side effects of opioids including nausea, vomiting, pruritus, urinary retention, sedation, and respiratory depression [24]. Pleural puncture and pneumothorax are also potential procedural complications, but both appear to be rare [35].

Paravertebral Nerve Blocks

Paravertebral blockade (PVB) is a regional anesthesia technique with a large number of indications including surgical anesthesia for breast surgery [36–39], surgical anesthesia and postoperative analgesia during and after thoracic [40] and abdominal surgery [41] and pain therapy for fractured ribs [3, 42–44], postherpetic neuralgia [45, 46], hyperhidrosis [47], and liver capsule pain after abdominal trauma [48, 49].

Thoracic paravertebral block is becoming increasingly popular in recent years. Paravertebral analgesia has been studied as a possible alternative to epidural analgesia for thoracotomy. Because the analgesic effects of paravertebral blockade are comparable to epidural analgesia, paravertebral nerve blocks may avoid the risks of thoracic epidural analgesia such as hypotension and urinary retention [50]. Davies et al. reported a systematic review and meta-analysis of ten randomized trials comparing paravertebral blockade with thoracic epidural analgesia [51]. They found that both provide comparable pain relief after thoracotomy, but paravertebral blockade had a better side effect profile and fewer pulmonary complications. However, recent various trials have achieved different results [52–54]. An updated meta-analysis in 2014 by Ding et al. comparing the efficacy and adverse effects of paravertebral blockade and thoracic epidural analgesia in preventing pain associated with thoracotomy included 777 patients in 18 randomized controlled trials. Their analysis showed that PVB provided comparable analgesia with TEA and furthermore has a better side effect profile. In particular, PVB is associated with less urinary retention, postoperative nausea and vomiting, and hypotension. This makes paravertebral blockade a desirable technique for regional blockade for the thoracic chest wall and a viable alternative to thoracic epidural analgesia [55]. Thoracic anatomy relevant to these analgesic techniques is portrayed in Figs. 12.1, 12.2, and 12.3.

Paravertebral Anatomy

The paravertebral space (Fig. 12.3) is the shape of a four-sided pyramid with its apex facing posteriorly into the neural foramen and its base bordered anteriorly by the parietal pleura. The thoracic paravertebral space is defined by the following four borders: (1) the bone and articular capsules of the rib and transverse process above, (2) the rib below, (3) medially by the vertebral body, and (4) laterally by the intercostal space and the costotransverse ligament. The costotransverse ligament runs from the transverse process to the superior root and its continuation, the intercostal nerve. The intercostal nerve branches into dorsal and ventral rami in the paravertebral space. Gray and white rami communicates course through the space to and from the respective sympathetic ganglion at that level, which is also contained within the paravertebral space. Other contents include areolar tissue, fat, and blood vessels. It is important to keep in mind that the paravertebral space is contiguous with the epidural

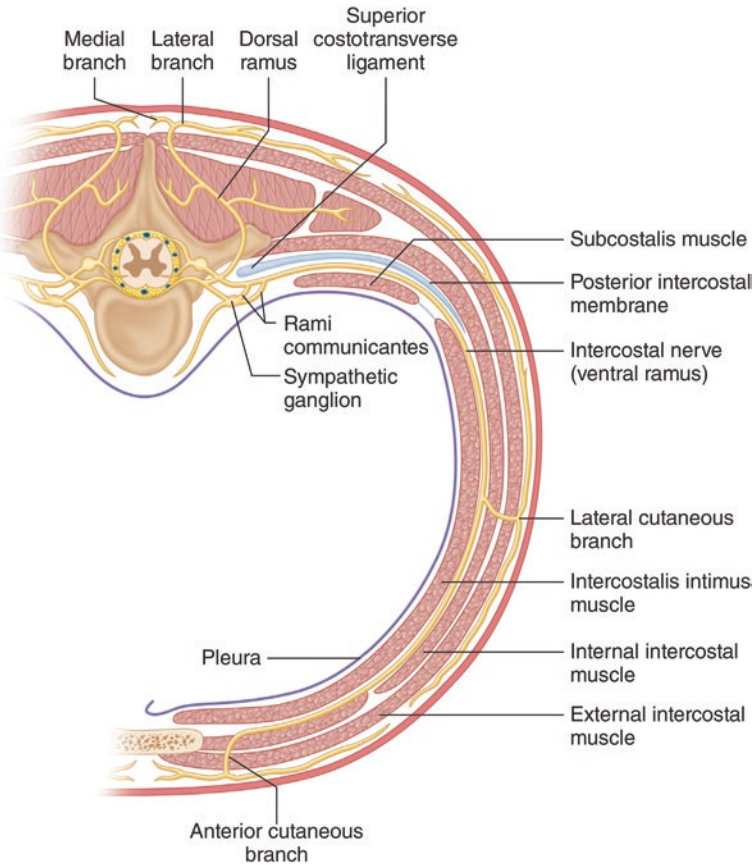

Fig. 12.1 A transverse section through a typical thoracic dermatome at the level of the intervertebral foramen (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

and intercostal spaces as it lies between these two other spaces. Any substance injected into the paravertebral space may potentially spread cephalad and caudad to adjacent paravertebral spaces as well as medially and laterally to the epidural and intercostal spaces, respectively [56]. Rarely, an injection into the paravertebral space will spread to the contralateral space, and this has been demonstrated radiologically [19–21, 57–59].

In general, topographic spread is variable and difficult to predict [60, 61]. Naja et al. performed a series of paravertebral blocks using nerve stimulator guidance to determine the effect of varying injection points on spread of solution [61]. Their findings indicated that injection in the more ventral aspect of the thoracic paravertebral space resulted in a multisegmental longitudinal spreading pattern. Injecting at the dorsal aspect of the space showed a cloud-like spread with limited distribution to adjacent segments (Fig. 12.4).

The similarity in the anatomic distribution and density of block produced by continuous paravertebral block and continuous epidural infusion would seem to indicate that some cases of unilateral "epidural" block might be attributable to inadvertent continuous paravertebral blockade. This phenomenon has been confirmed radiologically [62].

Paravertebral Nerve Block Technique

Patient comfort during performance of a paravertebral block is improved by good technique, the use of small-gauge needles, and the avoidance of paresthesias while performing the block [63]. Generous infiltration of local anesthetic also makes the procedure more tolerable. Sedation before the procedure is strongly recommended and adds greatly to patient comfort.

Classic Technique—Lateral Approach

The classic technique for paravertebral blockade involves insertion of a needle 4.0 cm lateral to the midline, level to the caudad aspect of the spinous process one level above the level to be blocked (Fig. 12.5). The caudad angle of the thoracic spinous process brings the inferior tip of the spinous process to the superior aspect of the spinous process at the level below [64]. The needle is advanced perpendicular to the skin in all planes until it contacts the transverse process. The depth of the needle is noted. A sterile hemostat can be clamped to the needle to mark the depth of the needle at the skin. The needle is then "walked off" the transverse process in

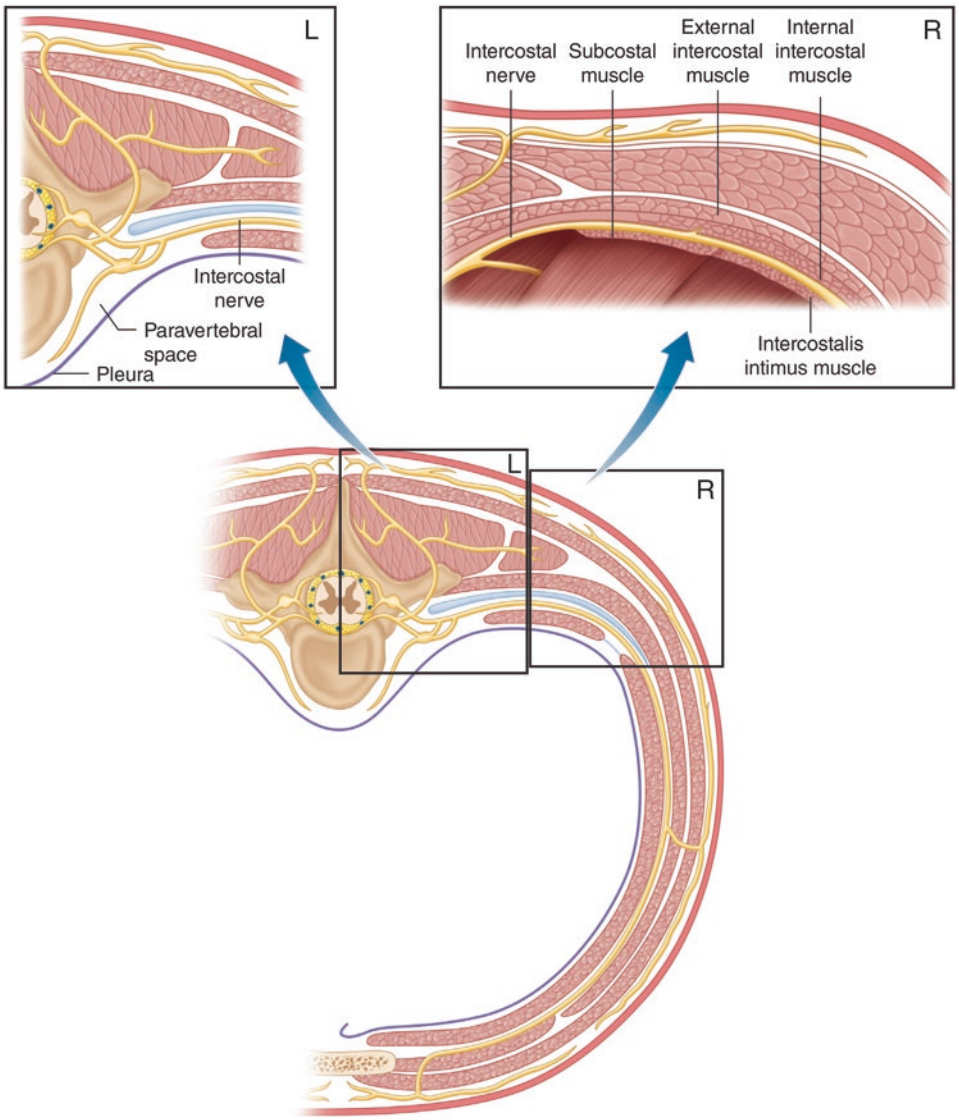

Fig. 12.2 Paravertebral nerve blocks and interpleural nerve blocks act in the area of the left upper and lower boxes. Intercostal nerve blocks are applied to the anatomy depicted in the right upper and lower boxes (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

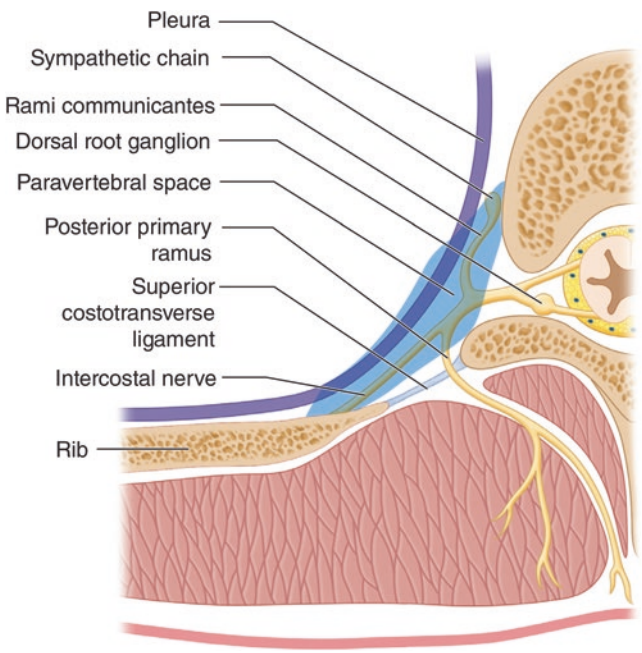

Fig. 12.3 The paravertebral space is defined by four borders: (1) medial, vertebral body; (2) lateral, intercostal space, and the costotransverse ligament; (3) superior, bone, and articular capsules of the rib and transverse process above; and (4) inferior, the rib below. In three dimensions, the space is a four-sided pyramid with its base at the pleura and apex at the intervertebral foramen (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

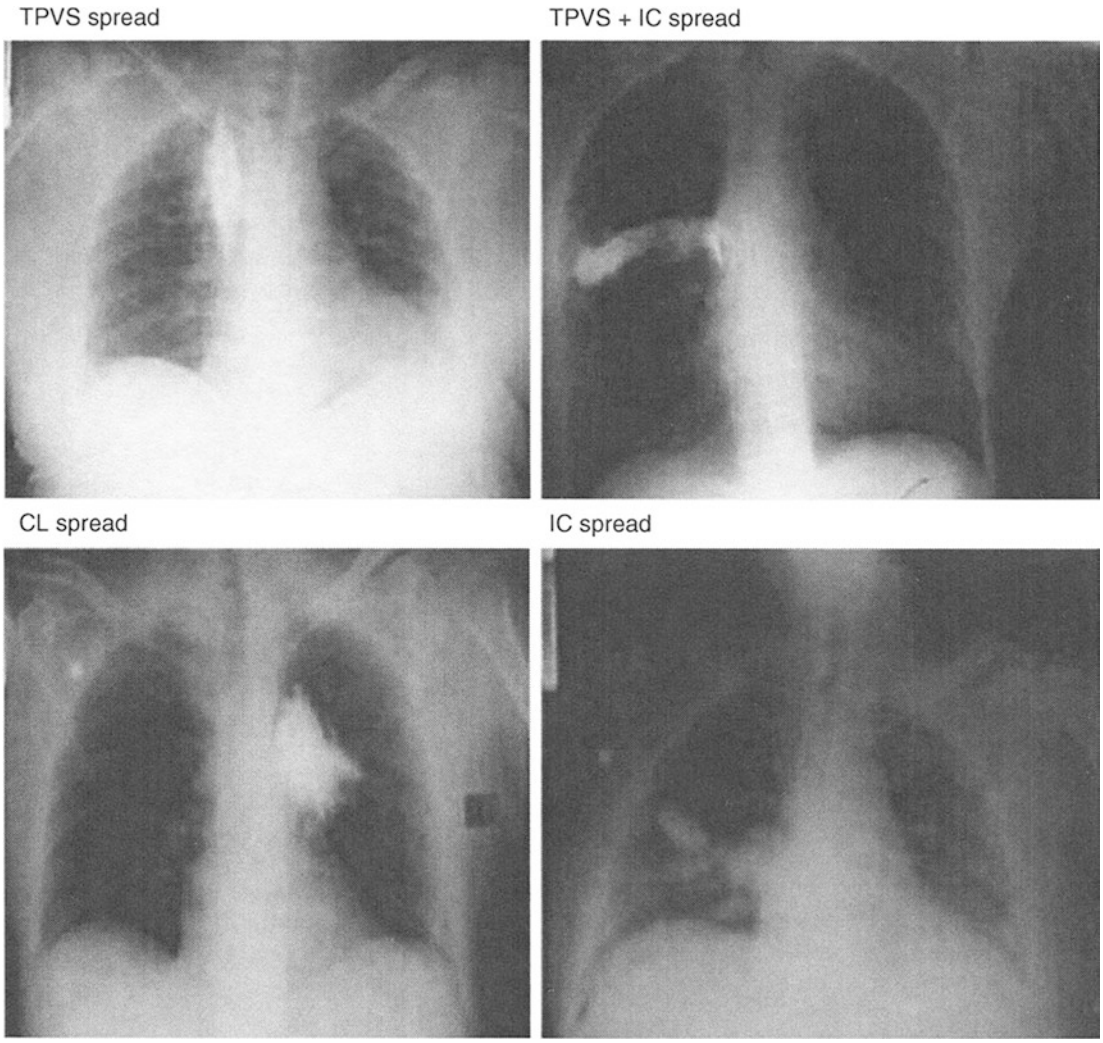

Fig. 12.4 Thoracic paravertebral space (TPVS). TPVS + IC TPVS +Intercostal. *CL*, cloud like; *IC*, intercostal (From Naja et al. [46] reprinted with permission from Blackwell Publishing)

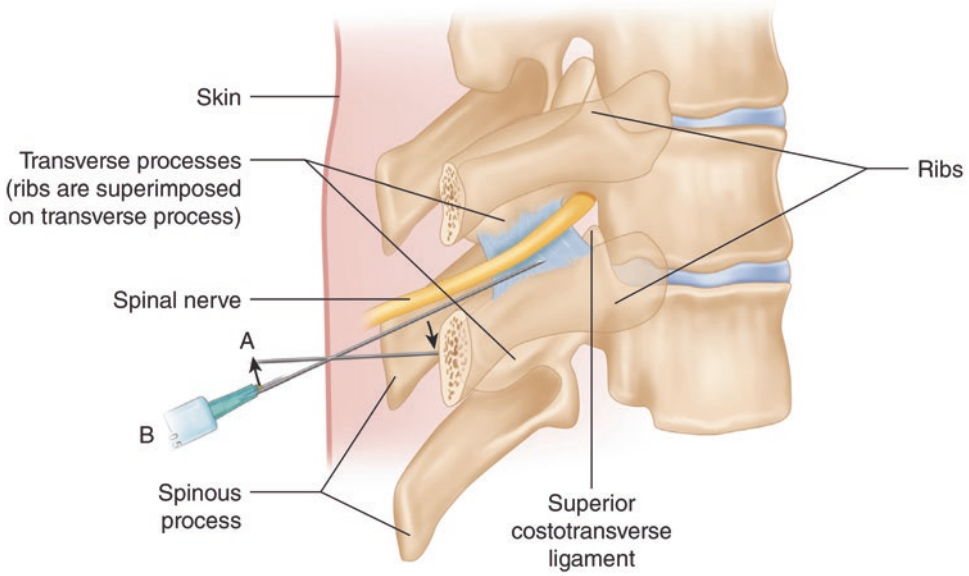

Fig. 12.5 Insert needle 4 cm lateral to the midline at the level of the caudad tip of the spinous process, one segment above the level to be blocked. Advance needle to the transverse process (TP) **A**. "walk off" TP in a cephalad direction **B**. Advance needle 1 cm into the PVS (Reprinted from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

a cephalad direction and advanced 1 cm, placing the tip of the needle in the paravertebral space. Modification of this technique by advancing the needle medially to contact the vertebral body affords relative confidence that an intraneural or subarachnoid injection will not occur. (See detailed description later.) Because the epidural space is contiguous with the paravertebral space via the intervertebral neural foramen, epidural spread is always possible if enough volume is injected.

Medial Approach

To avoid intrathecal injection, Shaw recommends a medial approach [65]. The needle insertion point is approximately 1 cm from midline. The needle is advanced until the lamina is contacted and then directed laterally off the bone. With this technique, the tip of the needle is directed away from the neuraxis, but intraneural injection and epidural extravasation are still possible. Tenicela and Pollan modified and strongly advocate performance of the medial approach in the following manner: after a skin wheal is placed, generous infiltration of local anesthetic into the paraspinal muscles is performed 3–4 cm lateral to the midline in the thoracic region and 2–3 cm lateral to midline in the lumbar region [17]. A 22-gauge, 9-cm spinal needle is inserted and advanced at a 45° angle to the transverse plane in a medial direction until the lamina is contacted. The approximate depth required to make contact with the lamina is 5–6 cm in males and somewhat less in females. Gentle aspiration is performed to confirm negative return of blood or cerebrospinal fluid (CSF). At this point, a small amount of local anesthetic is injected at the periosteum. A sterile hemostat is clamped to the shaft of the needle about 1–1.5 cm from the skin, marking the depth of the lamina. The needle is then withdrawn and guided laterally off the lamina and advanced until the hemostat is flush with the skin. After negative aspiration for blood, CSF, and air, a test dose of 3 mL is given. The remaining dose can be given if there was no adverse response to the test dose. If bone is contacted at increasingly superficial levels, the needle has contacted the transverse process and is too cephalad. It must be reinserted approximately 1 cm caudad. These authors claim good to excellent results in 97 % of 380 performances of paravertebral block.

Continuous Technique

Further modification of the injection technique allows placement of a catheter for continuous infusion. Eason and Wyatt proposed that this technique achieves the closest possible approximation of the needle tip with the common intercostal nerve (i.e., before division into dorsal and ventral rami) [66]. By using an epidural needle, a catheter can be advanced for repeated bolus dosing or continuous infusion. Beginning 3 cm lateral to midline, a needle is passed perpendicular to the skin in all planes. The needle is advanced until it contacts bone, which may be rib or transverse process. From this point, the needle is walked cephalad off the bone. This technique was proposed to be safer than using the caudad direction for performance of the block (Fig. 12.6). Loss of resistance with an air-filled syringe is used to identify entrance of the needle tip into the paravertebral space. When the needle is in the costotransverse ligament, there is significant resistance

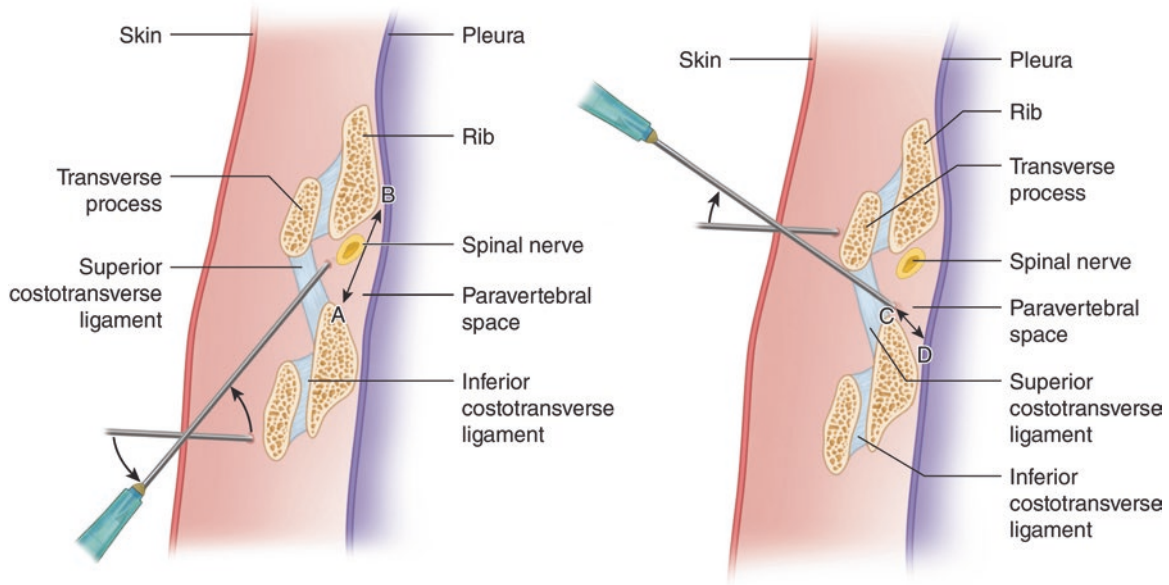

Fig. 12.6 The distance from the superior costotransverse ligament to the pleura is longer with the cranial approach (line **a**, **b**) than it is with a caudad approach (line **c**, **d**). The risk of pneumothorax may therefore be decreased with a superior approach (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

to attempted injection of air. Once the needle tip passes into the loose areolar tissue of the paravertebral space, the air can be injected. If a catheter is advanced, it should have a single orifice at the tip to ensure that aspiration will give accurate information about the location of the tip. An insertion depth of 1 cm is suggested.

The authors report that manipulation of the epidural needle may be necessary to actually insert the catheter into the paravertebral space. An easily advancing catheter may indicate interpleural localization [57]. Injection of 15 mL of 0.375 % bupivacaine reliably blocks four dermatomes.

Ultrasound-Guided Paravertebral Nerve Block

A linear high-frequency ultrasound transducer is used in the transverse plane with its medial border just lateral to the previously identified spinous process of the vertebral body at the level of the facet joint, and an ultrasound survey scan is obtained. Once the transverse process is identified, the transducer is slowly moved superiorly or inferiorly until the space between the two adjacent transverse processes is identified. One can identify the pleura that appears as a bright hyperechoic downward curving line, which can be seen to slide back and forth with respiration. Just above the hyperechoic pleural line as it curves down as it moves medial toward the vertebral body is the triangular-shaped thoracic paravertebral space. Just above the paravertebral space is the linear hyperechoic internal intercostal membrane. The depth of the posterior border of the paravertebral space is noted. When these anatomic structures are clearly identified on the transverse ultrasound scan, the skin is prepped with anesthetic solution, and a 3 ½ in. needle with stylet is advanced from the middle of the inferior border of the ultrasound transducer using an out-of-plane approach with the trajectory being adjusted under real-time ultrasound guidance until the needle tip is at the previously identified depth of the posterior border of the paravertebral space. After careful aspiration, a small amount of solution can be injected to aid in identification of the needle tip position. The needle is then advanced slowly with attention paid to the relative location of the bright hyperechoic pleura line until the needle tip is seen to be within the paravertebral space. After careful aspiration, the remainder of the solution is slowly injected. The needle is then removed and sterile pressure dressing placed at the injection site [67].

Complications/Treatment

The most important factors for safe performance of paravertebral neural blockade are a solid knowledge of pertinent anatomy, meticulous attention to injection technique, and anticipation of all possible physiologic changes associated with the block. The clinician must have a comprehensive understanding of the potential complications. Early recognition facilitates rapid treatment, thus minimizing more serious sequelae. Utilization of a nerve stimulator-guided technique is associated with a higher success rate and fewer complications than standard techniques [68]. It is strongly suggested that an intravenous line be in place before performing the block.

It is imperative that low-osmolarity contrast agents be used when performing these blocks, because spread of high-osmolarity solutions into the subarachnoid space can lead to significant neurologic harm. The proximity of the paravertebral space to the central nervous system creates the obvious potential for needle entrance into either the epidural or subarachnoid space. Iodinated contrast has been injected into the epidural space with and without spread into the paravertebral space. In performing 45 paravertebral blocks, Purcell-Jones et al. showed contrast confined to the paravertebral space in only 18 % of procedures. There was epidural extravasation in 70 % and exclusive epidural spread in 31 % of cases [56].

In addition to epidural [13] and subdural [69] injection, unrecognized subarachnoid puncture can occur. Headaches not associated with obvious dural puncture occurred in 3 of 24 cases in one series of paravertebral blocks. Aspiration was negative for CSF before injection [70]. Negative aspiration for CSF is not an absolute guarantee of proper needle placement, especially with small-gauge needles or long, small-bore catheters. The headaches resolved with conservative management within 5–14 days postoperatively. The medial approach proposed by Shaw and modified by Tenicela and Pollan has shown excellent results with low complication rates [17, 65]. Of the 384 blocks performed by Tenicela and Pollan, there was one incident of pneumothorax (0.26 %), one recognized dural puncture, two intrathecal injections of the test dose, 18 incidents of hypotension (4.6 %), five bilateral blockades (1.3 %), and 27 incidents of fair to poor block (7.0 %). Poor results were attributed to centralized pain disorders. There were no incidents of serious or permanent sequelae.

Intravenous, intra-arterial, and intraneural injection can occur using any approach to the paravertebral space [68]. In addition, infection, hematoma formation, or damage to the neural fascicle may occur from dry needling. The type of needle can also affect the incidence of sequelae. Short-beveled needles have been shown to cause less nerve damage than long-beveled needles [71].

Aspiration will not reveal the presence of an intrafascicular needle tip. Injectate can dissect back through an epineural injection to the contiguous pia mater [72, 73]. This is driven by the occurrence of severe sequelae (death, paraplegia, transverse myelitis) from injection of a long-acting formulation of procaine [74–76]. The diffuse tissue necrosis was attributed to the carrier solution [77]. For this reason, the use

of fluoroscopy and injection of low-osmolarity iodinated contrast to confirm proper needle placement are recommended when performing paravertebral blockade.

When using a continuous technique, there is always a risk of shearing the catheter if it is withdrawn back through the needle. Predictably, there will almost always be some pain at the site of needle insertion. Infection and hematoma are also possible risks. Monoplatythela (unilateral flat nipple) may occur with a successful block [78].

Other potential complications involve interpleural or intrapulmonary injections. If the tip of the needle is in the interpleural space, aspiration should reveal air. Injection of a small volume of radiocontrast under live fluoroscopy can quickly and easily detect an interpleural or intrapulmonary injection.

Prolonged anesthesia and motor block after inguinal hernia repair under general anesthesia with paravertebral blockade was observed in a patient with multiple sclerosis [79]. Abnormal uptake of local anesthetics into the spinal cord secondary to the presence of demyelination was proposed as the mechanism.

Contraindications to paravertebral block are infection at the site, patient refusal, and allergy to any of the solutions to be injected.

Intercostal Nerve Blocks

Intercostal nerve blocks are an alternative to thoracic epidural analgesia. Intercostal nerve blocks can be used in the acute setting for rib fractures, postthoracotomy pain, and trauma. Potential pitfalls of intercostal nerve blocks include difficulty in placement, high rate of local anesthetic absorption, and risk of pneumothorax. Ultrasound guidance has diminished these risks.

Intercostal Anatomy

The anatomy of the intercostal nerves and spaces is depicted in Figs. 12.1, 12.2, 12.7, and 12.8. Intercostal nerves are derived from the spinal roots of the respective thoracic segments. They are composed of dorsal horn sensory afferent fibers, ventral horn motor efferent fibers, and postganglionic sympathetic nerves that join the nerve via the paravertebral gray rami communicantes. Thus, each intercostal nerve has autonomic and somatic sensory and motor functions. Soon after the sympathetic contribution occurs within the paravertebral space, the intercostal nerve divides into ventral and dorsal rami. The dorsal ramus provides sensory innervation to the posteromedial structures of the back (synovium, periosteum, fascia, muscles, and skin) and motor innervation to the erector spinae muscles. The ventral ramus travels between the ribs. It is protected within the subcostal groove by the rib and two layers of intercostal muscle.

Each intercostal nerve (ventral ramus) is associated with a vein and artery. The intercostal vein is derived from the confluence of venules along the thoracic cage and empties into the azygous vein on the right and the hemiazygous vein on the left. The most cephalad intercostal veins join and empty into the respective brachiocephalic veins bilaterally. The intercostal arteries are derived directly from the aorta.

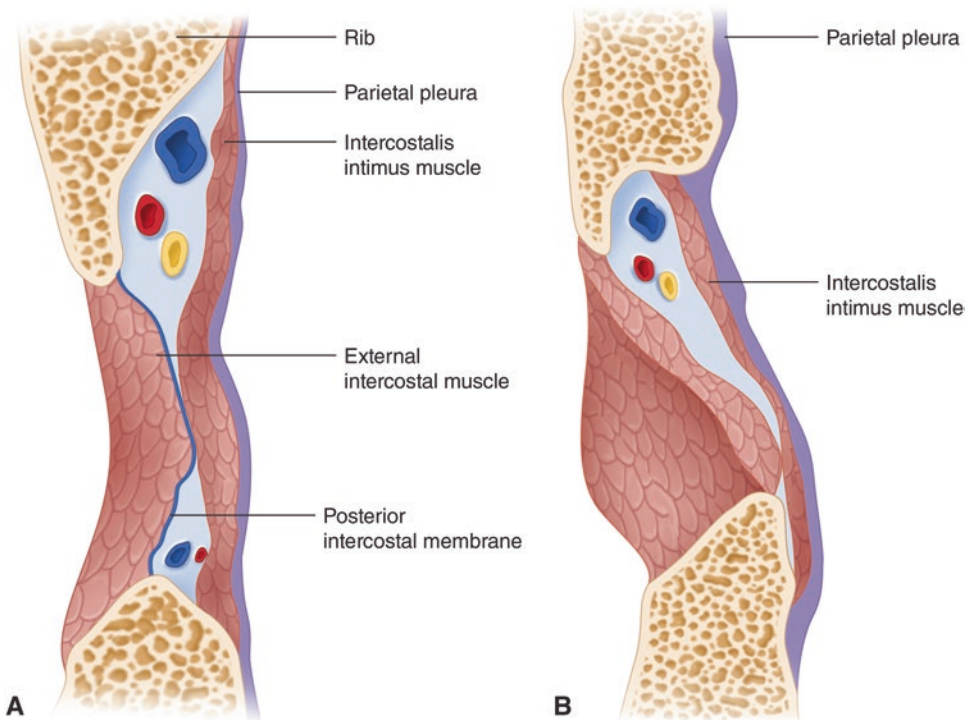

Fig. 12.7 Anatomic cross section through the intercostal space at (**A**) angle of Rib and (**B**) Laterally at the posterior axillary line (Reprinted from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

The neurovascular structures are always superficial to the parietal pleura and thin aponeurotic-areolar tissue called the intercostalis intimus muscle. The aponeurotic-areolar tissue has muscle fibers embedded within its substance, and despite its name, its classification as a true muscle is a matter of debate among anatomists. There is various cutaneous branching of the ventral rami. In general, there are anterior and lateral branches, which divide and innervate skin and intercostal muscles of an individual segment along with variable collateral innervation of the adjacent segments. Because of this collateral innervation, it is necessary to block a level above and below the desired level. Because there is minimal adhesion of the aponeurosis to the parietal pleura, and the intercostalis intimus muscle is a rather flimsy structure, cephalad and caudad spread of injected solution to the adjacent intercostal spaces is not impeded (Fig. 12.7 and 12.8). It is important to keep in mind that the intercostal and paravertebral spaces are contiguous at all levels. Spread of local anesthetic to the paravertebral space produces unilateral segmental sympathetic blockade.

Intercostal Nerve Block Techniques

Intercostal neural blockade can be achieved intermittently or continuously in one or several segments depending on the technique used. Careful attention to technique decreases the rate of complication. Percutaneous injection of 2–5 mL of local anesthetic in at least three adjacent levels will ensure anesthesia/analgesia in the distribution of the middle intercostal nerve because of collateral innervation. Although relief is temporary, this technique is very effective in alleviating somatic pain in the chest wall and abdominal wall. Prolonged blockade requires either multiple reinsertions with the attendant risk of pneumothorax, placement of a catheter for bolus dosing or continuous infusion [80], injection with a neurolytic agent [81], or cryoablation [82].

Another important risk to keep in mind is local anesthetic toxicity. Blood levels of local anesthetic after intercostal blockade and interpleural analgesia are significantly greater than after any other frequently performed regional anesthetic

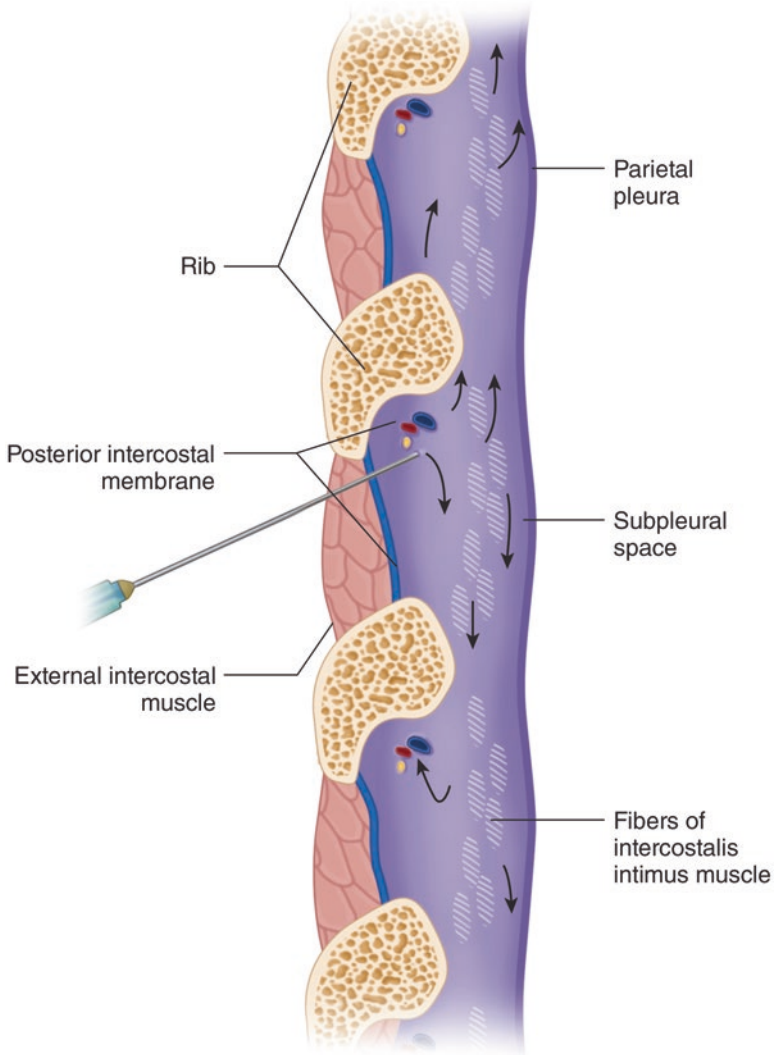

Fig. 12.8 The aponeurosis or intercostalis intimus, does not impede spread of injectate to adjacent intercostal spaces when the needle or catheter is placed in the correct tissue plane (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

techniques. Tucker et al. performed epidural, caudal, intercostal, brachial plexus, and sciatic/femoral nerve blocks with a single injection of mepivacaine 500 mg (1 % and 2 % solutions) with and without epinephrine [83]. When measuring arterial plasma levels, the highest levels were found after intercostal nerve blocks without epinephrine (5–10 μg/mL). When epinephrine was added to the solution (1:200,000 concentration), the plasma level decreased to 2–5 μg/mL. Epinephrine should be uniformly added to local anesthetic for performance of intercostal nerve block to minimize the potential for systemic toxicity.

Posterior Approach

Traditionally, intercostal nerve blocks are performed with a posterior approach at the angle of the rib, 6–8 cm lateral to the respective spinous process [84]. This target point allows direct palpation of the rib in most patients. It also allows blockade of the lateral intercostal cutaneous branch, which usually originates distal to the angle of the rib, ensuring good medial as well as lateral analgesia. The immediately adjacent intercostal nerves must also be blocked, because there is collateral innervation from the levels above and below. Neurolytic injections and cryoablative procedures must also be performed in a similar manner.

Figure 12.9 shows a technique for safely performing an intercostal nerve block. The skin above one intercostal space is retracted in a cephalad direction by the index and middle fingers of the nondominant hand. The rib corresponding to the nerve to be blocked is now between the fingers. A short-beveled, 25-gauge needle is advanced toward the inferior margin of the rib until bone is gently contacted. The fingers then release the skin to its original position. The needle is carefully walked off the inferior margin of the rib and advanced 3–5 mm, passing the external and internal intercostal muscles and placing the tip in the intercostal space. The width of the posterior intercostal space at the angle of the rib is approximately 8 mm [84]. Aspiration must be negative for blood and air. A volume of 2–5 mL of local anes-

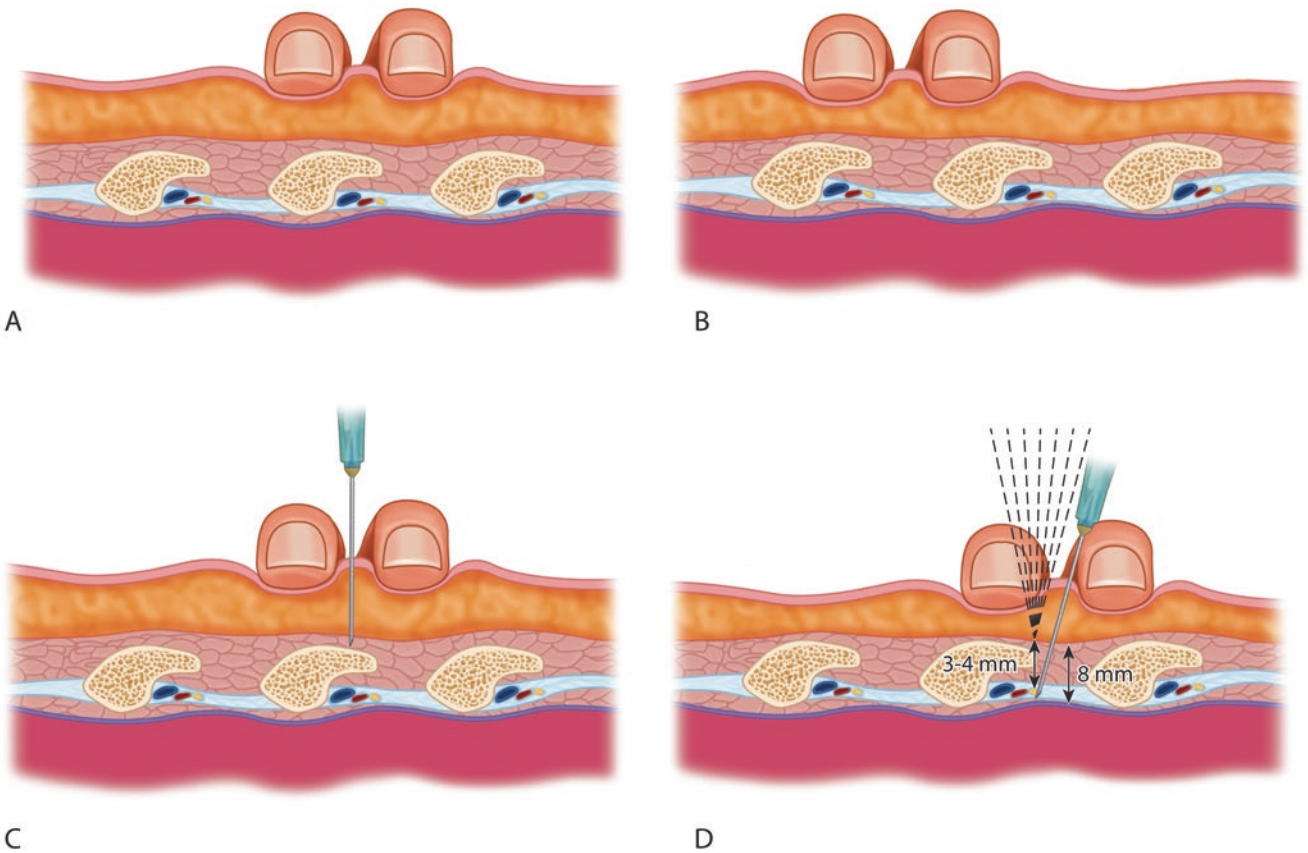

Fig. 12.9 Technique for intercostal nerve block. (**a**, **b**) The skin is retracted cephalad by two fingers straddling a rib. (**c**) A 25-gauge needle is advanced toward the inferior aspect of the rib until bone is contacted. (**d**) The cephalad traction on the skin is released, the needle is "walked off" the inferior border of the rib and advanced 3–5 mm beyond the rib to pass through the external and internal intercostal muscles (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

thetic with 1:200,000 epinephrine is then slowly injected. This exact procedure is then repeated at the level above and below the targeted intercostal nerve. If multiple dermatomes need to be blocked, one level above and one below the targeted levels must also be blocked.

For pain associated with video-assisted thoracoscopy procedures, the utilization of intercostal nerve blockade with 0.375 % bupivacaine resulted in a significant decrease in the postoperative use of intravenous morphine [2]. This technique may be particularly useful for outpatient video-assisted thoracoscopy procedures.

Lateral Approach

A variation of this technique is entry at the posterior or midaxillary lines. These approaches may be adequate for blocking the anterior chest or abdominal wall, but will often miss the lateral cutaneous branch, thus providing less than satisfactory blockade of the back and flank regions.

In patients undergoing thoracotomy, the surgeon may perform the blocks under direct visualization just before closure. However, these blocks are often placed at a site more medial than what would be chosen for a percutaneous approach. Thus, there seems to be a higher incidence of complications because of the proximity to the spinal nerve roots.

Continuous Technique

Nunn and Slavin described the ability of a single intercostal injection of India ink to spread subpleurally to multiple intercostal spaces [84]. The minimally adherent parietal pleura and the thin intercostalis intimus muscle did not hinder the multidirectional spread of the injectate (Fig. 12.8).

Based on morphometric measurements of the intercostal space, Nunn and Slavin placed the needle tip 3 mm past the inferior margin of the rib, leaving approximately 5 mm to the pleura. In a study by O'Kelly and Garry, a continuous catheter was placed through a 19-gauge epidural needle with the tip directed medially [85]. After first injecting 10 mL of solution through the needle, the catheter was advanced 2 cm and then secured to the skin. Appropriate spread of local anesthetic was confirmed by radiographic imaging.

Satisfactory analgesia has been documented using continuous infusion [86]. Seventy-five patients (92 %) had good analgesia without requiring supplemental medications during the first postoperative day using an infusion of 0.5 % bupivacaine at 7 mL/h. Sixty-six patients (81.5 %) remained satisfied with their analgesia over the following 4 days. Patients who experienced inadequate analgesia early in their course were thought to have leakage of anesthetic into the interpleural space. Subsequent decrements in analgesic efficacy were attributed to tachyphylaxis. The same authors modified the protocol to increase the infusion rate to a maximum of 10 mL/h [87]. This resulted in a significant improvement in pulmonary function over the control group, which required higher doses of intravenous rescue pain medications than the continuous intercostal infusion group.

Ultrasound-Guided Intercostal Nerve Block

The rib at the level to be blocked is by palpation and traced posterior to the posterior angulation of the affected rib. A linear high-frequency ultrasound transducer is then placed in the longitudinal plane with the superior aspect of the ultrasound transducer rotated about 15° laterally over the affected rib at the posterior angulation of the ribs. The rib can be seen as a hyperechoic curvilinear line with an acoustic shadow underneath it. The three layers of intercostal muscle, the external, internal, and innermost, are identified in the intercostal space between adjacent ribs. Color Doppler helps identify beneath the adjacent intercostal artery and vein. This space between adjacent ribs provides an excellent acoustic window, which allows easy identification of the intercostal space and the pleura beneath it. The depth of the pleura is noted. Usually, both the rib inferior to the targeted rib and the targeted rib can be visualized in the same window. 22-gauge echogenic needle is advanced from the inferior border of the ultrasound transducer using an in-plane approach with the trajectory being adjusted under real-time ultrasound guidance until the needle tip is resting in the internal layer of the intercostal muscle. At that point, after careful aspiration, a small amount of solution is injected under real-time ultrasound imaging to utilize hydrodissection to reconfirm the position of the needle tip. Once the position of the needle tip is reconfirmed, the needle is carefully advanced into the innermost layer of the intercostal muscle just short of the previously identified depth of the pleura. After careful aspiration, a small amount of solution is again injected to aid in identification of the position of the needle tip with attention paid to the relative location of the bright hyperechoic pleural line. After careful aspiration, the remainder of the solution is slowly injected. There should be minimal resistance to injection. The needle is then removed and a sterile dressing is applied at the injection site [88].

Complications/Treatment

The most common complications of intercostal nerve block are associated with the aberrant needle placement (pneumothorax, hemothorax, hemoptysis, hematoma, intravascular injection, neuritis, subarachnoid block, failed block) or problems associated with the injectate (allergic reaction, toxic reaction, epinephrine reaction, tissue necrosis, respiratory insufficiency).

The actual incidence of pneumothorax secondary to intercostal nerve block is quite small. A large, retrospective study reporting 50,097 intercostal nerve blocks in 4333 patients undergoing surgery or therapeutic nerve blocks revealed only four clinically significant pneumothoraces (0.092 %) and no other significant complications [89]. The technique for intercostal neural blockade was similar to the posterior approach described by Nunn and Slavin [84]. There was some minor discomfort at the injection sites in 5 % of patients. A prospective study by the same authors in 200 consecutive patients undergoing intercostal nerve block compared pre- and postinjection films to evaluate for pneumothorax [90]. There were only four pneumothoraces in a total of 2610 needle punctures, of which three pneumothoraces were attributed to the actual surgical procedure itself and not performance of the blocks. In the largest retrospective study with more than 100,000 needle punctures, Moore reported an incidence of pneumothorax of 0.073 % without any other serious complications [90]. It is important to note that residents still in training performed most of these blocks [91].

There are sporadic case reports of other types of complications. Hematoma has occurred in a heparinized patient [92]. Bilateral intercostal nerve blocks have resulted in postoperative respiratory failure in patients with preoperative pulmonary compromise [93, 94]. Motor blockade and the loss of accessory respiratory muscle function were the hypothesized etiologic mechanisms. In a study looking at the efficacy of continuous epidural versus intercostal analgesia, one intercostal catheter led to rib osteomyelitis which had to be treated surgically [80]. Local anesthetic toxicity can occur due to higher absorption due to the close proximity of the intercostal vasculature.

Intraoperative intercostal nerve block performed by the surgical team has resulted in total spinal anesthesia. Presumably, this serious complication occurred because of the proximity of the injections to spinal nerve roots [95, 96]. Paravertebral neural block has also occurred with attempted intercostal nerve block during surgery [97]. Total spinal anesthesia has occurred during performance of percutaneous intercostal nerve blocks [98]. Dissection of the injectate through the endoneurium in continuity with the pia mater was the presumed etiologic mechanism. Retrograde spread could also occur through the dural cuff, which surrounds the peripheral nerves at the perineurium.

Intrapulmonary injection is a risk, especially when there has been an alteration in the pulmonary anatomy secondary to previous surgery. Acute bronchospasm from intrapulmonary injection of 8 % phenol has been reported [99]. The characteristic odor of phenol was detected in the patient's exhaled air.

In addition to the issue of epidural blockade with continuous intercostal neural blockade, there is concern regarding misplacement of the catheter. The actual technique of catheter placement is somewhat imprecise, lacking a definitive end point. Mowbray et al. performed intercostal catheterization in 22 patients scheduled for thoracotomy or median sternotomy [59]. At the time of surgery, it was found that only 12 catheters (54.5 %) were actually placed correctly in the intercostal space. There was also a report of neuritis with catheter placement. Catheter dislodgment and interpleural or intravenous catheter migration can occur.

Relative contraindications to intercostal blockade include patient refusal, history of allergic reaction to injectates, coagulopathy, and infection at the proposed site of injection.

Interpleural Analgesia

Because interpleural analgesia is rarely performed in modern times, our discussion of this technique will be brief. Interpleural analgesia has been evaluated for multiple uses, including surgery of the upper abdomen, flank and thoracic wall [100, 101], chronic regional pain syndrome [102], multiple rib fractures [3], and chronic pancreatitis [103, 104]. The literature is ambivalent as to the ultimate efficacy of interpleural blockade. Direct comparison has been made to intercostal neural blockade and the latter technique was deemed to be superior [105, 106]. Interpleural analgesia was compared with thoracic epidural analgesia after minimally invasive coronary artery bypass surgery and was found to be a safe and effective alternative [107].

Pleural Anatomy

The lungs are sheathed in a glossy membrane called the visceral pleura. This membrane develops embryonically from the lung tissue. This closely attached serous membrane is continuous with the membrane that lines the chest wall, mediastinum, and diaphragm, where it is called the parietal pleura. The cupola of the lung is adjacent to a portion of

cervical parietal pleura. The potential space between the visceral and parietal pleura, the pleural cavity, is only evident when filled with air (pneumothorax), pus (empyema), or fluid (hydro- or hemothorax). The costal and diaphragmatic parietal pleurae meet and descend in a groove with no lung tissue between them, caudad and anterior to T6 and posterior to T10. This is the costophrenic sulcus, which opens to accommodate vital capacity lung expansion.

Interpleural Block Technique

The block is easy to perform when clear landmarks are present and usually involves the placement of a continuous catheter for infusion. The technique can be performed percutaneously. Alternatively, it may be performed intraoperatively under direct vision. The seated or lateral decubitus position (side to be blocked uppermost) can be used. After prepping the insertion site with appropriate sterile technique, the needle is placed at the superior border of the rib to avoid the neurovascular bundle. Because the paravertebral gutter is the eventual target for the catheter, a posterior approach is beneficial. The angle of the rib correlates to the widest aspect of the intercostal space, which may provide the best location for placement of the catheter.

The needle is advanced until it is felt to "pop" through the fascial layer of the parietal pleura. Entry into the pleural space is evidenced by visual techniques (Fig. 12.10) which rely on entrance of fluid into the interpleural space with negative inspiratory interpleural pressure [101]. A saline-filled syringe, a column of saline in a syringe without a plunger, and a hanging drop have all been used to visually confirm entry [108, 109]. A multiport catheter should be easily advanced 5–10 cm through the epidural needle. If the catheter does not advance smoothly, either pleural adhesions or misplacement of the catheter is present. In spontaneously breathing patients, air will always be entrained when a needle and/or catheter are placed into the pleural space. Thus, it is important to minimize the total time of needle and catheter placements.

Once the catheter is in place, the patient should be positioned so the local anesthetic injected will pool in the paravertebral gutter. The amount of local anesthetic injected can vary from 10 mL to 30 mL, and most will select an intermediate volume (20 mL of 0.25 %–0.5 % bupivacaine with epinephrine) [110, 111]. The mechanism of blockade is believed to be a "retrograde" intercostal blockade at multiple levels [112]. Local anesthetic diffuses from the interpleural space to the intercostal nerves and paravertebral spaces where it pools (Fig. 12.11). The area of spread for a given volume is greater in the supine position compared with the lateral position [113].

Fig. 12.10 Visual techniques using fluid aspiration by negative interpleural pressure to recognize entry into the interpleural space. (**a**) Hanging drop. (**b**) A saline column in a syringe without a barrel. (**c**) A saline-filled glass syringe (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

Complications/Treatment

Complications associated with interpleural block are related to all phases of the procedure: needle and catheter placement, injection of local anesthetic, and infection as a result of indwelling catheter. It is possible to cause direct damage to neurovascular structures if the needle is angled toward the inferior margin of the rib during placement.

Because of the nature of the technique, which involves the passage of a needle through the pleura, entrainment of small amounts of air occur during catheter placement, and practically all patients (by definition) develop a pneumothorax (although usually less than 5 % of lung volume) [114]. Stromskag et al. reviewed the incidence of significant pneumothorax in 703 patients, demonstrating an incidence of 2 % [114]. Most of these were asymptomatic. The potential for significant pneumothorax or bronchopleural fistula occurs in patients with adhesions or bullae or in patients on positive pressure ventilation. Tension pneumothorax has been reported and attributed to a loss of resistance technique [115].

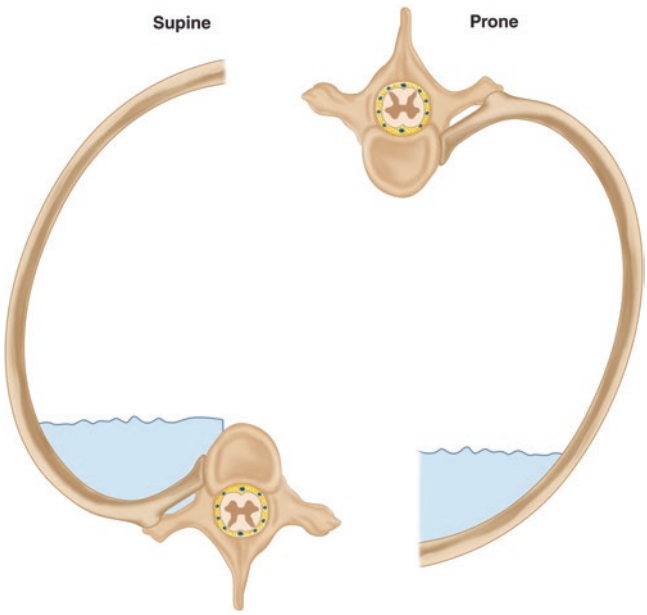

Fig. 12.11 Gravity and volume are important factors in distributing interpleural anesthetic to the targeted nerves. The position of the patient is critical to obtaining and maintaining an effective block in the desired dermatomal distribution. The patient must be positioned so that the instilled local anesthetic pools in the paravertebral gutter of the desired levels (Modified from Ferrante FM, VadeBoncouer TR. Postoperative Pain Management. New York: Churchill Livingstone; 1993, with permission from Elsevier)

In a series of 21 patients, an interpleural catheter was placed under general anesthesia before thoracotomy. When the catheters were viewed after thoracotomy, ten catheters were misplaced (seven were within the lung parenchyma). There were eight cases of lung damage, and three pneumothoraces (two tension). Thus, the authors concluded that interpleural catheterization can be dangerous [115]. Additional complications mentioned in the literature include local anesthetic toxicity, unilateral Horner's syndrome, and phrenic nerve blockade [116–118].

Contradications of interpleural blockade include preexisting pleural effusions or hemothorax, because the fluid will make diffusion of the local anesthetic unpredictable and diminish the efficacy of the block. Infection at the insertion site or within the pleural cavity is an absolute contraindication to this technique. Finally, in any patient with a chest tube connected to continuous suction, the full dose of local anesthetic will not be administered. In fact, one study found that up to 30 %–40 % of an administered dose of bupivacaine was found in the thoracostomy drainage [119]. All things considered, it seems unreasonable to expose patients to these aforementioned risks when other, more effective means of anesthesia and analgesia are available.

Thoracic Wall Nerve Block

Chest wall surgeries are relatively common and can have significant pain sequelae. Ultrasound-guided injections techniques have allowed for the development of intermuscular along the planar fascia between the muscles. This technique has been increasingly used in breast surgery. Studies have also shown efficacy of serratus anterior block being used for postthoracotomy pain [120].

Anterior Thoracic Wall Anatomy

Anterior thoracic wall muscles include the pectoralis major, pectoralis minor, latissimus dorsi, teres major, and serratus muscle. Neural innervation of the chest wall and breast include the pectoral nerves from the brachial plexus cords, thoracic 2–6 spinal nerves, and the long thoracic and thoracodorsal nerve. The lateral pectoral nerve is from Cervical 5–7 and runs between pectoralis major and minor to supply the pectoralis major muscle. The medial pectoral nerve comes from Cervical 8-Thoracic 1 and runs deep to the pectoralis minor to supply pectoralis major and minor. The lateral and anterior branches of Thoracic 2–6 run in a plane between the intercostal muscles and become the lateral and anterior branches. Lateral spinal nerves pierce the intercostal muscles and serratus anterior in the mid-axillary line to give off anterior and posterior cutaneous branches. The anterior branches of Thoracic 2–6 nerves pierce the intercostal muscles and serratus anterior to supply the medial breast. Thoracic 2 spinal nerve becomes the intercostobrachial nerve. The long thoracic nerve from the cervical 5–7 runs on the outer portion of serratus anterior. The thoracodorsal nerve from cervical 6–8 runs deep into the posterior axillary wall and supply the latissimus dorsi [121, 123–124].

Thoracic Wall Block Techniques

We will discuss the serratus anterior block as described by Blanco et al. [14]. He describes a safe and easily performed regional anesthetic technique to block the thoracic intercostal nerves and to provide complete analgesia of the lateral part of the thorax. With the patient in supine position a linear ultrasound probe (10–12 Hz) should be placed in the mid-clavicular region of the thoracic cage in the sagittal plane. Ribs should be counted inferiorly and laterally, until the fifth rib is identified in the mid-axillary line. The latissimus dorsi (superficial and posterior), teres major (superior), and serratus muscles (deep and inferior) are identified by the ultrasound over the fifth rib. The needle is placed in the

planar fascia between the latissimus dorsi and the serratus anterior muscle [14]. Previously, Blanco et al. have described pectoralis muscle blocks (Pec I and II) where local anesthetic is injected between the chest wall muscles. In the Pec I block, local anesthetic is injected between the pectoralis major and minor at the third rib level to block the lateral and medial pectoral nerves [121]. In the Pec II block, local anesthetic is injected between the pectoralis minor and the serratus anterior at the third rib level to block the lateral branch of the T2–4 spinal nerves [122].

Complications/Treatment

These ultrasound-guided anterior chest wall planar blocks are still undergoing clinical trials. They are relatively low risk in terms of potential complications. These include possible pneumothorax, local anesthetic toxicity, intravascular injection, and nerve damage. Pain relief is limited to the duration of local anesthetic unless nerve catheter is used.

Summary

Paravertebral, intercostal nerve blocks and interpleural analgesia can all provide short- or long-term anesthesia and analgesia in a unilateral, dermatomal distribution in the thoracic and abdominal regions. Thoracic epidurals cover a larger area of the chest wall and come with associated physiologic changes such as hypotension. Thoracic epidurals and paravertebral blocks are also useful to manage chronic radicular and axial pain in this region. When performed correctly, all can provide good results. However, each technique has specific circumstances under which it should and should not be performed. Careful attention to every technical detail is mandatory. One should also be fully cognizant of the side effects and complications of each procedure. Good planning and careful attention to all technical details will aid in the successful performance of these techniques and at the same time minimize complications. When performing regional anesthesia, the operator should always have access to treatment for local anesthetic toxicity including emergency medications, resuscitation equipment, and intralipid therapy. Ultrasound can be helpful in decreasing complications by avoiding vascular structures and providing direct visualization of needle placement. However, success depends on operator knowledge and comfort level with various ultrasound-guided techniques.

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Abdominal Wall Blocks: Safe Practice and Management of Adverse Events

13

James D. Griffiths and Peter D. Hebbard

Key Points

- Abdominal wall blocks have gained popularity in recent years as an alternative to epidural anesthesia. Due to the vascularity of the target area, the risk of local anesthetic toxicity is heightened.
- The key to safe abdominal wall blockade is anatomical knowledge, ultrasound scanning skill, and adherence to local anesthetic dose limits.
- Although rare, trauma to the abdominal wall itself and intra-abdominal structures has been reported. Another rare complication that should be considered is inadvertent femoral nerve block.
- Absorption of local anesthetic following TAP block is rapid and, although peak plasma concentrations are comparable to other blocks, several reports of seizures have been published, usually following injection of large local anesthetic doses.
- Abdominal blocks can be challenging in certain populations, including children, the obese, pregnant women, and individuals with coagulopathy. Awareness of needle size and trajectory and local anesthetic dosing are especially critical to avoiding complications in these patients.

J.D. Griffiths, MBBS, FANZCA, MEpi, PGCert CU (✉)
Department of Anesthesia and Pharmacology,
University of Melbourne, Royal Women's Hospital,
Parkville, VIC 3079, Australia
e-mail: james.griffiths@thewomens.org.au

P.D. Hebbard, MBBS, FANZCA, PG Dip Echo
Northeast Health Wangaratta, University of Melbourne,
Melbourne, VIC 3677, Australia
e-mail: p.hebbard@bigpond.com

Abbreviations

ASIS	Anterior Superior Iliac Spine
ED_{50}	Median effective dose
LA	Local anesthetic
TAP	Transversus abdominis plane

Introduction

The practice of abdominal wall regional anesthetic blocks has been revolutionized in the last decade by the evolution of small, portable, affordable, ultrasound machines. Short bevel needles and the seeking of fascial "pops" [1] have been substantially replaced by the capacity for real-time imaging of the passage of the needle and the spread of local anesthetic. Despite this, abdominal wall blocks remain predominantly "field" blocks, where a large volume of local anesthetic is injected into a fascial plane relying on wide spread to block the nerves within the plane. An exception to this is ultrasound-guided blocks of the ilioinguinal and iliohypogastric nerves, which may be imaged specifically.

In general, abdominal wall blocks appear to be safe, and serious complications are rare. Complications such as retroperitoneal hematoma and bowel perforation have been described following ilioinguinal nerve block but not after transversus abdominis plane (TAP) block. However, the ilioinguinal nerve block has been used for many years [2], and in comparison, the transversus abdominis block is relatively new (it has been in common use for less than 10 years). Also, the ilioinguinal nerve block has been traditionally performed using a blind technique, whereas the TAP block is usually performed with ultrasound guidance.

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_13

Key Risks and Complications

Abdominal Wall Trauma

Although the potential is present for trauma to abdominal wall structures, particularly blood vessels, there are no reports in the literature of significant hematoma related to TAP block. This is despite the fact that abdominal wall blocks make an attractive alternative to neuraxial analgesia (and therefore are commonly used) in patients with coagulopathy. Anecdotally, the situation may be complicated by the presence of surgical trauma, particularly laparoscopic port sites and drain tubes.

There are three main arteries in the abdominal wall, the superior and inferior epigastric arteries and the deep circumflex iliac artery (Fig. 13.1). These arteries may often be imaged on ultrasound, particularly using color Doppler imaging, and avoided. The superior epigastric, in particular, is vulnerable in an upper subcostal TAP or rectus sheath block where it emerges from the costal margin 2 to 5 cm lateral to the midline. It usually has a short course deep to the rectus muscle before penetrating into the muscle substance. Near to the anterior superior iliac spine (ASIS) the deep circumflex iliac artery turns from its lateral course on the iliacus fascia to pass into the TAP and run superiorly. It is vulnerable to a block targeting the ilioinguinal nerve in this area.

Nerve injury related to abdominal wall blocks has not been described. It is likely that the small, mobile, and robust nature of the abdominal wall nerves makes them likely to slide past rather than be cut by a block needle. The clinical presentation of isolated nerve injury in the abdominal wall is likely to be minimal and not reported by patients.

Transient relaxation of abdominal structures is seen when motor block is present, evident by bulging of the abdominal wall [3, 4]. This effect has not been reported to cause problems. Although some risk must exist, there have been no reports of significant infection such as abscess or fasciitis within the abdominal wall, following TAP or ilioinguinal nerve blocks.

Trauma to Intra-abdominal Structures

Reports of trauma to intra-abdominal structures resulting from abdominal wall blocks are rare. However, cases have included trauma to the liver [5–8] and bowel wall hematomas [9] (Figs. 13.2 and 13.3). Colonic perforation has been described following ilioinguinal nerve block in children [10, 11]. Performing nerve blocks of the abdominal wall without ultrasound has been shown to lead frequently to intraperitoneal needle tip placement [12, 13]. Ultrasound does not completely eliminate this risk as needle imaging and identification may be poor. Furthermore, there may be some difficulty in identifying the layers. A particular difficulty may be air or surgical gas in the abdominal wall. There may be greater risk in the morbidly obese (see later) or in pediatric patients, where the transversus plane may only be a few millimeters in thickness. The risk, however, does seem to be very low in experienced hands. If identification of the layers is uncertain or needle tip location undetermined, the needle should not be advanced further.

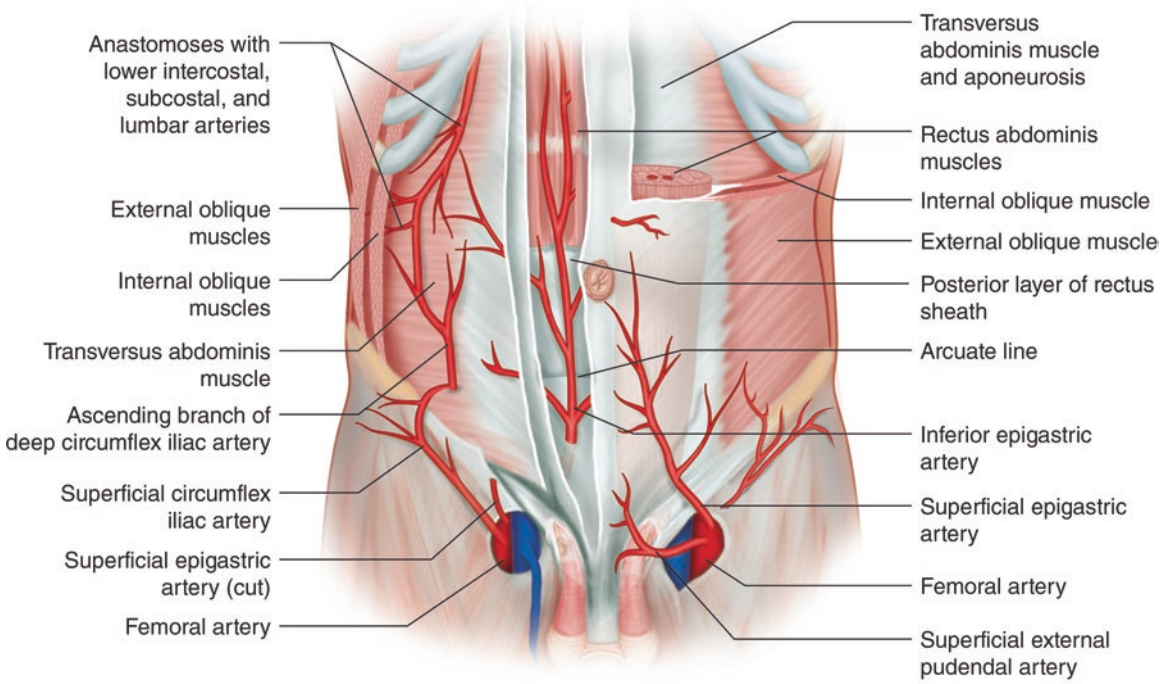

Fig. 13.1 Abdominal wall blood vessels

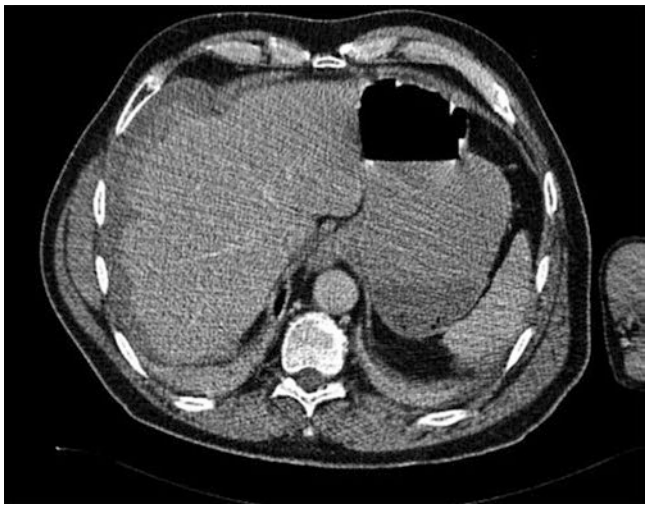

Fig. 13.2 CT scan of liver hematoma from Lancaster P, Chadwick M. Liver trauma secondary to ultrasound-guided transversus abdominis plane block. British Journal of Anesthesia. 2010; 104(4):509–10, by permission of Oxford University Press

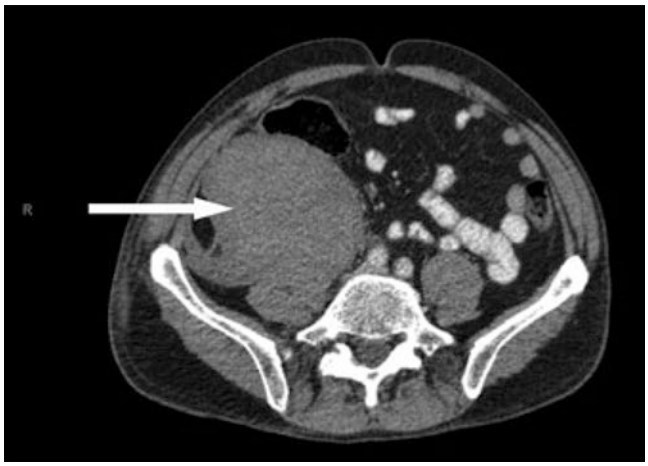

Fig. 13.3 Large Retroperitoneal hematoma from Parvaiz et al. Large retroperitoneal hematoma: an unexpected complication of ilioinguinal nerve block for inguinal hernia repair. Anesthesia. 2012;67(1):80–1. With permission John Wiley and Sons

Retroperitoneal injection in the inguinal area has been associated with retroperitoneal hematoma from deep circumflex iliac artery damage [5, 6, 14, 15]. The iliaca fascia is located immediately deep to the transversus abdominis muscle in the area near the ASIS.

Femoral Nerve Block

Inadvertent transient femoral nerve block has been described after nerve blocks of the abdominal wall including TAP block as well as ilioinguinal nerve block [16–19]. This potential should be considered in any block around the ASIS. However, it has not been reported after ultrasound-guided TAP or ilioinguinal nerve block. Femoral nerve block has also been described after posterior TAP injection in the area of the triangle of Petit without ultrasound guidance [10]. The authors speculated spread from deep to transversus abdominis to the iliac fossa, posterior to the fascia iliaca where the femoral nerve is located. Another anatomical route from injection in this location would be direct injection into the psoas muscle finding its way to the psoas compartment and femoral nerve. While uncommon, the potential for inadvertent femoral nerve block remains an important consideration when performing nerve blocks of the abdominal wall, especially in ambulatory or day surgery. Patients (and medical staff) are unlikely to anticipate leg weakness and this may increase the risk of postoperative falls.

Catheter entrapment from abdominal wall placement has also been described [20, 21]. The mechanism from this case was not clear as the catheter was eventually removed without a knot. Ultrasound imaging of the entrapped catheter was not undertaken.

Local Anesthetic Toxicity

Abdominal wall blocks are field blocks requiring the administration of large doses of local anesthetic. Efficacy clearly relies on an adequate volume of injectate to allow spread within the anatomical plane to bathe the required nerves; however, there are limited published data on the relative importance of dose, volume, and concentration of local anesthetic in the injectate. Cadaveric studies have been conducted to correlate the spread of injectate with the dermatomal anesthesia achieved [22–24]. There is a paucity of dose finding studies in the literature; however, Beloeil et al. demonstrated that large doses of local anesthetic were required to achieve ED_{50} [25].

Emerging evidence suggests that absorption of local anesthetic from the transversus abdominis plane is rapid, with peak levels typically achieved in 30 min (Fig. 13.4) and remaining elevated for up to 90 min [26–28]. If the block is administered following wound closure, it is important to recognize that peak plasma concentrations of local anesthetic are likely to occur in the Recovery Room and potentially after the departure of medical staff.

Plasma concentrations of local anesthetic have been studied following TAP block in several settings including following gynecological laparotomy and caesarean section [26, 27]. Peak total concentrations are comparable with local anesthetic concentrations following regional anesthesia elsewhere, including ilioinguinal nerve, caudal and scalp blocks for awake craniotomy [29–32]. However, these levels are also in the vicinity of those on the threshold of neurological toxicity as described by Knudsen and colleagues [33].

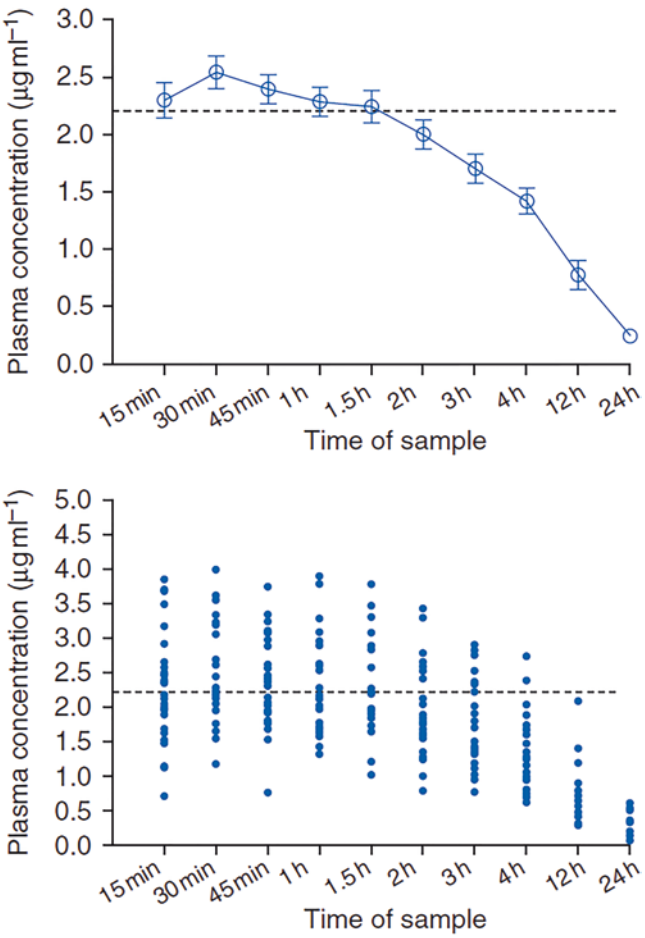

Fig. 13.4 Plasma ropivacaine concentrations following TAP block from Griffiths JD, Barron FA, Grant S, et al. Plasma ropivacaine concentrations after ultrasound-guided transversus abdominis plane block. British Journal of Anesthesia. 2010;105(6):853–6 [32]. By permission of Oxford University Press

Several case reports of seizures have been described, mainly involving large doses of local anesthetic although one case of seizures postcaesarean section involved only 2.7 mg/kg of ropivacaine [28, 34–36].

It is not known to what extent the accuracy of the deposition of local anesthetic within the transversus abdominis plane influences the resulting local anesthetic plasma concentrations. A variable amount of leakage of local anesthetic into surrounding musculature is occasionally observed during TAP blocks, particularly if the block is difficult, such as in the obese patient. It is possible that this leakage contributes to (or in fact, may reduce) the extent of systemic absorption. There is some evidence that the use of ultrasound guidance may decrease the plasma concentrations of local anesthetic following ilioinguinal nerve block [37].

There is some evidence to suggest that the addition of adrenaline (epinephrine) may reduce the systemic absorption of levobupivacaine [38]. This has not been studied in other local anesthetics, but would seem to offer potential, and also could serve as a marker of intravascular injection.

Catheters placed in the TAP can provide ongoing analgesia for 24–72 h [39, 40]. Hessian monitored bound and unbound plasma levels of ropivacaine for 72 h after an initial bolus and infusion into the TAP. Although one patient with low plasma ropivacaine levels reported symptoms consistent with local anesthetic toxicity, measured levels of ropivacaine remained below accepted toxic thresholds. Total ropivacaine levels continued to increase to 72 h although unbound ropivacaine peaked at 24 h.

Special Cases

Morbid Obesity

Morbid obesity increases the difficulty of performing abdominal wall blocks significantly. Ultrasound guidance is difficult due to the increased depth of imaging required and the narrow imaging window with linear ultrasound probes. Broadly curved lower frequency probes are helpful and improve the field of imaging at greater depths. However, it can be challenging to clearly observe the passage of a straight needle with a curved image. As shown in Fig. 13.5, it may be necessary to displace truncal adiposity with firm pressure from the ultrasound probe to improve imaging. This approach however has several problems. First, it may be difficult to accurately image the needle through its entire passage as the needle is long (typically 100–150 mm) and may bend in the tissues. An additional problem when performing these blocks on a very large patient is operator fatigue. Strength and endurance are required in the arm holding the ultrasound probe. Image quality tends to deteriorate as the operator gets tired, an issue which seems particularly prominent in trainees (who generally take longer to perform the block). Helpful strategies may include having an assistant support the abdominal wall and optimizing conditions such as the operating table or bed height and having the patient close to the operator.

Pediatrics

There is a significant body of evidence supporting the use of abdominal wall blocks in children [2, 12, 32, 41–43]. However, studies also demonstrate that the deposition of the injectate in pediatric population is frequently inaccurate, especially when using blind techniques [37]. Higher

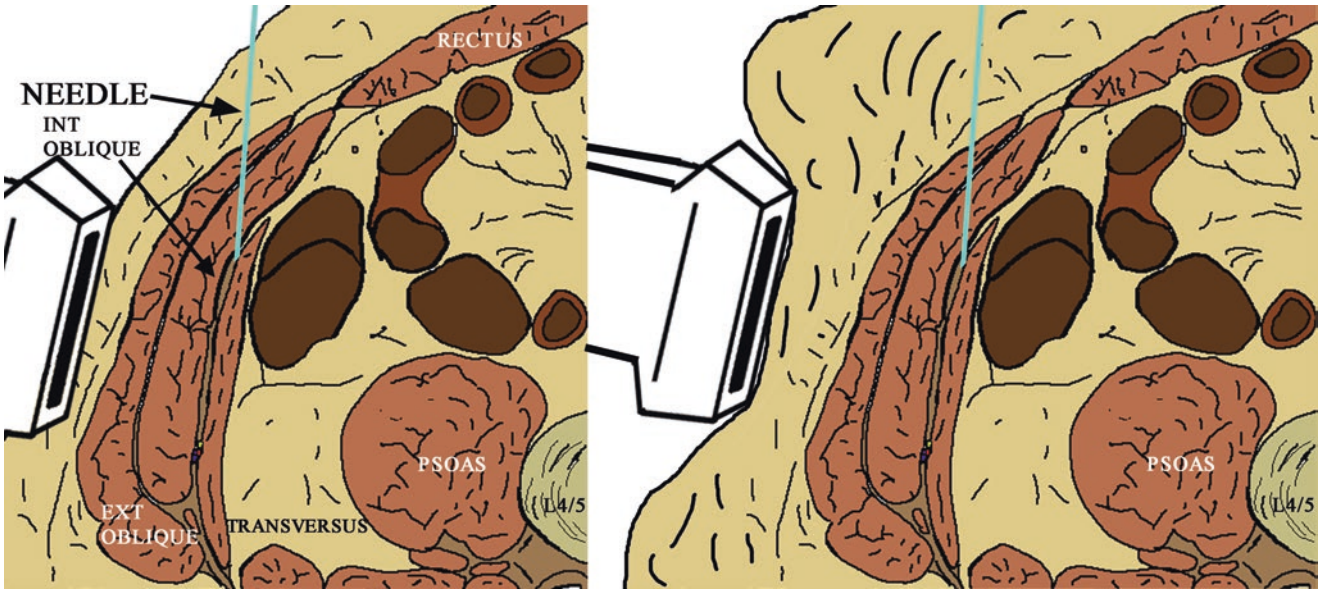

Fig. 13.5 TAP block in the morbidly obese

frequency small footprint ultrasound probes may be required and strict attention to dose limits is even more important.

Pregnancy

There are many publications involving the use of TAP blocks to provide analgesia following caesarean section [44–47]. The blocks are generally performed following wound closure and therefore whilst the patient still has many of the physiological changes of pregnancy, they are technically no longer pregnant. There are a number of these changes, which may be relevant to performing TAP blocks in the pregnant (or recently pregnant) patient. Dilatation (and potentially varicosities) of the abdominal wall veins may increase the risk of abdominal wall hematoma. Theoretically, the gravid uterus represents an additional intra-abdominal organ at risk of trauma from a misplaced block needle. Plasma-free (unbound) local anesthetic concentrations may be increased following TAP block due to the decrease in plasma-binding proteins and the increase in cardiac output and tissue blood flow in late pregnancy.

Coagulopathy

Truncal nerve blocks present an attractive alternative for providing analgesia in patients where neuraxial anesthesia is contraindicated. This would include patients with coagulopathy, hepatic and renal disease, and systemic sepsis. Patients with coagulopathy must be at an increased risk of significant abdominal wall hematoma, although this has not been described in the literature. This risk could potentially be minimized by reducing the size of the block needle. Smaller needles are more difficult to visualize using ultrasound, and are also more prone to bending, so are therefore more reliant on operator expertise. Also, patients with intra-abdominal sepsis undergoing laparotomy could theoretically be at risk of providing a locus of infection in the abdominal wall. Impaired clotting and sepsis should not be considered absolute contraindications for abdominal wall blockade or catheters. These cases should be assessed individually.

Summary

The key to safe abdominal wall blockade is anatomical knowledge, ultrasound scanning skill, and adherence to local anesthetic dose limits. Adequate training and equipment are critical to the safe performance of all regional anesthesia [48, 49]. Practitioners need to be aware of the neuroanatomy of the abdominal wall relevant to the site requiring anesthesia [22, 50]. Abdominal wall blocks often require a long needle to traverse a relatively long distance. As with other regional techniques [51], care needs to be taken to visualize the needle throughout its passage in order to avoid intraperitoneal injection and potential trauma to intra-abdominal structures. The transversus abdominis muscle is often very thin, so the risk of entering the peritoneal cavity (and therefore potentially causing trauma to intra-abdominal structures) must always be considered. Abdominal wall blocks are "field" blocks requiring a large dose and volume of local anesthetic solution; therefore, practitioners should always consider the potential for local anesthetic toxicity. Systemic absorption of

drug is similar to other comparable techniques, however unexpectedly high plasma levels and toxicity have been reported. Practitioners should always be cognizant of the likely time course of peak plasma concentrations of local anesthetic. Finally, ultrasound has been shown to result in more accurate placement of local anesthetic [12, 37, 41]. It has been proposed that the practice of "blind" placement of transversus abdominis plane and ilioinguinal nerve blocks should be discontinued [13].

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Epidural Blockade: Safe Practice and Management of Adverse Events

14

Steven J. Gaff

Key Points

- Epidural anesthesia and analgesia has been the mainstay for pain control following many surgical procedures. Despite a gradual decrease in popularity, it remains a relevant and important modality for certain subspecialties such as obstetrics.
- In this chapter, key themes in the safety and quality of epidural anesthesia, including combined spinal–epidural (CSE) techniques, are highlighted.
- Practice points which might help to make our epidural procedures as safe as possible are presented in this chapter and complication rates should improve by incorporating these measures.
- Complications may arise from block-induced physiological changes, wrong drug/adverse drug effects, or issued with needle/catheter insertion. Although rare, serious neurologic injury is a risk that must be considered, and the decision to perform an epidural should be made on a patient-by-patient basis.
- Certain risk factors exist that may predispose to complications with an epidural, and the anesthesiologist must be aware of these and any coincidental conditions that could mimic neurologic injury following epidural anesthesia.
- Intravertebral hematoma can result in spinal cord compression, which may lead to serious neurologic consequences; practice guidelines should be followed when considering an epidural for an anticoagulated patient. Intravertebral infection can lead to abscess and, in severe cases, meningitis; proper antiseptic technique should be followed to minimize the risk of introducing bacteria into the epidural space.
- Spinal cord ischemia, trauma to the spinal cord/nerve root, and arachnoiditis are other potential complications associated with epidural anesthesia. Care should be taken to eliminate any chance of wrong route errors or infusing the wrong drug.
- As with all anesthetic procedures, the safety of epidural blockade reflects the psychomotor skills and judgment of the operator, as well as the possibility of human or system error.

Introduction

Epidural analgesia provides excellent analgesia which is satisfying for the patient and the anesthetist. Some authors have suggested that gold standard pain relief is reason enough for siting an epidural [1], but the advantages should go beyond simply demonstrating better pain scores and fewer opioid-related side effects. The decision to proceed should be based on the evidence for outcome benefit and the potential for adverse effects.

Randomized controlled trials (RCTs) have shown epidural infusion of local anesthetic, when compared to systemic opioid analgesia, provides superior analgesia and attenuates the neurohumoral stress response to surgery [2–5]. In the MASTER trial, an RCT conducted in 888 patients with significant comorbidities undergoing major abdominal surgery, respiratory failure occurred less frequently in patients managed with an epidural compared to a systemic opioid-based technique [5]. In certain at-risk subgroups, such as those undergoing abdominal aortic surgery, epidural analgesia may reduce cardiorespiratory morbidity as well as facilitating earlier extubation and discharge from the intensive care unit (ICU) [6, 7]. A recent large population-based cohort study found that the use of an epidural-based technique slightly reduced 30-day mortality in patients undergoing noncardiac surgery, but the absolute risk reduction was only 0.2 % (number needed to treat 477) and the authors concluded that this small improvement was not compelling

S.J. Gaff, MBChB, FCARCSI, FANZCA (✉)
Department of Anaesthesia and Perioperative Medicine, The Alfred Hospital, Melbourne, VIC 3004, Australia
e-mail: steven.fowler@alfred.org.au

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_14

[8]. Cohort studies have found an association between regional anesthesia and lower rates of metastasis or tumor recurrence but there is currently no higher level evidence to support this [9]. A retrospective analysis of data from the MASTER trial to assess whether postoperative epidural analgesia had an effect on tumor recurrence found no effect [10], and a recent consensus statement has concluded there is currently insufficient evidence to support any change in clinical practice [11].

Epidural use in the perioperative setting has been declining around the world and it is interesting to note that this decline started before the MASTER trial was published [8, 12, 13]. One of the most common reasons given for this is lack of evidence for outcome benefit. Improvement in early functional recovery has not been shown to contribute to longer term outcome and no prospective RCT has demonstrated a reduction in mortality using epidural analgesia. It is unlikely that one will do so because extrapolating from the MASTER trial this may require a study enrolling 55,000 participants [8].

Another reason for declining epidural use in the perioperative setting is that comparable analgesia can often be achieved using modern multimodal analgesia, with fewer minor side effects or serious adverse events, and equivalent functional outcome [14]. Peripheral nerve or plexus block (PNB) [15], high-volume local anesthetic infiltration (HVLIA) [16], and trunk blocks such as transversus abdominis plane (TAP) block [17, 18], can all provide equivalent analgesia to epidural blockade without the risk to the neuraxis. Other alternatives include intrathecal opioid and paravertebral block [19], although the relative safety profile of the latter technique is debated [20]. Even systemic opioid-based techniques have become much safer and more effective during the last 40 years whereas the technique of epidural analgesia is little changed [21].

Other factors which make it increasingly difficult to demonstrate a significant benefit from postoperative epidural analgesia are the introduction of less invasive (e.g., endovascular and laparoscopically assisted) surgical techniques, as well as comprehensive enhanced recovery after surgery (ERAS) programs [3, 7]. The concept of ERAS is small, incremental improvements in perioperative management combined in a protocol to improve outcome and reduce hospital stay [22]. As an example in the setting of total knee arthroplasty (TKA), techniques utilizing peripheral nerve blockade (PNB), intrathecal opioid, or high-volume local anesthetic infiltration (HVLIA) have largely replaced epidural analgesia because they provide equivalent analgesia and fewer adverse effects [15, 16, 23, 24]. It is highly relevant that this patient population is also prone to serious neuraxial complications following epidural catheterization [25].

Benefits of Epidural Blockade in Special Patient Populations

Because of the potential benefits, epidural analgesia remains widely used in high-risk subgroups undergoing major thoracic, abdominopelvic, or lower limb surgery. Epidural block (or CSE) also remains a cornerstone of labor pain management and operative obstetric anesthesia worldwide [26]. The safety of epidural analgesia compared to opioid delivered using a patient-controlled analgesia (PCA) device among adult patients undergoing major surgery has been examined in two pooled, uncontrolled studies of more than 120,000 patients [27, 28]. Respiratory depression requiring treatment with naloxone and sedation occurred more commonly with PCA opioid, although hypotension was much more frequent with epidural analgesia (5 % vs. 0.5 %) and no mortality difference was shown. These two large series underline the usefulness of regional techniques in opioid-sensitive patients, including the population with suspected or diagnosed obstructive sleep apnea (OSA). An epidural technique (including CSE) is also more titratable than single-shot spinal anesthesia, which may be relevant in frail patients with relatively fixed stroke volume, for example, who may not tolerate general anesthesia well. Similarly, in the setting of opioid tolerance or significant pre- or postoperative pain, regional analgesia can be very useful. In any case, a multimodal, multidisciplinary approach should be employed.

Infrastructure for Safe Epidural Blockade

Important aspects of organizational structure which ensure safe and effective epidural analgesia are listed in Table 14.1. Attention to these facets of care promotes both effective analgesia and patient safety [2, 29, 30]. In many centers, acute pain services assume responsibility for postoperative management, encompassing staff training and patient education.

Training in Epidural Techniques

Epidural block is a core skill for anesthesiologists and a clear understanding of the relevant anatomy, physiology, and pharmacology is required. As well as technical aspects of safe epidural blockade such as gentle technique and meticulous asepsis, it is essential that the importance of patient preassessment and case selection, consent and documentation is understood. Utilization of a test dose (e.g., lidocaine with adrenaline) to detect inadvertent intrathecal or intravascular catheterization and awareness of warning ('red flag') symptoms and signs which may signal an

Table 14.1 Organizational factors for safe epidural analgesia

Nursing staff education and accreditation
Pain assessment using validated tools
Setup and change of pump and infusion circuit
Monitoring including sensorimotor block, pain, and sedation scores
Recognition of adverse effects
Discontinuation of epidural analgesia and catheter removal
Medical protocols and/or guidelines
Standardized prescribing
Frequency of patient assessment and handover
Mobilization and enhanced recovery
Identification and management of serious complications
Follow-up
Quick reference guide
Resuscitation team, oxygen, drugs, and equipment available
Documentation
Patient information (pre- and postprocedure)
Audit and quality assurance

evolving neurological complication are key teaching points [31, 32]. The Australian and New Zealand College of Anesthetists requires 50 labor epidurals, 20 other lumbar epidurals, and five thoracic epidurals to be performed during anesthesia training [33]. However, it has been shown using CUSUM analysis, a useful tool to assess proficiency in practical skills, that this number may not be sufficient for all trainees to achieve competency and training should be tailored to the individual [34]. Konrad and colleagues reported in a learning curve study that 90 epidural attempts are needed to achieve a success rate of 80 % [35]. In our experience, the use of peripheral nerve and trunk blocks as well as local infiltration techniques has reduced training in epidural analgesia. This trend should be monitored by training bodies as it could lead to deskilling of trainees although workshops and simulators can supplement in-theatre training. Ultrasound can be useful to confirm the position of the interspinous space (i.e., midline) and the depth of the ligamentum flavum, especially when attempts at conventional insertion have failed or the procedure is expected to be difficult [36]. The evidence for ultrasound-assisted epidural catheter placement is limited but utilization is likely to increase as image quality and needle visualization improves [37, 38].

Risks of Epidural Anesthesia

Complications of epidural block may arise from physiological changes resulting from the block, adverse drug effects, problems associated with the needle or catheter, or wrong drug/route error. The adverse effects and nonneurological complications which should not result in permanent harm if treated appropriately are listed in Table 14.2.

Table 14.2 Adverse effects and nonneurological complications of epidural blockade

Adverse effects
Hypotension
Urinary retention
Pruritus
Motor block
High block
Block failure
Allergy
Complications (excluding neurological)
Local anesthetic toxicity
Postdural puncture headache

Table 14.3 Causes of neurologic damage attributable to epidural blockade.

Cord compression
Hematoma
Needle or catheter trauma
Coagulopathy
Abscess
Exogenous infection via needle/catheter
Hematogenous
Local spread (e.g., paravertebral)
Cord ischemia
Anterior spinal artery syndrome
Cord and nerve root trauma
Needle/catheter/injectate
Arachnoiditis (inflammation)
Wrong drug or toxic injectate
Infection
Local anesthetic neurotoxicity

Intravenous access should be secured prior to commencing epidural blockade and maintained for the duration of the infusion. Death or major morbidity from wrong drug or route error is idiosyncratic and rare. In contrast, neurological complications of centroneuraxial block assume two distinct patterns. Temporary neuropathies are typically patchy sensory deficits whereas a serious neurological complication can be defined as having the potential to cause permanent functional impairment (usually from weakness or pain). Mechanisms and causes of damage to the neuraxis attributable to epidural blockade are listed in Table 14.3.

Coincidental Causes of Neurologic Injury

Consideration of noniatrogenic causes is mandatory (see Table 14.4). Coincidental pathology such as spinal stenosis can lead to cord compression when triggered by the additional volume of local anesthetic injection. It is well known

Table 14.4 Coincidental conditions mimicking neurologic injury from epidural blockade

Spinal tumors
Spinal vascular malformation
Prolapsed intervertebral disc
Guillain–Barré syndrome
Multiple sclerosis
Spinal hematoma
Metastases
Thalassemia
Infections (e.g., viral)
Embolic
Iatrogenic (e.g., hypotension, surgery, positioning, drugs)

that temporary obstetric palsies occur with and without neuraxial blockade [39]. Surgical damage [40] and patient positioning [41, 42] are both likely to be more common causes of permanent nerve injury than regional anesthesia. In a recent large retrospective 10-year single-center study of 380,000 consecutive patients undergoing all types of procedures, Welch and colleagues reported that the use of general or epidural anesthesia increased the risk of postoperative peripheral nerve injury, but there was no difference with the use of peripheral nerve blockade or spinal anesthesia [43]. In this study, nerve injuries resulting from the surgical procedure were excluded. Proving that the regional technique was not responsible may be impossible, even with advanced diagnostic techniques, and there is significant potential for misclassification of these injuries.

Serious Neurological Complications of Epidural Anesthesia

Whereas general anesthesia techniques have gradually become safer and less disruptive of normal physiology, the invasiveness of regional techniques is little changed; serious complications of centroneuraxial block still occur and they are often severe. Discussion of material risk remains topical [44, 45]. Although it is highly desirable to provide an estimate of the risk of a severe complication prior to a neuraxial procedure, the incidence of severe neurological complications quoted to the patient varies widely and the issue is reported to be a source of "confusion and concern" for anesthesiologists [46, 47]. Although a number of large studies have been published during the last 15 years, which help to provide contemporary data, it remains difficult to estimate incidence confidently for an individual patient.

The range of reported incidence figures reflects varied methodology—different patient populations have been studied and there is no consistent definition for a serious neurological complication. For example, some studies include patients who recovered, drug errors and cardiovascular complications [48, 49], or exclude major categories such as spinal hematoma and epidural abscess [50]. Sources of numerator and denominator data include voluntary reporting [49], postal questionnaire [25, 48], hotline reporting [51], pharmaceutical sales [25], and analysis of litigation or no-fault insurance systems [40, 48, 49]. Better studies corroborate their figures using multiple sources including referrals to neurology, radiology, and neurosurgery but this heterogeneity makes comparison difficult and the incidence figures quoted must be seen as estimates only.

Also, many studies are not powered to detect severe complications because very large numbers of patients are needed. Studies reporting no adverse events (i.e., zero numerators) in seemingly large series are easy to misinterpret. The "rule of 3/n" should be used; it states that for n observations with a zero numerator the upper 95 % confidence limit is 3/n [52]. For example, if a study reports that no neurological complications are observed in 4000 procedures, then according to the rule of 3/n which describes the upper 95 % CI for the actual incidence, the rate of permanent injury may be approximately 1:1400 [53, 54].

Third, an overall figure for incidence of serious complications of epidural analgesia should not be provided because the risk of a severe complication may differ up to 100-fold between patients at low risk [55] and those with multiple risk factors [25, 49]. The importance of considering risk: benefit on a patient-by-patient basis is highlighted in a retrospective study published in 2004 by Moen and colleagues [25]. This key study reported the incidence of serious neurologic complications associated with centroneuraxial blocks performed during the 1990s in Sweden and achieved the participation of 85 % of anesthesiology departments. The estimated denominator was 1,260,000 spinals and 250,000 epidurals (including CSE). In the general population, severe neurologic complications occurred after 1 in 3600 epidural procedures but the rate was higher in women undergoing total knee arthroplasty (1 in 1800) and much lower in obstetric patients (1 in 25,000). Major neurologic complications most commonly occurred in patients undergoing orthopedic, general, vascular, and urologic surgery. The authors proposed this was related to important risk factors in this group of patients including disordered coagulation, osteoporosis, spinal stenosis, and immunosuppression. In this study, patients who recovered after treatment for a serious complication were included.

The 3rd National Audit Project of The Royal College of Anesthetists (NAP3) was a 1 year prospective audit published in 2009 which included adverse events relating to wrong drug/route error and cardiovascular collapse, as well as serious neurological complications of centroneuraxial blockade [49]. Participation of 100 % of public hospitals in the United Kingdom was achieved and the estimated denominator included 293,000 epidurals and 42,000 CSEs. The majority of severe complications occurred after epidural or CSE procedures in the perioperative setting where the incidence of permanent harm was

approximately 1:5700 compared to 1 in 166,000 epidural blocks and 1 in 25,000 CSEs in obstetric patients. Although the authors concluded that the results were largely reassuring, 22 patients were excluded from analysis because complete recovery was documented by 6 months. These cases included epidural abscesses, spinal cord trauma, and an intravertebral hematoma as well as an unknown number of other cases with full resolution prior to reporting. When these 22 known serious complications with full recovery are included, the overall incidence in NAP3 was very similar to that found in the Swedish study by Moen and colleagues [25, 56].

It is important to note that the incidence of severe complications associated with spinal anesthesia is low and relatively consistent across subgroups—around 1 in 20,000 or less [25, 49, 57]—and all neuraxial block techniques (i.e., epidural, CSE, and spinal anesthesia) are associated with very low complication rates in obstetric patients [25, 49, 55].

Risk Factors for Neurologic Injury

The recognized patient- and technique-related factors which increase the chance of a serious neurological complication after neuraxial block are presented in Table 14.5 [58–60]. Older patients with multiple comorbidities undergoing epidural blockade in the perioperative setting are particularly at risk of serious neurological complications [48, 49]. Coagulation abnormalities and degenerative conditions of the spine, including spinal stenosis and osteoporosis, a common combination in older female patients, are also important risk factors [25]. Degenerative changes in the spine reduce the compliance of the intravertebral space and injection of a large fluid volume into the epidural space can cause transient paraplegia [61]. If the diagnosis is known in advance, other regional techniques such as plexus, trunk or peripheral nerve blockade, local infiltration, or spinal anesthesia can be selected, avoiding cord compression risk [62]. However, a serious complication can occur in the absence of any risk factors, [25, 63] and significant hemorrhagic complications of peripheral nerve and plexus block have also been reported [64].

Table 14.5 Risk factors for severe neurologic complications after epidural blockade

Patient factors
Female sex
Atherosclerosis
Diabetes
Advanced age
Spinal disorders
Osteoporosis
Ankylosing spondylitis
Spinal stenosis
Osteoarthritis
Other spinal deformity
Neuropathy
Coagulation abnormality (including liver disease; bleeding disorder)
Technique factors
Epidural catheter
Traumatic puncture
Dysesthesias during insertion
Prolonged continuation of block
Hypotension

Diagnosis of Neurologic Injury

Because compressive causes such as spinal hematoma and abscess are reversible if treated promptly, dilute solutions of local anesthetic, which avoid motor block, should be used so that pathologic lower body neurological deficit can be identified as early as possible. Initial presentation as cauda equina syndrome is a feature of several etiologies and it should be readily recognized by all practitioners. The fine autonomic fibers of the cauda equina are often the first to be affected by compression, ischemia, or neurotoxicity [65]. Damage to S2-S4 roots produces an atonic bladder although continence may be preserved if intravesical pressure is low. Progression of the syndrome leads to weakness of muscles below the knee as well as the hamstrings and gluteal muscles, with loss of ankle jerks and preservation of the knee jerk. Sensory loss in the sacral roots produces the characteristic saddle-shaped anesthesia of the perineum, buttocks, and thighs, extending to foot and calf if L5 and S1 roots are involved. Even using the lowest possible effective concentration of local anesthetic for epidural infusion, detection of the onset of painless cauda equine syndrome may be difficult in an immobile postoperative patient with a catheterized bladder. Patient outcome depends on vigilance and a high index of suspicion, especially in at-risk cases. The cardinal signs of new or progressive sensorimotor deficit, bladder dysfunction, and back pain can usually be detected using serial neurological assessment every 4 h until 24 h after epidural catheter removal. If these ‘red flag’ features become apparent, the epidural infusion should be discontinued to exclude a local anesthetic or volume effect. Magnetic resonance imaging (MRI) should be performed within 4 h after the infusion is stopped if the situation has not improved, as well as neurosurgical referral and early decompression if indicated. Should there be a delay in stopping the epidural infusion after onset of new ‘red flag’ signs, MRI scanning may need to proceed before the local anesthetic effect resolves [66]. In summary, the key management principles are

(1) diligent serial clinical neurologic assessment; (2) early MRI; and (3) consultation with colleagues in radiology, neurology, and neurosurgery.

Intravertebral Hematoma

Bleeding into a relatively enclosed bony space such as the intravertebral canal can result in permanent neurological sequelae with minimal volume by compressive effects (Fig. 14.1). Spinal cord compression from a hematoma developing in the subarachnoid, subdural, or extradural space can rapidly produce irreversible paraplegia but the deficit is potentially reversible if treated early [66].

Etiology

It is clear that an epidural Tuohy needle is more traumatic than a single-shot spinal anesthetic using a fine pencil point needle. The study by Moen and colleagues reported that the incidence of spinal hematoma in the nonobstetric population was 1:10,300 after epidural versus 1:480,000 after spinal blockade [25]. Intravertebral hematoma is more likely to occur in the presence of the 'red flags' listed in Table 14.5 but may occur in the absence of recognized risk factors [63]. In the study by Moen and colleagues [25], coagulation abnormality was documented in only one-third of spinal hematoma which underlines the importance of vigilance and postoperative neurologic monitoring. Some of these cases may be caused by puncture of epidural veins or Adamkiewicz's artery, which usually lies close to the midline along the L3 spinal root or in some cases L4/5 [67].

Incidence

After low-molecular-weight heparins (LMWHs) were introduced for routine thromboprophylaxis in 1993, an unfortunate cluster of nearly 60 cases of spinal hematoma occurred in the United States that were associated with administration of relatively high doses of LMWH. Those affected were typically older female orthopedic patients undergoing joint replacement surgery with epidural analgesia, for whom the estimated reporting rate of spinal hematoma was 1 in 3100 during 1993–1997 [57]. But this is not a problem which is confined to the United States; the similar incidence in Sweden [25], Australia [13], Germany [21], and the United Kingdom [68] suggests that this is a worldwide phenomenon. In contrast, the incidence of spinal hematoma after obstetric epidurals is probably less than 1:100,000 [48, 55]. In Moen and colleagues' study [25], there were two spinal

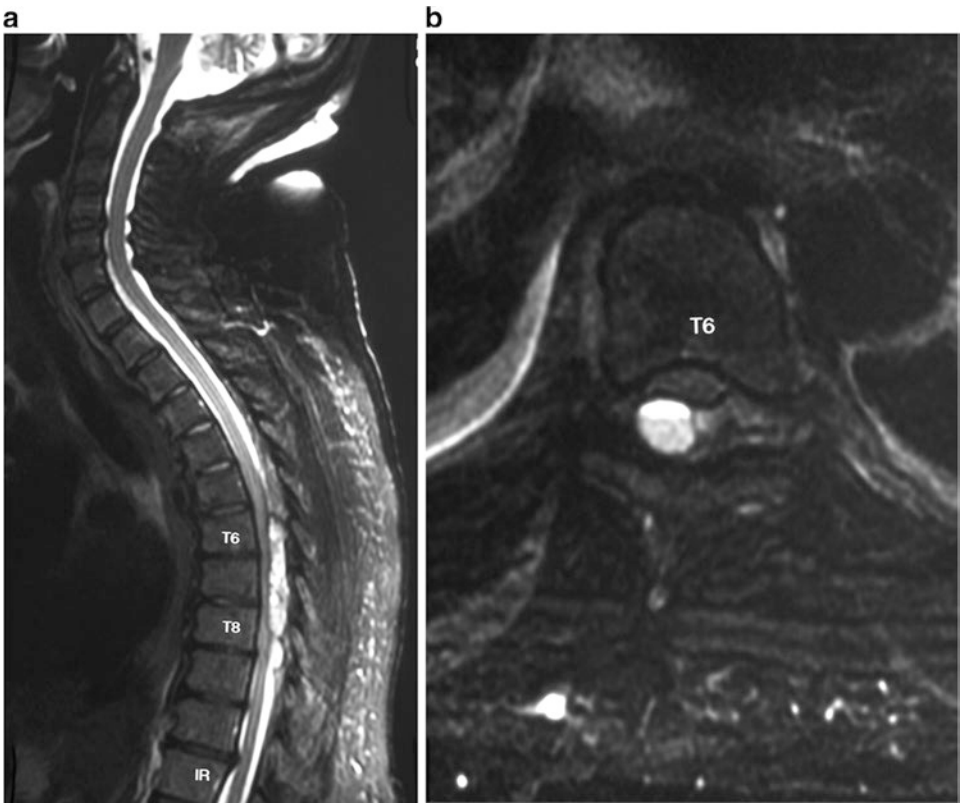

Fig. 14.1 Thoracic epidural hematoma demonstrated by MRI. Sagittal (**a**) and axial (**b**) T2 MR images of cervicothoracic spine showing acute epidural hematoma posterior to the cord at T5–T9 level. Note well-defined layering of blood in (**b**) (Courtesy Dr. Ayton Hope, Auckland City Hospital.)

hematomas reported among 255,000 obstetric blocks, but both occurring in patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP).

Diagnosis and Treatment

Because prognosis is better when preoperative neurologic deterioration is less severe, early diagnosis of spinal hematoma should be a central aim of postoperative surveillance. In a neurosurgical review of all 613 cases of spinal hematoma identified in the literature until 2003 [67], only one in ten reported cases was related to "a needle in the back," the largest group being idiopathic/spontaneous (38 %). Of the cases related to neuraxial blockade, symptoms appeared within 24 h in two-thirds of evaluated cases (31/46). Overall, complete neurologic recovery from spinal hematoma was achieved in about 40 % of cases. Comparing prompt surgical intervention (laminectomy and clot evacuation within 12 h) with treatment delayed beyond 12 h, the rate of complete recovery was 66 % versus 29 %. Although recovery after conservative treatment occurred in 25 of 33 cases (76 %), these patients were carefully selected [67].

Prevention

Formalized guidelines for centroneuraxial blockade in the presence of anticoagulation have subsequently been developed and implemented in several jurisdictions including the United States [64], Scandinavia [69], and Europe [70]. The American Society of Regional Anesthesia (ASRA) guidance for use and timing of neuraxial block in the context of drugs which affect coagulation is summarized in Table 14.6 [64]. These expert recommendations are not based on high-level evidence but on pharmacology of hemostasis-altering drugs or published case reports and case series. Partial or complete hemostatic failure from any cause (or combination of causes) produces a spectrum of risk, which may be negligible in the case of low-dose aspirin, and very high in fully heparinized patients [71], or in the presence of thrombolytic therapy [72]. Drug half-lives can be longer in the elderly and in patients with renal impairment and other comorbidities. The guidelines stress the importance of other precautions for safe practice, including frequent clinical neurological surveillance and avoidance of local anesthetic solutions which cause motor block [64].

Data from a large retrospective audit from Finland during the period 2000–2009 [48], as well as the NAP3 audit from the United Kingdom [49], suggest that guidelines for neuraxial blockade in the setting of anticoagulation have reduced the incidence of spinal hematoma but not eliminated the risk [20]. In the Finnish study, timing of antithrombotic drug administration was not in accordance with current recommendations in six out of 13 cases of intravertebral hematoma following neuraxial puncture, reinforcing the fact that serious complications can be avoided when practice guidelines are followed [20, 48].

Acceptable Laboratory Values for Safe Institution of Epidural Blockade

The minimum platelet count below which it is safe to place an epidural is not known. It is generally accepted that isolated thrombocytopenia to a platelet count of 100 × 10 [9]/L does not pose a risk for spinal hematoma, in the absence of other risk factors, and there is some evidence that the safe level may be as low as 75 × 10 [9]/L in obstetrics [73, 74]. Use of bleeding time as a screening test is not recommended but in an individual patient with a history of bleeding or easy bruising, platelet function analysis can be useful to identify platelet function disorders [75].

It is probably inadvisable to perform epidural blockade if any abnormality in other coagulation parameters (e.g., prothrombin time (PT) or activated partial thromboplastin time (APTT)) is present. However, where the anticipated benefits are great or if general anesthesia is contraindicated, there is some evidence that minor abnormalities are acceptable for single-shot spinal anesthesia although a nonneuraxial technique would be preferable [63]. There are very limited data in the setting of congenital disorders such as hemophilia and von Willebrand's disease [76]. Factor levels should be certainly be corrected to normal if centroneuraxial block is warranted although in our institution neuraxial blockade is avoided in these patients [76]. Coagulopathy associated with other conditions such as major trauma, sepsis, uremia, and liver failure is incompatible with centroneuraxial block until platelet abnormalities and clotting pathways are corrected [74]. For deeper block techniques such as paravertebral or lumbar plexus block, it is recommended that neuraxial precautions are followed but single-shot peripheral nerve blocks performed using ultrasound are relatively safe in the setting of abnormal coagulation [64, 70].

Unfractionated Heparin and LMWH

Centroneuraxial blockade can be performed in patients receiving subcutaneous UH or LMWH as long as guidelines setting out appropriate timing of needle placement and catheter removal relative to anticoagulant drug administration are carefully followed. Routine monitoring of the anti-Xa level in the setting of LMWH is not necessary but patients receiving heparin for more than 4 days should have a platelet count measured to exclude heparin-induced thrombocytope-

Table 14.6 2010 ASRA guidelines for neuraxial anesthesia and anticoagulation [64]

Drug class	Recommendation
Antiplatelet drugs	
(a) Aspirin/dipyridamole/NSAIDs[a]	No contraindication; perform block at any time[b]
(b) Thienopyridine derivatives	Discontinue agent 7 days (clopidogrel) to 14 days (ticlopidine) before CNB[c]
(c) GP IIb/IIIa receptor antagonists	CNB contraindicated within 8 h (eptifibatide, tirofiban) to 48 h (abciximab) of administration
UH	
(a) Subcutaneous	No contraindication with twice daily dosing (<10,000 U/day)[d]
(b) Intravenous	Perform CNB or remove catheter 2–4 h after last dose and confirmed normal APTT; delay heparin administration for 1 h after CNB (e.g., intraoperatively)[e]
LMWH	
(a) Prophylactic	Single daily dosing: CNB or catheter removal 10–12 h after LMWH; administer LMWH 4 h after CNB/catheter removal[f]
	Twice daily dosing: Delay LMWH for 24 h after surgery and remove epidural catheter 2 h before first dose
(b) Therapeutic	Delay CNB at least 24 h after LMWH; otherwise as above
Oral anticoagulants	
(a) Warfarin	After stopping warfarin, document normal INR before CNB; when starting warfarin, remove catheter when INR still ≤ 1.5
(b) Factor Xa inhibitors	Rivaroxaban: CNB 48 h after last dose[g]
(c) Direct thrombin inhibitors	Fondaparinux: CNB 72 h after last dose[g]
	Dabigatran: CNB 72 h after last dose[g]
Thrombolytics	Insufficient data; extreme risk[h]
Herbal medicines	No contraindication; perform block at any time[b]

CNB centroneuraxial block, *GP* glycoprotein, *UH* unfractionated heparin, *LMWH* low molecular weight heparin
[a]Including cyclooxygenase-2 inhibitors
[b]Caution when combined with other anticoagulants
[c]Clopidogrel can be restarted within 24 h after neuraxial manipulation
[d]Delay heparin after block if technical difficulty anticipated. European guidelines [70] recommend withholding CNB for 4–6 h after low-dose subcutaneous UH and waiting 1 h after CNB or catheter removal before administration
[e]European guidelines [70] recommend deferring surgery 6–12 h after traumatic CNB if intraoperative intravenous heparinization planned but ASRA guidelines state no mandatory delay
[f]Delay LMWH administration for 24 h after traumatic CNB
[g]Not stated in ASRA guidelines. Interval based on four drug half-lives (see text) and normal renal function. Nordic guidelines [69] state that administration of newer oral anticoagulants should be delayed for at least 6 h after CNB or catheter manipulation although other groups recommend an interval of 24 h (see text)
[h]Recommend neurologic monitoring at least two hourly

nia [64]. Although the presence of therapeutic blood heparin levels is a clear contraindication to epidural or spinal insertion, the situation is more reassuring with therapeutic heparinization shortly after the block procedure which is common in the setting of vascular surgery. Heparin administration should be delayed for at least an hour after needle placement and variables, such as other antiplatelet or anticoagulant therapy or traumatic procedure (e.g., bloody tap), may increase the chance of a spinal hematoma [64]. A number of case series comprising several thousand patients in which attention was given to these risk factors point to the relative safety of spinal/epidural anesthesia in patients subsequently heparinized for vascular surgery, although cases of spinal hematoma still occur in this high-risk population [60]. Thoracic epidural catheterization before full systemic heparinization for cardiopulmonary bypass remains very controversial because the potential benefits may not be worth the risks [77]. If performed, then the precautions in Table 14.7 should be observed. If a patient unexpectedly requires therapeutic anticoagulation (e.g., myocardial infarction in the postoperative period), at what stage should one remove the epidural catheter? At our institution, we prefer to remove the catheter before anticoagulating the patient rather than leaving it in situ because the treatment period is often prolonged. In the setting of fibrinolytic or thrombolytic therapy, a fibrinogen level may be helpful for timing of catheter removal [64]. The key message is that when neuraxial block is proposed or already established in the setting of anticoagulation—and it may be the best choice for the patient—experienced clinicians should be involved in decision-making and diligent postoperative surveillance for abnormal motor block is essential.

Table 14.7 Precautions for safe use of epidural blockade

1. Careful patient selection, i.e., assess risk–benefit of epidural blockade
2. Experienced clinicians should be involved in higher risk cases
3. Consider a nonneuraxial technique in 'red flag' patients
4. Follow guidelines for anticoagulation and centroneuraxial block
5. Perform in awake or lightly sedated patient
6. Minimize number of attempts; consider a time limit per operator
7. Avoid intraoperative hypotension; care with positioning
8. Use dilute epidural local anesthetic solutions which avoid motor block
9. Strict neurologic surveillance with a high index of suspicion
10. Communication with postoperative and acute pain teams
11. Advise patients to report back pain and sensorimotor symptoms
12. Ideally MRI should be available within 4 h

Oral Anticoagulants

It is not recommended that epidural (or other neuraxial blocks) are undertaken in patients with a therapeutic INR level. Although neuraxial puncture can be undertaken concurrently with initiation of warfarin therapy (as long as the INR level is < 1.5), much more caution is required in patients recently discontinued from warfarin with a falling INR level [64]. Adequate levels of factors II, VII, IX, and X may not be present until the INR is within normal limits (≤ 1.2) which is likely to take 4-5 days.

There are insufficient data on newer classes of oral anticoagulant such as direct thrombin inhibitors (e.g., dabigatran), direct factor Xa inhibitors (e.g., rivaroxaban, fondaparinux), and phosphodiesterase inhibitors. These drugs tend to be potent and difficult to reverse. Although appropriate window for neuraxial blockade after discontinuation is determined by the predicted drug half-life, the actual risk of spinal hematoma is unknown [69]. The European [70], and Scandinavian [69], guidelines adopted two half-life intervals between discontinuing the drug and neuraxial puncture as the shortest safe interval to provide adequate hemostasis while providing protection against venous thromboembolism (VTE). Although two to three half-lives may be appropriate when risk factors for VTE are present, in the remainder of patients an interval of five to six drug half-lives assures a more complete elimination of the drug [78]. A compromise would be an interval of four drug half-lives; bridge therapy with LMWH can be administered if indicated to prevent VTE. An interval of eight to 24 h is advised after the neuraxial procedure before restarting the oral anticoagulant depending on the bleeding risk [78]. Dabigatran activity can be monitored with the thrombin time or ecarin clotting time while the best tests for the direct factor Xa inhibitors are prothrombin time and anti-Xa assay [78].

Antiplatelet Agents

The minor hemostatic defect caused by the use of aspirin, dipyridamole, or nonsteroidal anti-inflammatory drugs (NSAIDs) alone does not seem to increase the risk of spinal hematoma after epidural blockade. A number of case series amounting to many thousands of patients receiving these drugs preoperatively and subsequently given spinal or epidural anesthesia without complication attest to the safety of this combination [63]. However, COX-2 selective inhibitors should be considered as an alternative to conventional NSAIDs in patients receiving other anticoagulants who require centroneuraxial block [64]. On the other hand, neuraxial blockade is contraindicated in the presence of newer antiplatelet agents such as clopidogrel (an adenosine diphosphate receptor antagonist) and ticlopidine (a thienopyridine). Clopidogrel induces a maximum 60 % inhibition of platelet function and this can be achieved after a single dose [78]. This platelet effect is irreversible and recovers completely 7 days after discontinuation [79]. Although a case of spinal hematoma occurring after a 7-day clopidogrel-free interval has been reported, the patient had other risk factors [80]. Clopidogrel can usually be restarted within 24 h of the neuraxial intervention (e.g., catheter removal) [78]. Platelet function monitors appear to give limited prognostic information on bleeding but reversal can usually be achieved with platelet administration if required [78].

Intravertebral Abscess and Meningitis

Serious infectious complications happen more frequently than spinal hematoma and greater emphasis should be placed on these. Unfortunately intravertebral abscess often presents late and the classic triad of fever, back pain, and neurological changes is only present in a minority of patients [81]. Fever usually occurs first, followed by back pain and tenderness; progressive neurological signs appear later. The incidence is difficult to define accurately but it is clear that serious neuraxial infection occurs more frequently in the nonobstetric population and presentation is late in some cases [49].

Although intravertebral infection is thought to be most frequently caused by bacterial migration along the catheter [82], other possibilities are colonization from hematogenous spread, contamination of the infusate/delivery system, or directly during the procedure itself by the anesthesiologist's nasal flora [83]. The reported incidence of bacterial colonization of the epidural catheter is as high as 53 % [82]. One study of 205 epidural catheters reported 38 % of patients had positive cultures in the skin surrounding the epidural insertion site and the positive culture rate for the tip section of the catheter

was 17.6 %. Positive skin cultures (odds ratio (OR) 18), transfusion (OR 15), and catheter-related events on the ward, such as accidental disconnection (OR 35), were strong risk factors for tip colonization although no patient had a clinical infection during the 3 months follow-up period [82].

Prognosis after intravertebral abscess and meningitis is better than that reported for spinal hematomas [48, 68], but outcome is no better in anesthesia-related abscesses than in those occurring spontaneously, suggesting our index of suspicion needs to be higher [84]. Many cases occur in patients who are immunocompromised (NB. diabetes mellitus), a relatively high proportion occur after thoracic epidural catheterization and longer duration of use is also a risk factor [81, 85]. In a large retrospective Finnish study, all five cases of epidural abscess occurred with epidural catheters left in situ for more than 3 days [48]. If serious neuraxial infection is suspected, the catheter should be removed and the tip sent for culture. Blood tests including cultures and early imaging should be performed but lumbar puncture should only be undertaken when local abscess has been excluded. Appropriate antibiotics should be administered in consultation with an infectious diseases physician and neurosurgical opinion obtained [86]. In a review by Kindler et al., 80 % percent of patients were treated with surgery, although only 45 % made a full recovery. In selected cases, spinal abscesses were treated successfully with nonsurgical management [85]. Intravenous antibiotics for 3–4 weeks (extending to 8 weeks if there is associated osteomyelitis) is recommended for primary epidural infection [81].

Prevention

There seems to be no doubt that a meticulous aseptic technique will prevent some cases—these precautions are formalized in guidelines produced by professional bodies [86–89]. Removal of jewelry; hand washing with surgical scrub or alcohol-based solution; full barrier precautions including mask, cap, gown, a large drape, and sterile gloves; avoidance of multidose drug vials; and use of bacterial filters for epidural catheters are recommended. Chlorhexidine in 70 % alcohol should be used for skin asepsis and the solution allowed to dry for 30 s before needle insertion [86–89]. Chlorhexidine has superior bactericidal effect as well as faster onset, longer duration of action, and a lower incidence of skin reactions compared to povidine iodine [89]. Chlorhexidine-impregnated discs significantly reduce colonization at the epidural catheter skin entry point [90]. Prophylactic antibiotics are recommended before the block procedure in patients who are suspected to be bacteremic [86], although in our institution neuraxial blockade would be relatively contraindicated in this scenario. Any interruptions to the sterile circuit may increase the possibility of superficial or deep infection [91]. In the event of accidental disconnection from the hub, the epidural catheter should be cut using sterile scissors 20 mm from the exposed proximal end before reconnection [92]. Because duration of catheterization is a risk factor for intravertebral abscess, a discussion of the risk–benefit for continuing the epidural should occur at 3 days, preferably involving the clinician who placed the catheter, along with a change of the infusate set and bacterial filter [81]. It is strongly advised that large volume infusate bags prepared commercially or in the hospital pharmacy according to International Standards Organization (ISO) criteria are used instead of epidural solutions prepared on the ward [81, 91].

As is the case for spinal hematoma, the clear message from the literature is that a high index of suspicion (including checking the site regularly) is important, particularly in patients with a source of infection or immunosuppression from any cause. There may be a very long interval between the procedure and onset of signs—early diagnosis is crucial because outcome is related to duration and degree of neurologic impairment at the time of surgery. Poor prognosis is also associated with advanced age, with every decade the likelihood of poor outcome doubles [81].

Spinal Cord Ischemia and Infarction

Patterns of spinal cord injury resulting from inadequate local blood supply are a consequence of the anatomic arrangements (Fig. 14.2). The anterior two-thirds of any segment of the spinal cord are supplied by the single anterior spinal artery. This artery receives its blood supply from small paired segmental vessels arising from three distinct aortic origins with poor vertical anastomoses between the cervical, thoracic, and lumbar territories, although there is considerable anatomic variation. The largest of these is usually the radicularis magna (artery of Adamkiewicz), entering on the left between T8 and L3. Damage to this artery from any cause (and needle damage to vessels traversing the intervertebral foramen is possible) can lead to ischemia in the entire lumbar cord. The midthoracic region comprises a watershed area of the cord and is also thought to be particularly vulnerable to hypoperfusion.

Usually causation is multifactorial—age, hypotension, and intraoperative positioning seem to be especially important (Table 14.8) [93, 94]. In patients with vascular disease, proactive management of perioperative hypotension will reduce the risk of cord ischemia. This is imperative in elderly patients undergoing major abdominopelvic surgery in hyperlordotic or 'jack-knife' operating positions—especially when general anesthesia is combined with an epidural technique [49]. The NAP3 audit undertaken in the United Kingdom reported that inappropriate lower limb motor block postoperatively was a common presentation, MRI may be inconclusive early, and the prognosis of spinal cord infarction was universally poor [49].

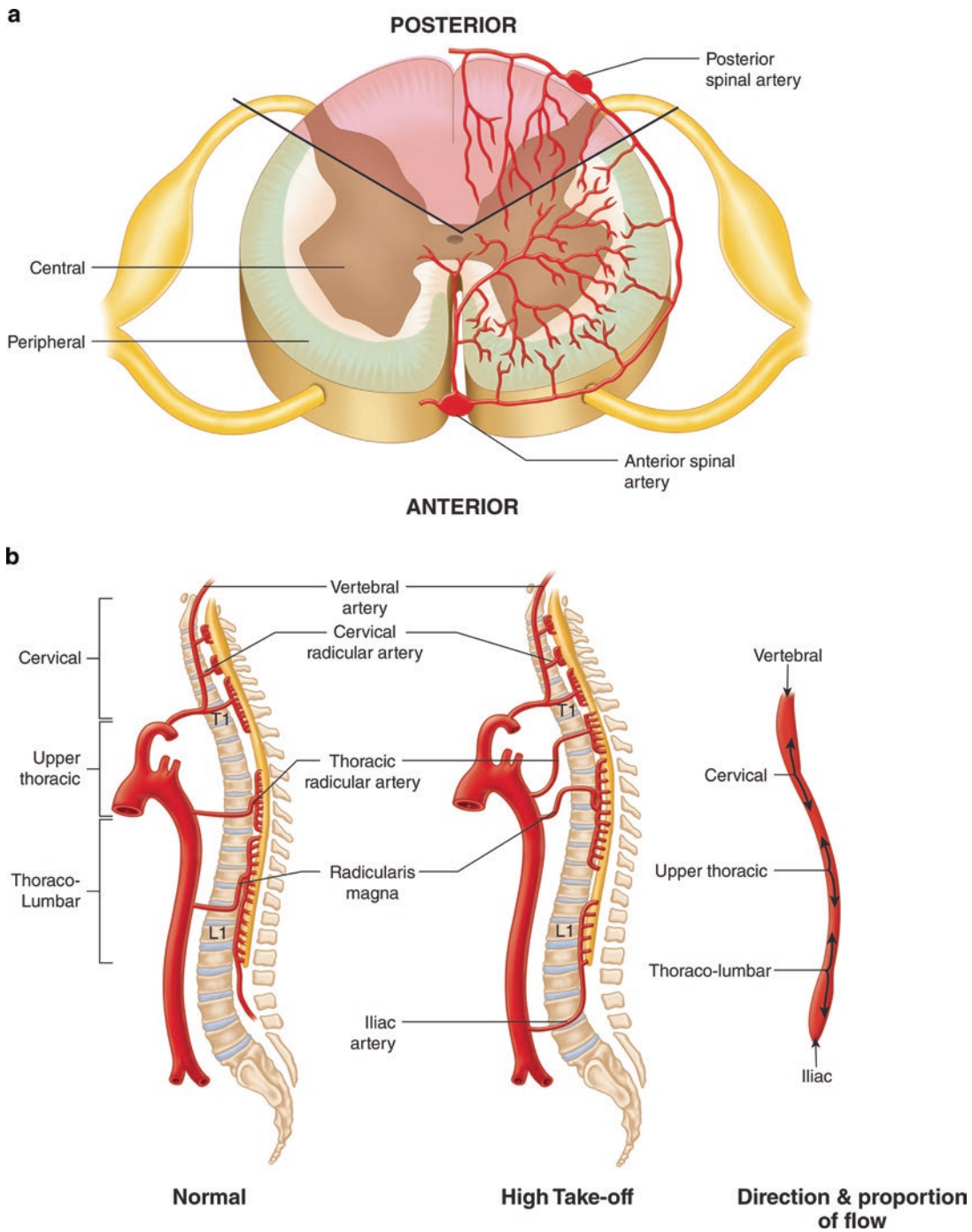

Fig. 14.2 (**a**) Horizontal section of spinal cord showing territory supplied by anterior and posterior spinal arteries. (**b**) Vertical arrangement of three zones of aortic blood supply to the anterior spinal artery. High take-off occurs in around 15 % of cases (From Cousins MJ, Bridenbaugh PO, eds. Neural Blockade in Clinical Anesthesia and Management of Pain. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1998:212. Reprinted with permission from Publisher.)

Spinal Cord and Nerve Root Trauma

Temporary neuropathy related to incomplete single nerve root damage is the most common neurological complication of all and resolves within a year. Generally, only a sensory deficit develops which often follows the same distribution as the painful paresthesia reported during the procedure, although occasionally paresis is seen (most frequently foot drop) [40]. Electromyography and MRI are helpful to aid localization of the lesion [62]. Conversely, the consequences of cord injury or intracord injection can be disastrous.

The level of termination of the spinal cord assumes roughly a normally distribution. A few percent of spinal cords end at L2/3 interspace and around half at or below the L1/2 interspace [95]. With this in mind, spinal and needle-through-needle CSE anesthesia should be performed at or below L3/4, especially as Tuffier's line (the line between the iliac crests) is itself an inaccurate surface landmark, and avoid the common practice of going up a space in the event of difficulty [96–98]. The risk of damage to the conus medullaris may be greater with a needle-through-needle CSE technique than with single-shot spinal anesthesia because of tenting of the dura by the Tuohy needle and potential for overshoot [98]. Accidental trauma to the cervicothoracic cord (including syrinx formation) during thoracic epidural insertion is rare but common themes include degenerative spinal disorders and difficult insertion under general anesthesia [99]. It is widely held that CNB should be performed awake where possible because of the strong correlation between radicular symptoms occurring during the procedure and persistent neuropathy [100].

Table 14.8 Important contributors to anterior spinal artery syndrome

Atherosclerosis
Hypotension
Positioning (e.g., lithotomy; hyperlordotic)
Aortic surgery and cross-clamping
Local vasoconstrictors
Embolism (thrombus, fat, air, bacterial)
Dissecting aortic aneurysm
Vertebral column surgery

Arachnoiditis and Neurotoxicity

Arachnoiditis is a rare cause of cauda equina syndrome after neuraxial anesthesia. The presentation is often catastrophic; the patient complains of a painful radiculopathy immediately after the block, usually bilateral and similar in character to the syndrome of transient neurologic symptoms, and often accompanied by bladder dysfunction. Progressive sensorimotor loss in the lower extremities develops as a marked adhesive inflammatory process involves the meninges, cord, and spinal roots. Subsequent intrathecal scarring impedes subarachnoid cerebrospinal fluid pathways and disrupts vascular supply. The clinical course often ends in complete paraplegia, hydrocephalus requiring ventriculo-peritoneal shunting, and occasionally death. The MRI features are tethering of the cord with either clumping of the adherent cauda equina roots peripherally or an 'empty thecal sac' sign (Fig. 14.3) [101].

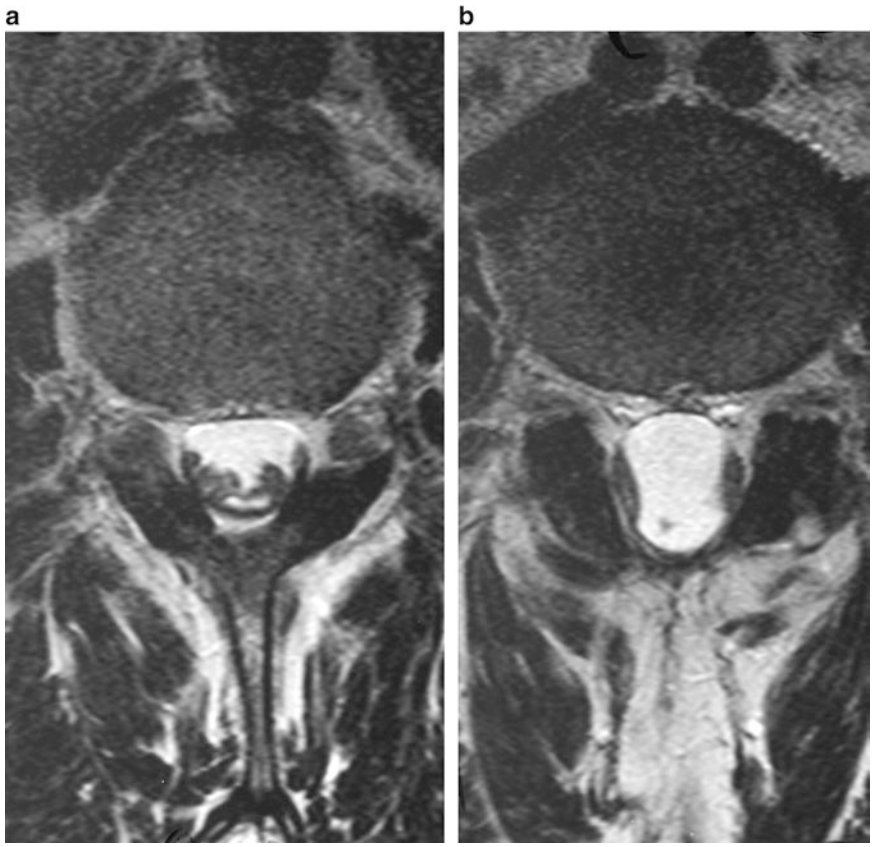

Fig. 14.3 (**a**) Axial T2-weighted MRI through the lumbar spine demonstrates moderately thickened nerve roots with an abnormal distribution within the thecal sac compatible with "clumping," typical of Type 1 arachnoiditis. (**b**) Axial T2-weighted MRI through the lumbar spine demonstrates thickened nerve roots that are peripheral displaced and adherent to dura giving the "empty thecal sac sign," typical of Type 2 arachnoiditis (Courtesy Dr. A. Hope, Auckland City Hospital.)

Table 14.9 Causes of arachnoiditis

Idiopathic
Infection (e.g., meningitis)
Spinal trauma, surgery, hemorrhage
Foreign substances introduced into the epidural and subarachnoid spaces
Intentional
Myelographic contrast agents
Corticosteroids
Antibiotics
Local anesthetic drugs
Accidental
Skin antiseptic
Detergents
Drug error
Unknown contaminant

Etiology

There are numerous causes of inflammation and adhesive scarring of the pia and arachnoid mater, some of which may occur coincidentally with regional anesthesia (Table 14.9). Although the link may be tenuous in some cases, inherent in centroneuraxial block is the risk of both drug error and accidental introduction of contaminants near the spinal cord and meninges. Arachnoiditis must always be included in the differential diagnosis for progressive cauda equina syndrome and it is critical that processes in such cases are examined methodically for lessons on safety.

There have been multiple cases of severe arachnoiditis linked to chlorhexidine in the last few years, invariably resulting in a devastating outcome for the patient as well as ongoing liability for the hospitals involved [101–103]. Meticulous care must be taken to avoid antiseptic contaminating the equipment or injectate being used for centroneuraxial block. The clinician should apply chlorhexidine separately (ideally by spray or single-use swabstick), away from the covered procedure tray and then remove it from the vicinity before preparing the medication for epidural injection [89, 101, 104]. It is recommended that 0.5 % instead of 2 % chlorhexidine in 70 % alcohol be used because antimicrobial efficacy appears equivalent between the two strengths and a smaller volume of the more concentrated solution could precipitate arachnoiditis [89].

Evidence from animal studies indicates that local anesthetics are neurotoxic in a concentration-dependent manner [105]. Although this is more relevant to single-shot and continuous spinal anesthesia than epidural catheter techniques [25], it is likely that existing polyneuropathy related to diabetes or other diseases confers a susceptibility to local anesthetic neurotoxicity [106–108]. Patients should always be told to report neurologic symptoms that develop after they go home.

Wrong Drug and Wrong Route Errors

Despite underreporting of iatrogenic medical errors because of medicolegal implications, wrong-drug case reports appear regularly [109]. Unfortunately, these include fatal events where a large dose of local anesthetic is accidentally administered into the intravascular or intrathecal compartments [48, 49]. Ampoules and bags intended for epidural and intravenous infusion may be very similar in size, shape, and labeling. Furthermore, they are often stored together and used concurrently [110]. In the UK NAP3 audit published this year, there were 11 cases of wrong route error—one of which resulted in death. Of six cases where bupivacaine intended for epidural use was given intravenously, five occurred in the obstetric setting [49]. In Australia, one parturient was injected with an estimated 8 mL of chlorhexidine to establish a labor epidural when the colorless solution in a receptacle on the procedure tray was confused for local anesthetic [103, 104]. Postoperatively, epidural catheters expose patients to the risk of wrong drug via the neuraxial route for several days—potassium chloride seems to be a particular culprit [111–114]. It is also possible for the catheter to be misplaced in a vessel or migrate to the intravascular compartment.

In the United Kingdom, best practice guidance for epidural injections and infusions has been produced by the National Patient Safety Agency [115], to reduce the risk of wrong route administration error but compliance and uptake is variable [110]. Infusion bags, catheters, and giving sets intended for epidural use should be stored separately from intravenous fluids and clearly labeled to minimize the risk of misconnection with a designated color (e.g., yellow) [30, 115]. Dedicated RA infusion pumps should be used with programmed limits for bolus administration and infusion rate [30]. Since 2013, non-interchangeable connectors for regional, spinal, and epidural anesthesia have been mandated in the United Kingdom although this does not preclude drawing the wrong drug up into the syringe [116]. Even with measures such as these, considerable responsibility lies with the anesthetist who places the catheter and subsequently delegates care to nursing staff.

Local Anesthetic Systemic Toxicity (LAST)

In a regional audit conducted in the United Kingdom, Jenkins and colleagues reported that the incidence of premonitory symptoms indicating suspected intravascular injection was 1 in 5000 labor epidurals and this is consistent with previous studies [31]. The improved cardiovascular and central nervous system toxicity profile of ropivacaine and levobupivacaine compared to racemic bupivacaine suggests that these agents are preferable for epidural administration [2]. However, maximum safe doses should always be observed, taking into account patient age and comorbidities.

Incremental, slow injection will provide a greater margin of safety because toxicity of a rapidly administered large IV bolus of any long-acting local anesthetic agent will render theoretical differences found under experimental conditions irrelevant [2]. When LAST is suspected or recognized it must be treated proactively because it is rapidly progressive when severe and a protocol for management of should be immediately available including use of lipid emulsion therapy (e.g., Intralipid®). The flowchart published by the Association of Anesthetists of Great Britain and Ireland has been endorsed by the Australian and New Zealand College of Anaesthetists [117], and ASRA has also produced a practice advisory [118], and checklist [119], for managing LAST. For more details on this topic, please refer to Chap. 3

Special Populations: Obstetric

The obstetric population represents a relatively homogeneous group at low risk of serious neurologic complications of epidural blockade [120]. Furthermore, neurologic deficits after childbirth may have many causes and there is often no definite link between an adverse event and the epidural [121]. Neuropraxia, which results from direct pressure applied by the fetal presenting part to the lumbar plexus as it traverses the pelvic brim during prolonged or obstructed labor, is a much more common cause of temporary deficit than anesthetic procedures [122]. An analysis published in 2006 with a denominator of 1.37 million obstetric blocks concluded that serious neurological complications are rare, occurring in 1 in 70,000 procedures, although temporary neurological injury (< 1 year) from presumed root lesions was sustained in 1 in 3900 cases [55]. Similarly, a survey of 300,000 obstetric epidurals performed in France over 5 years reported that the incidence of transient radiculopathy was 1 in 3277 [123]. In a multicenter retrospective survey of 505,000 obstetric epidurals [124], there were only five serious complications and only one of 38 single neuropathies lasted longer than 3 months. More recent major studies from the United States, Sweden, and the United Kingdom have confirmed that centroneuraxial block in parturients appears relatively safe [25, 49, 125].

Serious complications probably occur less frequently than in the nonobstetric (e.g., perioperative) setting because of the normal anatomy and intravertebral compliance in young, healthy subjects and relatively short duration of epidural catheterization. Data from the ASA Closed Claims database also supports the impression that significant deficits are less common in the obstetric population [60], although nerve injury was the leading maternal claim [126]. A meta-analysis published in 2006 reported that deep epidural infection occurred in less than one in 100,000 obstetric epidural procedures [55]. Meningitis is also rare in the obstetric setting and more likely to occur with intrathecal than epidural blockade [120].

The NAP3 audit from the United Kingdom highlighted that wrong route error occurs more commonly in the obstetric setting than in other areas of practice [49]. A large survey in the same country reported that over a quarter of maternity units had some experience of wrong route error (mostly accidental connection of local anesthetic solution to an intravenous line) [110]. The NAP3 audit from the United Kingdom also highlighted that presumed postdural puncture headache which does not resolve may rarely be a sign of intracranial subdural hematoma or meningitis [49]. Subdural hematoma is a known complication of dural leak and CT scan is recommended if headache is atypical or severe, persists after a second epidural blood patch (which is required in 10 % of cases) or if the presentation is late [125]. If the CT scan is negative and infective meningitis is suspected, lumbar puncture for cerebrospinal fluid analysis should be performed.

Inadvertent intrathecal injection of epidural solution occurs in approximately 1 in 3000 epidural procedures [31]. Although the incidence of high block is around 1 in 5000 cases, total spinal occurs in less than 1 in 10,000 parturients [31, 125]. Most unrecognized spinal catheters occur in the labor suite and risk factors for high block include obesity and intrathecal blockade after a failed spinal or epidural anesthetic [125]. Although high block may occur after an apparently normal test dose [126], routine testing of epidural catheters for intrathecal or intravascular placement is recommended—especially in a remote environment such as the labor suite where resuscitation is likely to be difficult.

Special Populations: Pediatric

There is good evidence for the use of continuous epidural analgesia in major pediatric surgery but unsurprisingly there are fewer studies of pediatric populations [127]. An audit of over 10,000 pediatric epidurals from the United Kingdom reported five serious complications, of which only one was permanent [128]. With respect to pediatric thoracic epidurals, a lack of statistical power limits the ability to draw conclusions [129]. The majority of centroneuraxial blocks in children performed in the United Kingdom and France are single-shot caudal anesthetics [49, 130]. Large surveys of pediatric caudal anesthesia have detected no permanent neurological injuries although there are case reports implicating caudal anesthesia in a spectrum of other complications [49, 131]. Dosing regimens for children must be carefully adapted for weight to minimize the risk of local anesthetic toxicity, especially in infants less than 3 months old. Local anesthetic spread is extensive in infants and block height should be monitored carefully [29].

Special Populations: Chronic Pain

Although most epidurals performed for chronic pain indications are single-shot injections, when a catheter is sited it is likely to remain for a long period. In a pooled analysis of 4628 chronic pain patients who had an epidural catheter in situ for at least 7 days, the deep infection rate was 1.2 % and among a subgroup of cancer patients with long duration catheters, the risk was one in 35 [132]. Although no serious complications were identified among 28,000 epidural blocks performed for chronic pain indications in a recent large prospective audit, the importance of careful technique with meticulous asepsis, availability of resuscitation equipment, and follow-up were highlighted [49]. A large retrospective study from Finland, on the other hand, reported that five severe complications (including three infectious complications) and one late fatality occurred among 12,000 epidurals for chronic pain [48]. The American Patient Safety Foundation has also highlighted the risk of spinal cord trauma and accidental intra-arterial injection during epidural steroid injection [133]. These procedures should ideally be performed awake or under light sedation.

Summary

Epidural analgesia (or CSE) remains the gold standard for labor pain relief and a valuable option for analgesia after major surgery, but the decision to proceed must be made after risk assessment on an individual patient basis. Practice points which might help to make our epidural procedures as safe as possible are presented in this chapter and complication rates should improve by incorporating these measures. There are some reassuring data emerging, but we need to maintain vigilance. As with all anesthetic procedures, the safety of epidural blockade reflects the psychomotor skills and judgment of the operator, as well as the possibility of human or system error.

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Spinal Anesthesia: Safe Practice and Management of Adverse Events

15

Pekka Tarkkila

Key Points

- Spinal anesthesia has been used effectively and safely for over 100 years, but its use should still be considered only after careful evaluation of each eligible patient.
- It is relatively simple to perform but requires an understanding of relevant anatomy and physiology in order to achieve safe and efficient anesthesia for the surgery.
- Spinal failures do occur and may be related to patient, equipment, or other specific factors.
- The degree and duration of spinal anesthesia can be modulated by the dose and baricity of the local anesthetic.
- Catheter techniques may be useful in certain circumstances
- Hemodynamic complications, including hypotension and bradycardia, may occur after spinal blockade; treatment with sympathomimetics, preloading with fluids, or even adjustment of patient positioning usually address these problems.
- Urinary retention is a common complication following spinal anesthesia; careful supervision of bladder function is important to prevent long-term bladder dysfunction.
- Thorough documentation of the spinal procedure can help determine the source of radiculopathy following spinal blockade. Early detection of nerve damage can help prevent long-term sequelae.
- Etiology of transient neurologic symptoms (TNS) is poorly understood and results from a variety of factors.
- Postdural puncture headache occurs as a result of CSF leakage through the dura at the site of puncture; symptoms are relieved by lying horizontally, and an epidural blood patch may speed recovery.

P. Tarkkila, MD (✉)
Department of Anesthesia and Intensive Care Medicine, Töölö Hospital/Helsinki University Hospital, Helsinki, Finland
e-mail: pekka.tarkkila@hus.fi

Introduction

Centennial celebrations to commemorate the introduction of spinal anesthesia occurred in 1998. Spinal anesthesia was introduced toward the end of the of the nineteenth century, utilized throughout the twentieth century, and is still being used in the twenty-first century, and we have no doubt that its use will continue into the foreseeable future, as it remains the centerpieces of modern regional anesthesia. The basic technique has changed very little since it was first described. August Bier from Germany was the first to publish a report of the first successful spinal anesthesia with cocaine on his friend and assistant Hildebrandt. Since then, spinal anesthesia has gained a worldwide popularity and an impressive safety record. However, the history of complications of spinal anesthesia is as old as the method itself [1]. The very first spinal anesthetic was followed by postdural puncture headache (PDPH) as August Bier and Hildebrandt both developed a headache after their experiment, that at least with Bier himself was posture related. The wine and cigars consumed during the celebration of a successful experiment may have augmented the development of headache.

In the early days of spinal anesthesia, it was claimed to be a safe method of anesthesia and was used successfully even in operations on the head, neck, and thorax with low mortality [2]. After initial great popularity, some tragic events occurred with spinal anesthesia, at a time when major advances were being made in inhalation anesthesia that almost made this technique obsolete, at least in United Kingdom. The most famous of these tragedies was the Woolley and Roe case in which two patients, in adjoining operating rooms, became paraplegic following spinal anesthesia for relatively minor surgery [3]. It is probable that this tragedy was caused by contamination of the spinal needles or syringes during the sterilization process [4]. In the 1950s, the reputation of spinal anesthesia was restored, mostly as a result of several reports from Vandam and Dripps involving

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_15

more than 10,000 patients [5]. They showed that spinal anesthesia was a safe technique and only rarely causes serious morbidity and mortality.

With modern equipment and developed techniques, this old anesthesia method remains an important and cost-efficient part of modern anesthesiology. With advanced knowledge of mechanisms, this versatile anesthesia method can be adjusted according to our needs. In the last decades, there have been many changes in the treatment of patients and spinal techniques. More and more operations are being performed on an ambulatory basis, and spinal anesthesia methods have been adjusted to meet the demands of a busy environment. The focus of complications with these patients has changed accordingly. Mortality or major complications are not usually an issue with short-stay patients, but we should be able to provide them fast track—anesthesia without side effects and with a high degree of patient satisfaction. However, we should be able to use spinal anesthesia safely for major operations in elderly patients with numerous comorbidities.

Technique

Prior to performing spinal anesthesia, the goal of preoperative assessment is similar to all anesthesia to techniques which is to determine all possible risk factors for complications. Laboratory investigations should not be ordered on a routine basis. The patient's medical status, the type of operation, or the drug therapy should be taken into consideration. ASA one or two patients without medical problems may not need more than a quick review. The preoperative evaluation should be performed in good time, if possible, in order to have the opportunity to optimize comorbidities.

The preoperative evaluation is basically similar regardless of the anesthesia method chosen. However, abnormalities of coagulation, whether the result of the patient's comorbidity or administration of drugs and the consequent hemorrhagic risks associated with spinal anesthesia should be taken into special consideration. There are many different guidelines presented by different societies, national authorities, hospitals and recommending when the spinal puncture can be performed safely in these patients. If the anesthesiologist decides to deviate from these guidelines, the patient with capacity should be given all the information he/she needs to make an informed choice. Also, it may be wise that an 'experienced anesthetist' should perform the procedure. It is likely that an experienced regional anesthetist will need fewer attempts to block success, and it is likely that the complications related to bleeding are in part related to the number of attempts at a block [6]. All equipment for spinal anesthesia should be collected and be ready to use before the procedure is started. Also the equipment for resuscitation and airway management should be immediately available. Before induction of spinal anesthesia, the first part of WHO Safe Surgery Checklist or similar ("sign in") is nowadays mandatory. After the appropriate monitors have been applied, the patient can be positioned for the block. The details of the spinal block are recorded either in the paper chart or into the electronic Anesthesia Information Management System.

Aseptic technique for spinal puncture requires that hands are washed thoroughly; the anesthesiologist wears cap, mask, and sterile gloves, and uses a large sterile drape. It remains controversial which antiseptic solution is most efficient and safest to use on the skin before spinal puncture. Chlorhexidine in alcohol might be the optimum skin preparation solution because in many studies it has been shown to be superior, reducing surgical site infections compared with other disinfectants. As both alcohol and chlorhexidine are neurotoxic, the anesthesiologist should be careful not to contaminate gloves or needles with the disinfectant. The solution must be allowed to dry before the skin is palpated or punctured so that no antiseptic solution is introduced into spinal canal.

Failure of Spinal Anesthesia

Failure of spinal anesthesia is one of the most embarrassing complications for the patient and the anesthesiologist. Spinal anesthesia, in contrast to many other regional anesthesia methods, has a clear end point indicating correct needle placement [free flow of cerebrospinal fluid (CSF) from the needle]. Despite this, there is, in common with other regional anesthesia techniques, a potential risk for failure. Correspondingly, even general anesthesia may be associated with failure, as patients can be aware of the surgical operation during anesthesia. Failure rates may be reduced by proper selection of patients, timing, and the skill of the anesthetist. The reasons for failure in spinal blocks are in most cases related to technical factors rather than to the anesthetic agent used [7].

The incidence of failures with spinal anesthesia varies in different studies, ranging from 3 % to 17 %. In some smaller studies, failure rates even up to 30 % have been reported. Spinal anesthesia can be classified as failure if the surgical operation cannot be performed without the addition of general anesthetic or an alternative regional block. The subarachnoid space may be impossible to locate or the needle may move during the injection of the anesthetic. The spinal puncture may be difficult to perform due to abnormal anatomy, obesity, or poor cooperation or pain experienced by the patient. Preprocedure ultrasound examination might decrease the number of passes and attempts needed to enter the subarachnoid space, at least with paramedian spinal anesthesia [8]. One cannot give unambiguous instructions, when the spinal technique should be abandoned and the anesthesia plan changed.

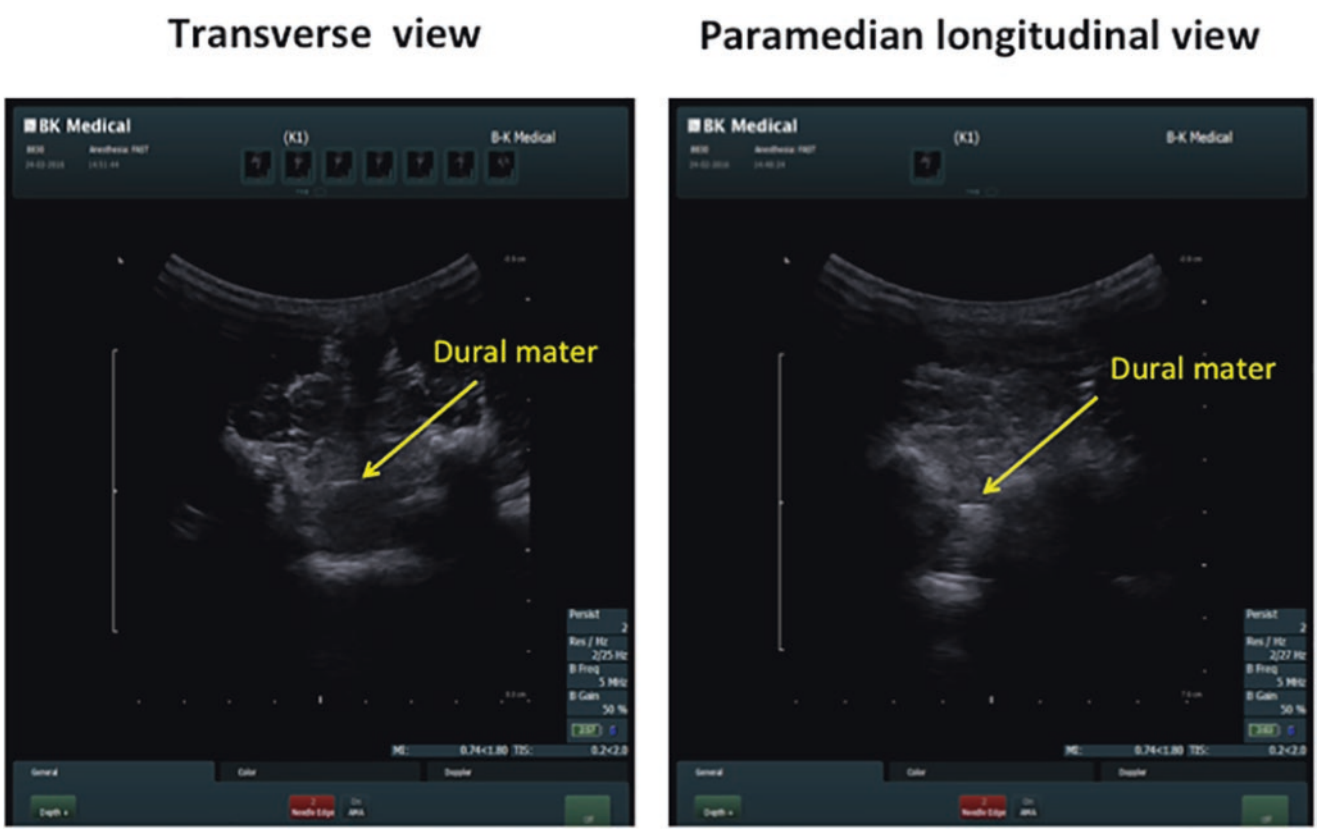

Fig. 15.1 Transverse and paramedian longitudinal ultrasound images at lumbar region

Regardless, if the spinal puncture does not succeed after several attempts and especially if many paresthesias have been elicited the anesthesiologist should change the planned anesthesia. Good clinical judgment and cooperation with the patient are essential in order to prevent complications associated with multiple punctures in in close proximity to spinal canal and nerve roots. Ironically quite often the patients that are at risk for unsuccessful spinal puncture tend to be poor candidates for general anesthesia as well (Fig. 15.1).

The anesthesiologist should make the best possible effort to prevent unsuccessful spinal anesthesia by careful technique which ensures free flow of CSF before injection of the local anesthetic and good fixation of the spinal needle during the injection to prevent needle movement. In some cases, failure occurs despite free-flowing CSF flow from the needle hub, and this may be caused by the needle entering an arachnoid cyst that is not in direct communication with the subarachnoid space. The Sprotte needle has been associated with higher failure rates, and this may be because the side hole is large and elongated and located distal from the tip. However, in a prospective study, comparing failure rates between Sprotte or Quincke needles, there was no difference noted [9].

The use of low-dose spinal anesthesia for day-case surgery has gained popularity in the recent years. Interestingly, the use of low-dose spinal anesthesia (bupivacaine less than 10 mg) for day-case surgery has not increased the risk for failure if a proper technique has been used [10–12]. Usually low-dose spinal anesthesia is used for surgery of the lower extremities although it can be used also for bilateral anesthesia, such as for tubal ligation. With low dose, selective, or unilateral spinal anesthesia, the proper technique is even more important that with higher doses. The position of the patient (sitting, lateral decubitus position, prone) is essential with respect to baricity of local anesthetic. The maintenance of the selected position affects the spread of anesthesia. With conventional (larger) doses of local anesthetics, even a longer period spent in the lateral decubitus position does not prevent bilateral block [13].

With hyperbaric bupivacaine and ropivacaine, the sensory level of analgesia can be modified with repositioning of the patient after local anesthetic injection. With isobaric bupivacaine, the sensory level of anesthesia is difficult to predict and more difficult to modify after puncture. However, there is a tendency for a higher level when a higher lumbar interspace for spinal anesthesia is used [14].

Hemodynamic Complications

Cardiovascular side effects are common during spinal anesthesia, hypotension being the most common [15, 16]. Decrease of blood pressure can be considered a normal physiologic effect of spinal anesthesia. In some cases, the decrease can be so severe that it can be considered a complication. There is no agreement at which level the low blood pressure should be treated. Clinical judgment is needed to decide when an individual patient needs treatment for a low blood pressure.

Hypotension

The reported incidence of hypotension during spinal anesthesia varies from 0 % to more than 50 % in nonpregnant patients. Pregnant patients are more susceptible to hypotension with incidences ranging from 50 % to more than 90 %. The high variation among publications may be explained by different methods used to prevent hypotension. Systolic blood pressures less than 85–90 mmHg or a decrease of more than 25 %–30 % from the preanesthetic value have been used to define hypotension [15, 16].

Hypotension during spinal anesthesia results principally from the preganglionic sympathetic blockade. Systemic vascular resistance decreases as a result of a reduction in sympathetic tone of the arterial circulation. This leads to peripheral arterial vasodilatation, the extent of which depends on the number of spinal segments involved. Other theories are proposed to explain hypotension during spinal anesthesia, among them: (1) Direct depressive circulatory effect of local anesthetics, (2) relative adrenal insufficiency, (3) skeletal muscle paralysis, (4) ascending medullary vasomotor block, and (5) concurrent respiratory insufficiency. Hypotensive effects of spinal anesthesia are exaggerated in advanced pregnancy because of aortocaval compression caused by the gravid uterus. Nerve fibers in pregnant patients are also more sensitive to the effect of local anesthetics [17], probably because of chronic exposure of progesterone altering the protein synthesis in nerve tissue [18].

Risk factors for hypotension include older patients, patients with peak block height greater or equal to T5, and patients undergoing combined spinal and general anesthesia [15, 16].

Bradycardia

Loss of sympathetic input to the heart, leaving vagal, parasympathetic innervation unopposed, and a decrease in cardiac preload are the main reasons for bradycardia during spinal anesthesia. The extent of sympathetic blockade is not always comparable with the sensory level [19], and this may be the reason why cardiovascular complications do not always occur despite high sensory levels [20]. Younger patients and those with sensory levels above T6 are more susceptible to bradycardia during spinal anesthesia [21]. Baseline heart rates less than 60 beats/minute and current therapy with beta-adenergic-blocking drugs also increase the risk for bradycardia [15].

The decrease in venous return to the heart leads to decreased stretch to the right side of the heart leading to decreased heart rate (Bainbridge reflex). Also a paradoxical form of Bezold–Jarisch reflex has been thought to occur rarely during spinal anesthesia leading to severe bradycardia and asystole [15]. During spinal anesthesia, a sudden decrease in ventricular volume (an empty ventricle) coupled with a vigorous ventricular contraction leads to activation of the mechanoreceptors, and subsequently increased vagal tone and decreased sympathetic activity as the heart perceives itself to be full [22]. Other possible mechanisms of bradycardia during spinal anesthesia include excessive sedation, preexisting autonomic dysfunction, heart block, vasovagal reaction [23], or athletic heart syndrome [24].

Treatment and Prevention of Hypotension and Bradycardia

Preventive procedures before spinal anesthesia are more frequently used for pregnant patients because these subjects are more susceptible to the hypotensive effects of spinal anesthesia. A decrease in blood pressure lasting more than 2 min may have a deleterious effect on the neonate [25].

Relative hypovolemia caused by spinal anesthesia may be successfully prevented either with sympathomimetic medication or by preloading with crystalloid or colloid. Even leg wrapping has been used with good success in patients scheduled for cesarean delivery [26]. Crystalloid preload has often been used but it does not seem to lessen the cardiovascular complication frequency even with elderly patients in good health [27]. However, if the patient is preoperatively hypovolemic, the hypovolemia must be corrected before establishing the block.

The most common sympathomimetic drugs used in the prevention and treatment of hypotension are ephedrine (combined alpha and beta effects, with predominant beta-adrenergic effects) and etilefrine (which has combined alpha and beta effects). They can be both infused according to blood pressure response or given as a boluses and have quite similar effects on patients. Methoxamine and phenylephrine (pure alpha-adrenergic agonists) are other sympathomimetics used. Ephedrine is mostly used for pregnant patients because it restores uterine flow despite the increase in maternal blood pressure [28]. Small increments of phenylephrine have also been considered safe for the fetus. The use of phenylephrine may be indicated if the increase in the heart rate in the mother is not tolerated. Because bradycardia during spinal anesthesia is most often caused by decreased preload to

the heart, restoring the blood pressure is the best treatment for bradycardia. Stimulating an empty heart with atropine may be deleterious, especially if the patient has coronary disease. Increased workload (tachycardia) increases the oxygen demand of the heart without increasing the oxygen supply.

Whenever serious hemodynamic instability occurs with spinal anesthesia, it is most likely attributable to some interference with the venous return. Therefore, one of the most important steps to take in the treatment is to check the position of the patient and if not optimal place the patient in a position that will enhance venous return. One should also make sure that the surgeon is not interfering with the venous return during surgical manipulation. In the words of one the great masters of spinal anesthesia, Professor Nicholas Greene, "the sine qua non of safe spinal anesthesia is the maintenance of venous return."

Nausea and Vomiting

Nausea and vomiting are quite rare during spinal anesthesia and most often associated with hypotension. Therefore, nausea in these cases is alleviated in combination with the successful treatment of hypotension and does not need any specific treatment itself. The other suggested mechanisms for nausea during spinal anesthesia are cerebral hypoxia, inadequate anesthesia, and traction-related parasympathetic reflexes provoked by surgical manipulation. Female gender, opiate premedication, and sensory level above T6 have all been shown to be significant risk factors for nausea during spinal anesthesia [15]. A history of motion sickness has also been associated with nausea during spinal anesthesia [16].

Cardiac Arrest

The incidence of cardiac arrest during spinal anesthesia has been between 2.5 and 6.4 per 10,000 anesthesias [29, 30]. Cardiac arrest is most often associated with a perioperative event such as significant blood loss or cement placement during orthopedic surgery. It is often difficult to determine whether surgical, anesthesia, or patient factors are the most significant leading up to the problem. Fortunately, the frequency of cardiac arrests has decreased significantly over the last decades [29]. The reason for this decrease is not clear. The awareness of this potential complication may have increased after Caplan and colleagues [31] reported 14 cases of sudden cardiac arrests in healthy patients who had spinal anesthesia for minor operations. Also, the use of pulse oximetry has become a standard during spinal anesthesia, although no randomized studies have been or will be done to confirm the effectiveness of pulse oximetry with this respect. Patients should be monitored during spinal anesthesia as vigilantly as during general anesthesia and side effects should be treated aggressively as soon as possible to prevent life-threatening complications. Cardiac arrest during neuraxial anesthesia has been associated with an equal or better likelihood of survival than a cardiac arrest during general anesthesia [29].

Urinary Retention

There is a high incidence of micturition difficulties postoperatively. Acute urinary retention can follow all types of anesthesia and operations. The etiology of postoperative urinary retention involves a combination of many factors, including surgical trauma to the pelvic nerves or to the bladder, overdistention of the bladder by large quantities of fluids given intravenously, postoperative edema around the bladder neck, and pain- or anxiety-induced reflex spasm of the internal and external urethral sphincters [32, 33]. Urinary retention is more likely to occur after major surgery and with elderly male patients. Opiates and confinement to bed may also be likely explanations for the development of urinary retention after surgery. The type of anesthetic and the management of postoperative pain may have little effect on the occurrence of postoperative urinary dysfunction [32].

Disturbances of micturition are common in the first 24 h after spinal anesthesia. There is a higher frequency of these disturbances after bupivacaine than lidocaine spinal anesthesia [34]. After administration of spinal anesthesia with bupivacaine or tetracaine the micturition reflex is very rapidly eliminated. Detrusor muscle contraction is restored to normal 7–8 h after the spinal injection. On average, patients recover enough motor function to be mobilized 1–2 h before the micturition reflex returns. Full skin sensibility is restored at the same time or slightly before patients are able to micturate. To avoid protracted postoperative bladder symptoms, careful supervision of bladder function is of great importance in patients receiving spinal anesthesia with long-acting anesthetics [35]. A single episode of bladder over distention may result in significant morbidity. Overfilling of the bladder can stretch and damage the detrusor muscle, leading to atony of the bladder wall, so that recovery of micturition may not occur when the bladder is emptied. Patients at risk for urinary retention should be stimulated to void and provided a quiet environment in which to do so. They should be encouraged to sit, stand, or ambulate as soon as possible [32]. A simple ultrasound measurement of the largest transverse diameter using a standard ultrasound device provides valuable aid in the management of patients at risk of urinary retention postoperatively [36]. Expedient catheterization when needed and the prophylactic placement of indwelling catheters in patients with previous disturbances are recommended [32, 34].

Urinary Retention and Outpatient Surgery

The reported frequency of urinary retention after intrathecal administration of opioids varies considerably. The risk for urinary retention is increased with higher doses of opioids or local anesthetics. Many patients who receive opioids intrathecally are usually catheterized because they are high-risk patients undergoing major surgery. On the other hand, 10–20 μg of fentanyl administered with small-dose bupivacaine for day-case surgery does not seem to increase the risk for urinary retention or prolong the discharge times [37–39]. Small-dose or unilateral spinal anesthesia is associated with smaller risk for urinary retention than conventional methods.

During the past few years, the home discharge criteria have been changed. The routine requirement of voiding before discharge can be considered mandatory only for high-risk patients. These high-risk patients include those with preoperative difficulties in urinating, operation in the perineal area, older men, etc. All patients must receive oral and written instructions before discharge regarding when, where, and who to contact in case of difficulty voiding. A follow-up phone call is recommended for all patients that are discharged before they have voided.

Transient Neurologic Problems

Radiculopathy

Damage to a nerve root can occur during identification of the subarachnoid space or during the insertion of a spinal catheter. Paresthesia with or without motor weakness is the presenting symptom and, while the majority of patients recover completely, a small number may be affected permanently. Although neurologic complications may present immediately postoperatively, some may require days or even weeks to emerge. Should neurologic dysfunction occur, early detection and intervention are required to promote complete neurologic recovery [40]. Documentation of critical data concerning spinal anesthetic technique, such as level of needle placement, needle type, and local anesthetic solution, is an important part of the anesthesia procedure. As demonstrated by the Closed Claim Study database, nerve damage is a major source of anesthetic liability. Therefore, the same consideration must be given to the documentation of prudent regional anesthetic practice as is given to its delivery [41]. Auroy et al. found in their prospective, multicenter study of 40,640 spinal anesthetics and 30,413 epidural anesthetics 19 cases of radiculopathy after spinal anesthesia and five cases of radiculopathy after epidural anesthesia [30]. In 12 of the 19 cases of radiculopathy after spinal anesthesia and in all five cases of radiculopathy after epidural anesthesia, the needle insertion or drug injection was associated with paresthesia or pain. In all cases, the radiculopathy was in the same distribution as the associated paresthesias.

Oblique lateral entry into the ligamentum flavum may direct the needle into the dural cuff region. This may result in direct trauma to a nerve root, with resultant unisegmental paresthesia; such a sign should warn the anesthesiologist not to persist with needle insertion in this position and not to attempt to thread a catheter [42].

To avoid trauma to nerves, careful technique and accurate anatomical knowledge are mandatory. Low lumbar interspace for puncture should be chosen as the spinal cord terminates in normal adults at L1 level although this is variable and it may be as low as L3. It has also been shown that the anesthesiologist quite often estimates the interspace for puncture incorrectly, although this has little clinical significance in most cases. Paresthesia during the insertion of a spinal needle is common with incidences varying between 4.5 and 18 % [43–47]. Fortunately in most cases, no harmful effects occur following paresthesia. In one study, elicitation of a paresthesia during needle placement was identified as a risk factor for persistent paresthesia [41]. If a paresthesia is elicited during spinal needle advancement into subarachnoid space, it is reasonable to draw the needle back 0.5–1.0 mm before injecting the anesthetic in order to avoid direct trauma to a single spinal nerve. One should never continue injecting anesthetic if the patient complains of pain during injection.

Backache

Backache after spinal anesthesia is quite common and rarely a major issue. Incidences of approximately 20 % have been described [9]. The long duration of operation is associated with higher incidence of back problems and the incidence is quite similar with spinal anesthesia as with general anesthesia. Relaxation of back muscles leads to unusual strain and this can lead to postoperative back pain. A pillow under the lumbar area is cheap and effective method to prevent at least some of the back problems.

If unusual back pain is encountered postoperatively, local infection and spinal hematoma should be excluded. Strict aseptic technique during the administration of spinal anesthesia should be used to prevent infectious complications. Local infection can be associated with tenderness, redness, and other usual signs of infection.

The increased use of low-molecular-weight heparins (LMWHs) for thromboprophylaxis has caused concern about the use of spinal anesthesia for these patients. Patients taking preoperative LMWH can be assumed to have altered coagulation, and the needle placement should occur at least 10–12 h after the LMWH dose. The decision to perform spinal anesthesia in a patient receiving antithrombotic therapy

should be made on an individual basis, weighing the small, though definite risk of spinal hematoma with the benefits of regional anesthesia for a specific patient. Alternative anesthetic and analgesic techniques exist for patients considered an unacceptable risk. It must be remembered that identification of risk factors and establishment of guidelines will not completely eliminate the complication of spinal hematoma [48]. Signs of cord compression, such as severe back pain, progression of numbness or weakness, and bowel and bladder dysfunction, warrant immediate radiographic evaluation because spinal hematoma with neurologic symptoms must be treated within 6–8 h in order to prevent permanent neurologic injury.

Transient Neurologic Symptoms (TNS)

For almost 70 years lidocaine was proven to be safe and reliable for spinal anesthesia in a hyperbaric 5 % solution [49, 50]. Hyperbaric lidocaine has been implicated as a causative agent in the cauda equina syndrome, associated with the use of spinal microcatheters [51]. The first report of transient neurologic symptoms (TNSs), termed initially transient radicular impairment or transient radicular irritation (TRI), after single-shot spinal anesthesia with hyperbaric 5 % lidocaine was published by Schneider and colleagues in 1993 [52]. This finding was later confirmed by several other studies [53–58].

TNS are defined as back pain and/or dysesthesia radiating bilaterally to the legs or buttocks after total recovery from spinal anesthesia and beginning within 24 h of surgery. Usually no objective signs of neurologic deficits can be demonstrated [47, 52, 58]. The pain is usually moderate and relieved by nonsteroidal anti-inflammatory agents, but opioids are also often needed [47, 56]. In some cases, the patients state that the transient neurologic pain is worse than their incisional pain [56].

Etiology

The etiology of transient neurologic symptoms has not been elucidated. Even the name of this syndrome is controversial and different suggestions appear in literature every now and then. To avoid confusion, it is not reasonable to change the name of the syndrome until the etiology is clear.

It is surprising that this new syndrome was not recognized until the beginning of 1990s. Lidocaine has been used since 1948 for spinal anesthesia in millions of patients without major central nervous system sequelae. The reason for a new syndrome may be either a change in methods or prior lack of recognition. One reason for the high number of reports of transient neurologic symptoms after spinal anesthesia may be that these symptoms were being sought more aggressively after the first case reports.

The practice of spinal anesthesia has changed significantly in recent decades. Use of premedication before spinal anesthesia has diminished. New small-gauge Quincke and pencil-point spinal needles have been introduced for everyday use. Patients are now ambulated as soon as possible after surgery. It is not clear if any of these changes could be responsible for the establishment of TNSs.

The delayed recognition of this phenomenon may be due to a high underlying rate of nonspecific back pain. A heightened awareness of the potential for local anesthetic-induced neurotoxicity after the recent association of lidocaine and microcatheters with cauda equina syndrome and the recognition of a distinct pattern of symptoms may play a part in the recognition of these symptoms [59].

Identification of Risk Factors

Possible causes or contributing factors to TNS include a specific local anesthetic toxicity, neural ischemia secondary to sciatic nerve stretching, spinal cord vasoconstriction, patient positioning, needle trauma, or pooling of local anesthetic secondary to small-gauge pencil-point needles. Patient diseases or some other undefined patient factors predisposing them to neurologic abnormalities and infection should also be ruled out. Musculoskeletal disturbances in the back and leg symptoms cannot be totally excluded. TNS frequency was noticed to be high with outpatient surgery and lithotomy position in one study [60]. However, in two randomized studies early ambulation did not increase the risk for TNS [61, 62].

After the initial report of TNS with lidocaine, this syndrome has also been associated with other local anesthetics. The incidence of TNS with 5 % lidocaine has been between 10 % and 37 % [44, 54, 56, 58]. The risk for TNS is highest with lidocaine and also with mepivacaine and there seems to be approximately seven times higher risk of developing TNS after intrathecal lidocaine than after bupivacaine, prilocaine, or procaine [63]. It is thought that a local anesthetic toxic effect may be an important contributing factor in the development of TNS after spinal anesthesia with concentrated solutions [64, 65]. Because the toxicity is believed to be concentration related, a rational approach to the problem would be to look at the comparative efficacy of lower concentrations of lidocaine for spinal anesthesia. However, in clinical studies, decreasing the concentration of lidocaine from 5 % to 2 % did not prevent the development of TNSs [54, 56].

The incidence of TNS after 4 % mepivacaine for spinal anesthesia has been high and up to 30 % [47]. Three randomized studies combined gave a similar incidence of TNS with mepivacaine as with lidocaine [63]. The incidence of these

symptoms with 0.5 % tetracaine-containing phenylephrine was 12.5 % but only 1.0 % when 0.5 % tetracaine without phenylephrine was used [46]. The incidence of TNS after hyperbaric 0.5 % or 0.75 % bupivacaine has been 0–3 % [47, 56, 66, 67]. The duration of symptoms after bupivacaine spinal anesthesia was less than 12 h compared with 12–120 h after mepivacaine spinal anesthesia [47]. Prilocaine, chloroprocaine, and articaine have also been associated with a low incidence of TNS.

The dorsal roots of spinal nerves are positioned most posteriorly in the spinal canal [52] and therefore hyperbaric solution pools in this area when the patient is supine. Individual physical characteristics of patients may predispose to the development of transient radicular symptoms after spinal anesthesia. Anatomical configuration of the spinal column affects the spread of subarachnoid anesthetic solutions that move under the influence of gravity [68]. Both lumbar lordosis and thoracic kyphosis will differ between individuals, particularly with respect to the lowest point of the thoracic spinal canal [69].

Sacral maldistribution of local anesthetic with pencil-point needles has been suggested to cause toxic peak concentrations of lidocaine. Maldistribution has been shown in spinal models when the side port of a Whitacre needle is sacrally directed and the speed of injection is slow. In contrast, the distribution from a sacrally directed Quincke needle was uniform even with slow injection rates [53]. However, in clinical practice transient neurologic symptoms have occurred following well-distributed blocks and with different types of spinal needles [43, 67, 70].

In addition to a toxic effect of the local anesthetic, the lithotomy position during surgery has been thought to contribute to TNS [52]. The lithotomy position may contribute to TNS by stretching the cauda equina and sciatic nerves, thus decreasing the vascular supply and increasing vulnerability to injury. During knee surgery, where the position of the operative leg is varied and nerve stretching may occur, there exists an increased risk for TNS. The incidence of TNS is higher after knee arthroscopy compared to inguinal hernia repairs [56]. Spinal cord vasoconstrictors may be implicated through either localized ischemia or prolonged spinal anesthesia due to decreased uptake of local anesthetic. Adding phenylephrine to tetracaine spinals increased the frequency of transient radicular symptoms [46]. Intrathecal tetracaine increases spinal cord blood flow and the effect can be reversed or prevented by epinephrine [71]. Lidocaine induces less vasodilatation in the spinal cord [72] and bupivacaine is a vasoconstrictor [73]. Epinephrine added to lidocaine did not increase the incidence of transient neurologic symptoms compared with lidocaine without epinephrine. However, different concentrations of lidocaine (5 % with epinephrine and 2 % without epinephrine) were used [56]. Preliminary animal data suggests that the concurrent administration of epinephrine enhances sensory deficits resulting from subarachnoid administration of lidocaine [74]. It is not clear whether animal data has clinical relevance for TNS.

It has been speculated that profound relaxation of the supportive muscles of the lumbar spine may result in straightening of the lordotic curve, and even transient spondylolisthesis, when the patient is lying on the operating table. This may be responsible in part for the radiating back symptoms which can occur after the intense motor block [47].

Needle-induced trauma is typically unilateral and closely associated with needle insertion or local anesthetic injection. TNS appear after otherwise uneventful spinal anesthetics and no correlation with paresthesias and incidence of symptoms has been found [46, 47, 56, 66, 67] Chemical meningitis or arachnoiditis is an improbable cause of these syndromes as there is no progression of symptoms and they usually resolve promptly without special treatment. However, result of the MRI of one case report with two patients with TNS after lidocaine spinal anesthesia shows enhancement of the cauda equina and the lumbosacral nerve roots that according to authors may support the theory of a direct toxic effect of lidocaine. The MRI findings are suggestive of pial hyperemia or breakdown of the nerve root–blood barrier by a non-infectious inflammatory process [75]. No association with TNS and patient sex, weight, or age has been found [47, 56]. Studies exploring a possible etiologic role of hyperosmolarity secondary to glucose suggest that it does not contribute to transient radicular symptoms [44, 46, 65, 76]. Glucose can also promote maldistribution of local anesthetics and thus contribute indirectly to neural injury. However, a similar incidence of TNS was found after spinal anesthesia with 5 % hyperbaric lidocaine with epinephrine and 2 % isobaric lidocaine without epinephrine [56].

The site of local anesthetic action is in sodium channels, and therefore a logical step toward determining a mechanism for the local anesthetic neurotoxicity is in establishing whether ongoing blockade of sodium channels is causative for neurotoxicity. According to Sakura et al. the local anesthetic toxicity does not result from the blockade of sodium channels, and they suggest that the pursuit of a Na channel blocker not associated with TNS is a realistic goal [76].

Clinical Implications

The clinical significance of TNS is still unclear. Although it is possible that transient neurologic symptoms represent the lower end of a spectrum of toxicity, their relationship to neurologic injury remains speculative [77]. There are not even any case reports that would indicate that TNS are permanent or haven't disappeared completely. Whether the use

of lidocaine or mepivacaine should be continued for spinal anesthesia is still controversial.

Adding epinephrine to lidocaine seems to potentiate persistent sensory impairment induced by subarachnoid lidocaine [74] and may explain cauda equina syndrome after single-shot spinal anesthesia [70]. There is no reason to add epinephrine to lidocaine as the solution can be substituted with bupivacaine [59, 77]. It has been suggested that lidocaine should be used sparingly—if at all—in anesthetic procedures where product pooling, nerve stretching, or both could compromise neural viability [78]. It may be wise to substitute lidocaine with other local anesthetics until the etiology and clinical significance of transient neurologic symptoms are determined. Decreasing the dose of bupivacaine makes it a suitable alternative for short-stay surgery [56]. However, there is still a place for a new nontoxic, effective, and short-acting local anesthetic.

Postdural Puncture Headache (PDPH)

PDPH used to be a common postoperative side effect of spinal anesthesia. With the development of thinner needles and needle tip design, this harmful complication has become rarer. But despite these positive developments, we still cannot promise our patients that they will not get this complication if spinal anesthesia is chosen for their anesthesia method.

Definition

PDPH is a typical headache that is usually bifrontal and occipital and is aggravated by upright posture and by straining. Nausea and vomiting are also common symptoms. The headache may first be experienced several hours to days after the dural puncture. It is relieved by lying down. The headache is different than any other headache that the patient has had before (except possible previous PDPH). PDPH needs to be differentiated from tension/migraine headache, aseptic or infective meningitis, cortical vein thrombosis, or cerebral/epidural hematoma.

The pain is often associated with other symptoms that can be related with the nerve involved. Usually these symptoms resolve with the recovery from the headache. Auditory disturbances may occur secondary to eight nerve dysfunction. These include unilateral or bilateral deafness that may go unnoticed if not specifically asked about from the patient. Traction of the abducens nerve can cause visual disturbances, diplopia being the most common symptom.

Etiology

The spinal dura mater extends from the foramen magnum to the second segment of the sacrum. It contains the spinal cord and nerve roots that pierce it. Usually after dural puncture the hole caused by the needle will close, but in some cases the hole remains open with subsequent loss of CSF through the hole. The dynamic relationship between dural and arachnoidal tear may have role in the closure of the puncture hole. There is a clear relationship between the loss of CSF and the severity of the symptoms. According to present knowledge, the typical headache in upright position is caused by the traction of the cerebral structures when the brain descends. Also, the compensatory cerebral vasodilatation due to loss of CSF can also cause headache.

Dura mater is a dense, connective tissue layer made of collagen and elastic fibers that are running in a longitudinal direction at least in the superficial layer of the dura. However, light and electron microscope studies of human dura mater have contested this classical description of the anatomy of the dura mater. Measurements of dural thickness have also demonstrated that the posterior dura varies in thickness, and that the thickness of the dura at particular spinal level is not predictable within an individual or between individuals [79]. Dural perforation in a thick area of dura may be less likely to lead a CSF leak than a perforation in a thin area and may explain the unpredictable consequences of a dural perforation.

Despite the new knowledge about dural anatomy, cutting spinal needles should still be oriented parallel rather than at right angles to these longitudinal dural (and also arachnoidal) fibers (or spine) to reduce the number of fibers cut. The cut dural fibers, previously under tension, would then tend to retract and increase the longitudinal dimensions of dural perforation, increasing the likelihood of postspinal headache. Clinical studies have confirmed that PDPH is more likely when the cutting spinal needle is orientated perpendicular to (versus parallel) the direction of the dural fibers [9, 80].

As previously mentioned, the risk for the occurrence of PDPH may be highest if the puncture is aimed at the thinnest part of the dura. However, the anesthesiologist does not have any possibility to aim the spinal needle to the thicker part of the dura. There are some patient groups that are at a higher risk to develop PDPH than the others (Table 15.1) especially, younger and obstetric patients and those who have had PDPH before having a higher risk for this syndrome.

There are differing opinions about the effect of gender, as in some studies it did not have any effect and in some other studies even nonpregnant women have been more susceptible to PDPH. There are also some risk factors that the anesthesi-

Table 15.1 Factors influencing likelihood of PDPH

• Needle size
• Age
• Number of punctures
• Bevel design
• Bevel orientation
• Pregnancy
• Previous PDPH
• Angle of approach

ologist can influence. If spinal anesthesia is chosen for a patient at risk, proper technique should be used. Multiple punctures should be avoided. Thin spinal needles should be used. However, the smallest available spinal needles (29-gauge) are more difficult to use and more expensive than the thicker ones. The anesthesiologist should use the spinal needle that he or she is familiar with to avoid technical difficulties during the puncture. Modern 27-gauge, pencil-point needles are quite easy to use after some practice and may offer the optimal balance between ease of puncture and incidence of complications. With these modern needles, CSF appears in the needle hub so fast that it does not hamper the procedure. Thus, even routine use of the 27-gauge (0.41 mm) Whitacre spinal needle when performing spinal anesthesia has been recommended [81].

Treatment

The anesthetic literature contains numerous publications about different treatment options for PDPH, and more than 50 different remedies have been proposed for the treatment of this syndrome. Fortunately, time heals PDPH in almost every case within a couple of days. The most effective curative treatment is epidural blood patch (EBP), in which the patient's own blood is injected into epidural space.

The symptoms of PDPH are alleviated by assuming the horizontal position. However, prophylactic treatment by placing the patient horizontal for a period of time (e.g., 24 h) after a dural puncture has no effect on the incidence or duration of a PDPH; it only delays the onset of PDPH until the patient ambulates [82]. Normal hydration of the patient should be maintained because dehydration can worsen the symptoms. Extra hydration has been suggested to help generate more CSF but does not alleviate the headache. Narcotic analgesics and, in some instances, nonsteroidal anti-inflammatory agents are often administered for symptomatic treatment of the headache.

Caffeine has been suggested as a mode of therapy to help constrict the vasodilated cerebral vessels with differing results. It is best administered early in the day so that patients can sleep at night. The dose of caffeine sodium benzoate is 500 mg intravenously which can be repeated once 2 h later if the first dose does not have the desired effect.

Boluses or infusions of epidural normal saline can help to transiently increase the epidural pressure, slowing the speed at which CSF leaks through the dural hole. This may speed the natural healing process. Bolus doses of 30–60 mL given six hourly for four doses have been used. Alternatively, a continuous infusion at a rate of 1000 mL administered over a 24-h period has been used. Colloids have also been used but probably their effect does not differ from the crystalloids. Although epidural saline or colloid can be a useful technique, higher success rates are achieved with EBPs and continuous epidural infusion or repetitive boluses necessitate that the patient stays at the hospital.

Epidural Blood Patch (EBP)

EBP has been shown to be the only curative treatment for PDPH that shortens effectively the duration of PDPH with a high incidence of success and low incidence of complications. Patient's autologous blood is injected into epidural space near the spinal puncture site to seal the hole and stop the CSF leak. EBP should be considered if the patient's PDPH is so severe that he or she is bedridden because of the headache and consents to the procedure. Breastfeeding mothers with newborn babies should be offered EBP if PDPH hampers breastfeeding and prevents them from enjoying the pleasures of recent motherhood.

The timing of EBP is controversial. Some authorities recommend a prophylactic blood patch if a dural tap is encountered during epidural puncture. However, not everyone gets PDPH even after dural puncture with a 16-gauge epidural needle. These patients would be exposed to an unnecessary procedure with potential side effects. Also, the results with prophylactic blood patches have not been convincing. The success rate has been higher if EBP has been administered 24 h after the dural puncture instead of the earlier [83].

According to present theory, the rapid effect of EBP is caused by the volume effect of the blood in the epidural space. The blood compresses the dural canal and increases the CSF pressure and the headache is relieved. An MRI study has confirmed the tamponade effect of the 20-mL EBP, which is believed to be responsible for the immediate resolution of PDPH [84]. In the later stage, the blood is clotting into dura and the hole will close, preventing the further leakage of CSF. There are no good studies indicating how long the patient should be treated in the hospital after EBP and what they can or cannot do to achieve the best possible results. Our practice is to keep the patient supine for 30 min after the EBP. Thereafter, sitting and standing is tried. Patients are released from the hospital 1 h after the procedure. They are advised to avoid any strain such as lifting during the first 24 h after the EBP. Thereafter, the patients can return to their normal activities. They can contact the hospital again if there are problems or the headache returns.

The contraindications to EBP are those that normally apply to epidurals (patient refusal, local infection, bleeding disorders, etc.). The anesthesiologist should interview the patient before EBP to find out if the symptoms are typical for PDPH. When in doubt, a neurologic opinion should be sought and perhaps a computed tomography scan or MRI taken to exclude other pathologic findings in the central neural system. Viral infection and malignancy are at least relative contraindications. There are not enough data to exclude the possibility that viruses or neoplastic cells introduced into the epidural space are potentially harmful to the patient.

The success rate with EBP has been approximately 70 %–90 %. In the first report by Gormley, only 2–3 mL

blood was recommended [85]. Higher blood volumes seem to lead to higher success rate of EBP. Volumes between 15 and 20 mL have been used most often, although even 30-mL volume has been used without complications. Strict aseptic technique should be used during the procedure. The administrator of EBP should be experienced with epidural technique because a dural tap with a Tuohy needle makes things only worse. According to Szeinfeld and colleagues, the blood spreads more in cephalad than caudad direction in the epidural space. Therefore, if the same interspace that was used for the lumbar puncture cannot be used, it may be wise to choose a lower one [86]. Usually, the patient feels a sensation of "fullness" during the injection. If there is persistent pain or paresthesia during the injection, the injection should be stopped. If the first EBP fails, the procedure can be repeated with a similar success rate. Usually, the PDPH is at least milder after EBP even if the headache returns. If two EBPs do not relieve the symptoms, even more caution than before should be used to exclude other reasons for headache.

Pruritus

Pruritus may be a problem if intrathecal opioids are used in combination with local anesthetics. Fentanyl is used quite often in combination with low-dose local anesthetic in order to intensify the block without delaying the discharge. Sufentanil and morphine are used more often for postoperative analgesia of inpatients. Most often the pruritus is mild and does not need any treatment. In some cases, itching can become a real problem and needs rescue medication. A 5-HT antagonist ondansetron has been shown to alleviate the symptoms effectively.

Continuous Spinal Anesthesia

Spinal catheters can be used for repeating dosing or continuous infusion of drugs into the subarachnoid space. Excessive block can be avoided with careful titration of the drugs into catheter. With more restricted block, there is a smaller risk for cardiovascular complications like hypotension and bradycardia. If the duration of surgery is prolonged, additional doses of local anesthetics can be injected. Continuous spinal anesthesia may also be used for on-going pain relief postoperatively.

In the beginning of 1990s, 14 cases of cauda equina syndrome were reported in association with small-gauge spinal catheters. This led to the withdrawal of the microcatheters from the market in the United States and Canada. The mechanism of these unfortunate events was probably attributable to direct toxic effects of local anesthetic. Maldistribution or potential pooling of local anesthetic administered through the catheters near the roots of cauda equina is the most likely explanation. Therefore, hyperbaric local anesthetics should be avoided with microcatheters. Injection of hyperbaric solution through a single-hole microcatheter may lead to neurotoxic concentrations of local anesthetics in CSF. The risk seems to increase when the catheter is directed caudad and glucose-containing solutions are injected. Unfortunately, it is impossible to predict the direction of a subarachnoid catheter despite attempts to direct it cranially at least with sharp-beveled needles [87]. More accurate positioning may be achieved by using directional puncture needles such as Sprotte or Tuohy needles. The catheter should not be advanced more than 2–3 cm into subarachnoid space.

Small-gauge spinal catheter systems with different techniques of dural perforation have been developed in order to reduce the risk of PDPH in continuous spinal anesthesia. Despite different catheter designs, the incidence of PDPH seems to be high in high-risk patients. An incidence of 78 % has been described with the over-the-needle catheter technique [88]. Spinal cutaneous fistula is a rare but harmful complication of continuous spinal anesthesia. In one reported case, the fistula followed a 5-h catheterization with an 18-gauge epidural nylon catheter. The fistula was closed with a single dural stitch, deep to the puncture site [89].

There are a lot of technical problems related to placement of small-diameter spinal catheters. Coiling and kinking of the catheters, catheter breakage, and failure to aspirate have been problems associated with these catheters. Over-the-needle devices have been associated with high failure rates [90]. Traumatic catheter placement can lead to spinal hematoma that fortunately is a rare but potentially catastrophic complication of spinal catheterization.

Spinal catheters should be properly marked and the personnel that manage the patients should be aware of the proper use of spinal catheters and the possible complications associated with them. Injecting the wrong solution into subarachnoid space can cause disastrous complications of spinal catheterization.

Strict aseptic routine should be used during the insertion and use of spinal catheters.

There are no prospective studies about the incidence of infective complications associated with the use of these catheters. Occasional case reports have been published about aseptic meningitis during continuous spinal analgesia. The preservatives have been suspected to be the cause of meningitis [91]. There are no data either about the safe time period that the spinal catheter can be used. In most studies, the spinal catheter has remained in situ for one or two postoperative days.

Catheter breakage can also occur during catheter withdrawal. During withdrawal of the catheter, the patient should be positioned preferably in the same position as during the insertion of the catheter. Excessive force should be avoided. Catheter removal is not acceptable during therapeutic levels of anticoagulation. The catheter must be checked after removal and if broken pieces are retained in the patient, they should be informed about the incident. It is recommended to leave possible broken pieces in situ if they do not cause problems such as CSF fistula.

Conclusion

Spinal anesthesia is one of the oldest and most reliable techniques of anesthesia today and its use now spans three centuries. The circumstances surrounding its introduction are fascinating. The basic technique has changed very little in more than 100 years of use. We now have better needles, local anesthetics, and catheters. We now add opiates to our local anesthetic solutions which have many benefits but also add to the list of complications. The phenomenon of TNS is fascinating and inexplicable. We have learned a great deal about the physiology of spinal anesthesia in the last 60 years thanks to outstanding contributions made by Sir Robert Macintosh and Professor Nicholas Greene. It is very likely that anesthesiologists will still be performing spinal anesthesia 100 years from now. We owe a debt of gratitude to Bier and Hildebrandt for the gift of spinal anesthesia.

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Part IV

Specific Patient Populations: Safe Practice and Management of Adverse Events

Complications of Regional Anesthesia in Chronic Pain Therapy

16

David Flamer, Rachael Seib, and Philip W.H. Peng

Key Points

- Various sympathetic, visceral, and somatic blocks are used to manage chronic pain, each associated with a specific set of potential complications.
- Complications of sympathetic blocks include direct trauma to structures in the path of the needle, inadvertent intravascular or intraspinal injection, inappropriate drug spread, negative response to the drug injected. In the case of celiac plexus blocks, additional complications include neurologic sequelae, hypotension, and diarrhea.
- Epidural steroid injection can be complicated by arachnoiditis, infection, and systemic side effects of the injectate. Some reports describe severe neurologic complications following transforaminal injection.
- Care must be taken when performing neural ablation, given the deleterious effects of injectates; motor paresis and postblock pain are some complications that have been reported following this procedure.
- Other procedures to treat chronic pain, including implantable catheters and spinal cord stimulation, may be complicated by infection/inflammation, adverse effects of drugs, or problems with the equipment.

D. Flamer, MD, FRCPC
Department of Anesthesia, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada
e-mail: david.flamer@uhn.ca

R. Seib, MD, FRCPC
Humber River Hospital, Toronto, ON, Canada
e-mail: rachaelseib@gmail.com

P.W.H. Peng, MBBS, FRCPC (✉)
Department of Anesthesia, Toronto Western Hospital, University of Toronto,
McL 2-405 TWH, 399 Bathurst Street,
Toronto, ON M5T 2S8, Canada
e-mail: Philip.peng@uhn.ca

Introduction

The specialty of pain management has continued to grow steadily in recent years, and the prevalence of treatment-related complications has also increased, as suggested in a 2004 closed claims study [1]. In this chapter, we discuss sympathetic, visceral, and somatic blocks commonly performed in the management of chronic pain. To understand how complications arise, it is necessary to review the anatomy and techniques of the blocks, which can be used for diagnostic or therapeutic purposes. It is also important to understand some of the unique drugs used in this setting (e.g., neurolytic agents and corticosteroids). In general, procedure-related damage can result from needle insertion, misplacement, or unanticipated spread of the drug, drug toxicity, injection of the wrong substance, or from an idiosyncratic reaction. Postblock physiological changes may also add to complications.

Sympathetic Blocks

Sympathetic blockade techniques are frequently employed in the diagnosis and treatment of sympathetically mediated pain syndromes, complex regional pain syndrome, limb ischemia or hypoperfusion, and visceral pain from cancer or nonmalignant conditions [2]. Diagnostic blocks with local anesthetic alone are often performed as a precursor to either a series of blocks or neurolytic block using phenol or ethanol.

Stellate Ganglion Block

The sympathetic fibers for the head, neck, and upper limbs arise from the first few thoracic segments and ascend through the sympathetic chains, and synapse in the superior, middle, and inferior cervical ganglion. The stellate ganglion is formed by the fusion of the inferior cervical and first thoracic

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_16

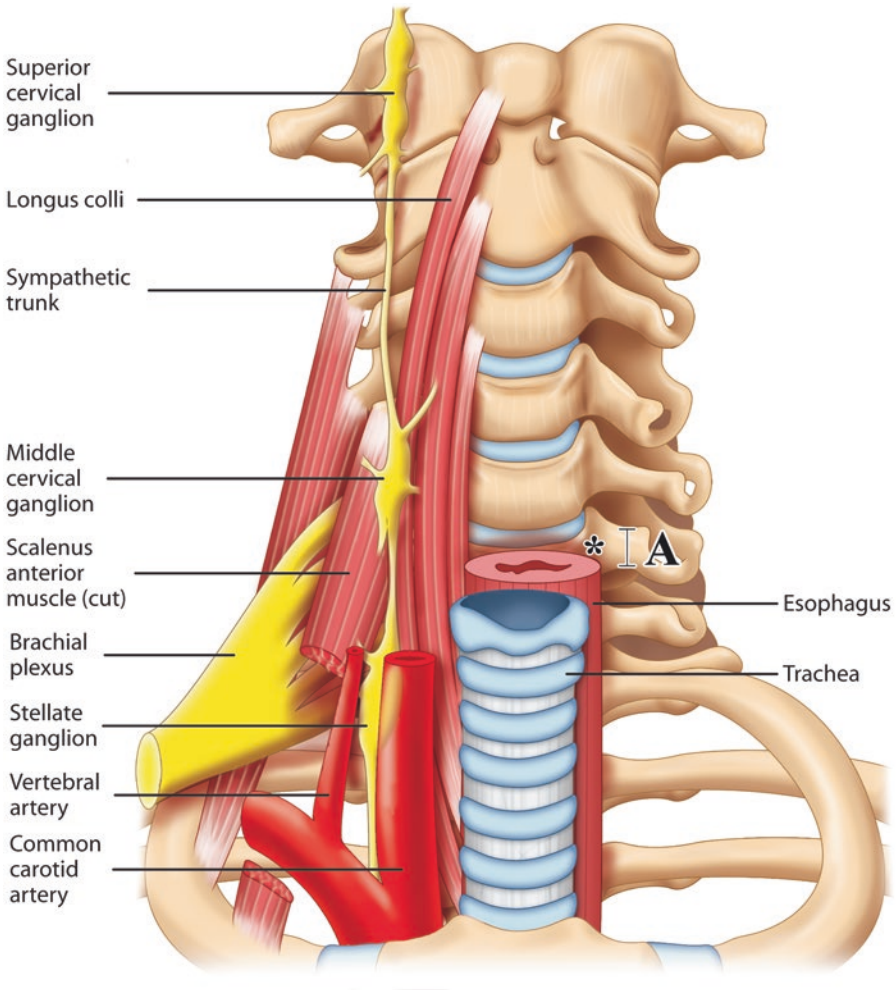

Fig. 16.1 Prevertebral region of the neck. The target site for needle insertion in classical approach is marked as *asterisk*. The breadth of the transverse process is marked as *A*. Reproduced with permission from Philip Peng Educational Series

sympathetic ganglia and extends from the level of the head of the first rib to the inferior border of the transverse process of C7 (Fig. 16.1). The postganglionic fibers from the stellate ganglion provide sympathetic innervation to the upper limbs via C7, C8, and T1 nerves. The preganglionic fibers of the head and neck region continue to travel cephalad to the superior and middle cervical ganglion through the cervical sympathetic trunk (CST). Injection of local anesthetic around the stellate ganglion interrupts the sympathetic outflow to head, neck, and upper limbs through inactivation of both preganglionic and postganglionic fibers, while injection of local anesthetic around the CST only result in sympathetic blockade of head and neck regions [3]. The CST is embedded in the prevertebral fascia dorsal to the posterior fascia of the carotid sheath [3, 4].

The most common approach to the stellate ganglion is an anterior paratracheal approach at the level of the cricoid cartilage (C6) with or without fluoroscopy guidance. This approach is essentially a blockade of the cervical sympathetic chain in proximity to the middle cervical ganglion instead of the stellate ganglion. Thus, the classical approach is better termed cervical sympathetic block. The sympathetic outflow to the head and neck region (cervical trunk) can be blocked independently of the fibers to the upper limb [5]. Thus, development of Horner's syndrome does not guarantee successful sympathetic blockade of the upper limb.

Also described are an anterior C7 paratracheal approach, medial approach to uncinate process [6], and a posterior T2 paravertebral approach [7]. The posterior approach aims to interrupt sympathetic outflow to the upper extremity with less chance of Horner's syndrome. Thus, it may be indicated for neurolytic blockade when long-term side effects are undesirable.

The overall complication rate for stellate ganglion block is estimated to be approximately 0.17 % [8]. These complications range from moderate to severe and can mostly be attributed to incorrect placement of the needle and anomalous spread of local anesthetic.

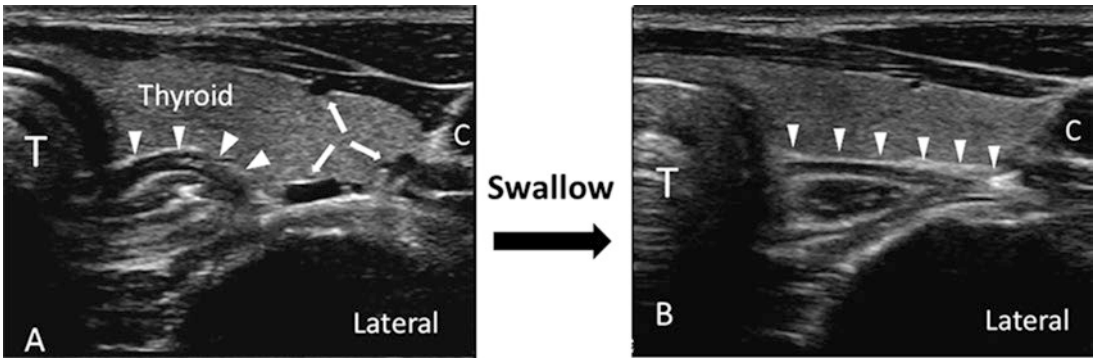

Fig. 16.2 Ultrasonographic image of neck at C7 level showing the variation of position of esophagus with swallowing. (**a**) Before swallowing, the esophagus (*arrow heads*) was seen covering half of the distance between trachea (T) and carotid artery (C); (**b**) during swallowing, the esophagus moved laterally toward the carotid artery, virtually covering the whole area between trachea and carotid artery. Note that the *bold arrows* showed the presence of three vessels in the preswallow scan. Swallowing action was evident by the increased in hyperechogenic shadow in the trachea. Reproduced with permission from Philip Peng Educational Series

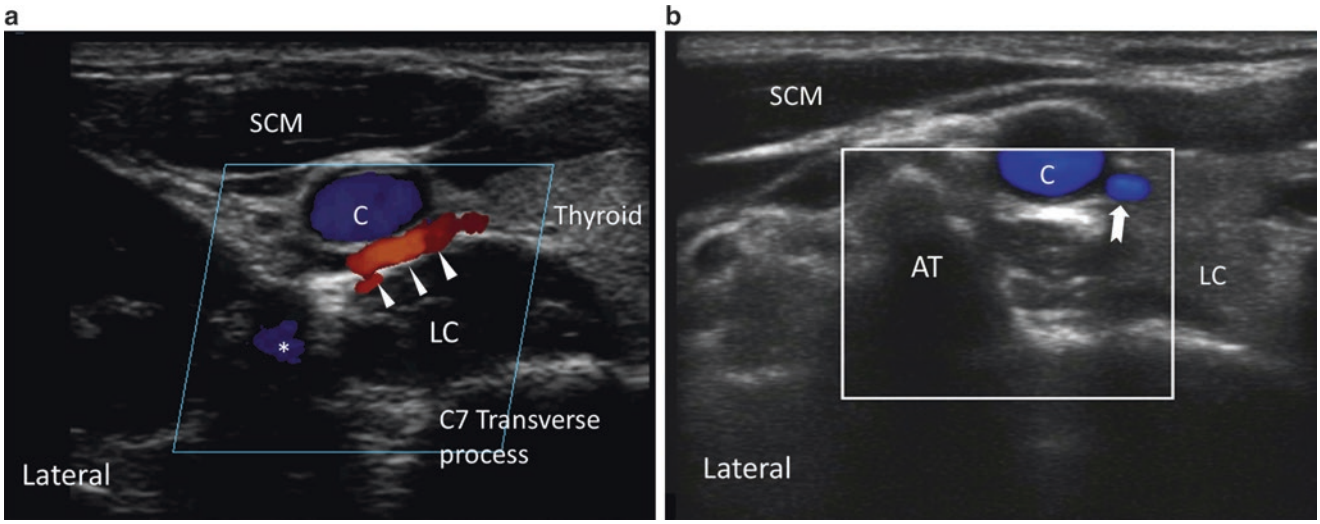

Fig. 16.3 (**a**) Ultrasonographic image of neck at C7 level on the right side showing the inferior thyroidal artery (*arrow heads*) in the long axis, crossing ventral to the paravertebral fascia. (**b**) Ultrasonographic image of neck at C6 level on the right side showing a vessel in the short axis (*bold arrows*). *LC* longus colli muscle, *C* carotid artery, *SCM* sternocleidomastoid muscle, *AT* anterior tubercle, * vertebral artery. Reproduced with permission from Philip Peng Educational Series

Complications

Needle Trauma

Structures that lie close to the path of needle insertion are either vessels or organs in the vicinity. Moore documented puncture of pharynx, trachea, and esophagus [9]. Literature confirms that the esophagus is displayed lateral to the cricoid in approximately 50 % of the individual (mostly left side) and the prevalence is even higher at C7 level (Fig. 16.2) [10]. When the esophagus is punctured, mediastinitis is a legitimate concern [11]. Pneumothorax is another recognized risk, especially with the anterior C7 approach, as the dome of the pleura may extend 2.5 cm above the level of the first rib, especially on the right side. The risk of pneumothorax is increased further in tall, thin persons. The incidence of pneumothorax is up to 4 % with the posterior approach, which shares many of the risks of the thoracic paravertebral sympathetic block.

Retropharyngeal hematomas are another potential complication due to puncture or passage of the needle through local vessels, which include vertebral artery (aberrant course), inferior thyroidal artery, ascending and deep cervical arteries (Fig. 16.3) [3, 10, 11]. Such hematomas have been reported with symptoms ranging from minimal patient discomfort to complete loss of the patient's airway [12]. The frequency of catastrophic retropharyngeal hematoma after stellate ganglion block is approximately 1 in 100,000 cases [13]. However, the incidence of asymptomatic hematoma is much higher [14].

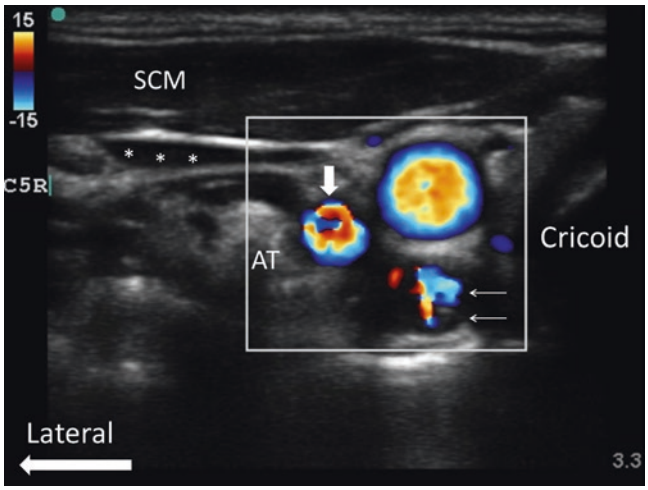

Fig. 16.4 Ultrasound image of the neck at the seventh cervical vertebral level (C7) with Doppler imaging. *Va* vertebral artery, *Ca* carotid artery, *LC* longus colli muscle, *SCM* sternocleidomastoid muscle, * internal jugular vein (compressed), *solid bold arrow* vertebral artery, *line arrows* artifact secondary to the shadowing of the carotid artery. Reproduced with permission from Philip Peng Educational Series

Intravascular Injection

The vessel most at risk is the vertebral artery. At the level of C7, the vertebral artery lies anterior to the stellate ganglion, before it swings posterior to enter the foramen transversarium of the sixth cervical transverse process. Thus, the anterior C7 paratracheal approach has a greater risk of vertebral artery puncture. However, the literature suggests that the vertebral artery enters the foramen transversarium at a level above C6 in 7–10 % (Fig. 16.4) [10, 15]. Kozody et al. have shown that as little as 2.5 mg of bupivacaine (a test dose) can cause major CNS effects when accidentally injected into the vertebral artery [16]. A smaller 1-mL test dose is recommended. Intravertebral artery local anesthetic injection may produce dizziness, nausea, light-headedness, and hypotension with low dosage and can result in coma, convulsion, and respiratory depression when higher doses are used [17]. These side effects are due to the direct effect of the local anesthetic on medullary and pontine centers. The duration and nature of the toxic effects depend on the dose injected and global and regional cerebral blood flow, as well as the precise neurovascular anatomy. Local anesthetic-induced neurologic symptoms, which appear after a low-dose injection, are often short-lived (minutes).

Accidental injection of air into the vertebral artery, with subsequent cerebral air embolism was reported by Adelman [18]. This complication represents two errors, not just one. Other vascular structures at risk are the carotid and jugular vessels, which lie lateral to the needle path, but there are no recent reports of puncture of these blood vessels.

Intraspinal Injection

Nerve roots of the brachial plexus exiting from intervertebral foramen may have an accompanying dural cuff. The vertebral canal and its contents lie posteromedial to the stellate ganglion. Thus, dural puncture may occur, either as a result of needle placement too medial or injection into a lateral extension of the perineural dural cuff of the cervical somatic nerve root [19]. Intrathecal injection of local anesthetic will produce a high spinal block, characterized by loss of consciousness, high motor block, hypotension, and apnea. This serious complication necessitates ventilatory and hemodynamic support until it wears off. Transient locked-in syndrome has been reported, as has subdural injection [20–22]. Wulf and Maier, in a survey of approximately 45,000 stellate ganglion blocks performed in Germany, reported six subarachnoid blocks and three high epidural injections [23]. Most important of all, care should be taken to avoid inadvertent injection of neurolytic agents into the epidural, subdural, or subarachnoid spaces, as this may lead to long-term neurologic deficit such as spinal cord infarction [24].

Anomalous Spread of Drug

Even when the drug is injected into the correct anatomical plane, anomalous spread may cause complications. Both bilateral recurrent laryngeal nerve palsy and contralateral Horner's Syndrome have been reported [25]. Bilateral block causes unopposed vocal cord adduction and airway obstruction. Local anesthetic spread posteriorly and anterolaterally can produce brachial plexus blockade in up to 10 % of patients, and phrenic nerve block, respectively [6]. Because of the possibility of somatic spread, it is necessary to check for normal sensory and motor function in the blocked limb when evaluating the success of the sympathetic block.

Drug Effects

Extensive blockade of the cardiac sympathetic nerves has been reported following a properly performed stellate ganglion block. This resulted in bradycardia, secondary to unopposed vagal tone [26]. This has resulted in at least one case of cardiac arrest [27]. Schlack et al. demonstrated in a canine model that left stellate ganglion blockade caused impairment of left ventricular function. The mechanism was asymmetric cardiac contraction and asynchrony, caused by loss of sympathetic tone in the antero-apical segment of the left ventricle, supplied by the left sympathetic chain [28]. Although it is difficult to extrapolate these animal data to humans, who may have different patterns of myocardial innervation, the authors suggest that it may remain a risk in patients with already compromised cardiac function. Data to confirm this are lacking.

One case of migraine has been reported following a stellate ganglion block, presumably due to an idiosyncratic reaction and a loss of unilateral sympathetic tone in the cerebral vasculature [29]. Although absorption of correctly injected local anesthetics to toxic levels would be considered unlikely in stellate ganglion blockade, Wulf et al. reported toxic plasma levels in 30 % of patients after injecting 10 mL of 0.5 % bupivacaine [23, 30]. There have been no recent reports of injection of the wrong drug, but it remains a theoretical possibility.

Ultrasound emerges as a popular method for the guidance of pain intervention [5]. The advantages of ultrasound over fluoroscopy are that it allows the visualization of the soft tissues and vessels, and precise delivery of the local anesthetic to the CST, which is defined by the fascia, not the bony structure. Therefore, ultrasound potentially minimizes the risk of direct trauma to the vessel and organs and reduces the total dose of local anesthetic injected. Typically, 3–5 mL of local anesthetic is required.

Thoracic and Lumbar Sympathetic Blockade

The sympathetic chain lies in the paravertebral region, receiving fibers from somatic nerve roots via the *rami communicantes*. In the thoracic region it lies adjacent to the neck of the ribs, relatively close to the somatic nerve roots and the parietal pleura, with pneumothorax being a possible complication. For this reason, transcutaneous approach to the thoracic sympathetic chain without radiologic imaging support is not commonly performed. Long-lasting thoracic sympathectomy is usually achieved by surgical ablation, using either thoracotomy or, more recently, thoracoscopy.

In the lumbar region, the sympathetic chain and its ganglia lie on the anterolateral border of the vertebral bodies, separated from the somatic nerve roots by the psoas muscle and fascia. The ganglia are found in variable locations but most consistently found at the L3 level (Fig. 16-5) [31]. The popular technique is fluoroscopy-guided needle insertion to the anterolateral border of the L2, L3, or L4 vertebrae. It requires the insertion of a needle 5–6 cm from the posterior midline with the patient in the prone position. The needle passes through the paravertebral muscles, "walks off" the transverse process, and passes through the psoas muscle and fascia to reach the lumbar sympathetic chain in the anterolateral aspect of the vertebra. The volume of local anesthetic injection varies, from high volume (e.g., 20 mL) at a single level to low volume at multiple levels.

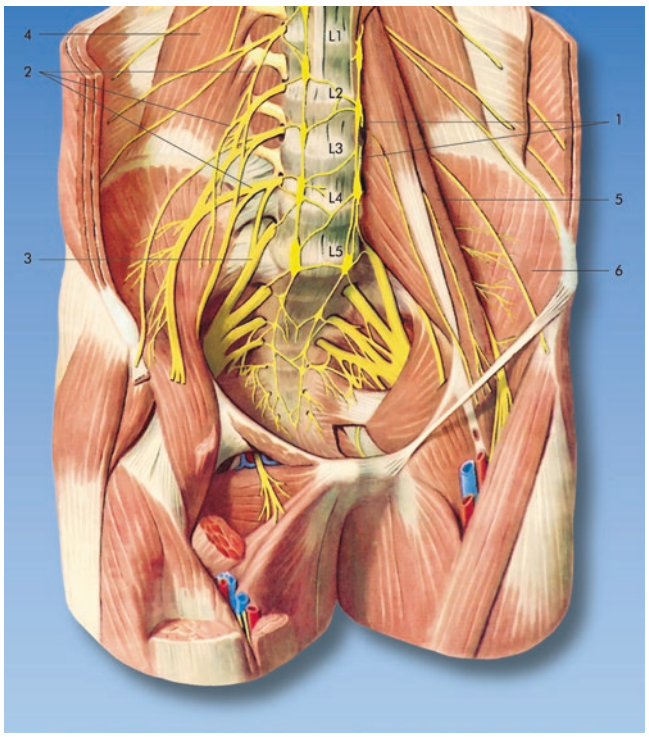

Fig. 16.5 Anatomy (*anterior view*): (*1*) sympathetic trunk with communicating branches, (*2*) lumbar plexus, (*3*) lumbosacral trunk, (*4*) quadratus lumborum muscle, (*5*) psoas major muscle, (*6*) iliac muscle Reproduced with permission from Dr. Danilo Jankovic

Complications

Intraspinal and Intravascular Injection

The vertebral column and the spinal canal lie posteromedial to the sympathetic chain. Injection of local anesthetic in the spinal canal is rare, but theoretically possible. Intraspinal injection (intrathecal, epidural, or subdural) and postdural puncture headache can follow puncture of either an extended dural cuff or the intraspinal dura [32, 33]. Intravascular injection is a possible complication, as both the aorta and inferior vena cava lie anterior to the sympathetic chain. Puncture of these structures is rarely reported, but it can occur in the clinical setting. The vertebral venous plexus is also at risk, as it is close to the path of the needle. The risk of intravascular injection into either a perivertebral vein or a major vessel is minimized by appropriate use of fluoroscopy and contrast medium before the injection of local anesthetics or neurolytic agents. Negative aspiration before injection yields false reassurance, as the sensitivity of this test is only 40.7 %. This low sensitivity can be explained by the fact that the veins of the vertebral plexus constitute a thin-walled, low-pressure system and collapse under aspiration [34].

Needle Trauma

Confirmation of needle position with fluoroscopy is necessary when performing neurolytic blockade of the lumbar sympathetic ganglia. The risks of 'blind' technique are needle trauma to the kidney, ureter, and bowel. In a cadaver study, three out of 80 "blind" needle attempts resulted in needle insertion into grossly osteoporotic vertebral bodies or the hilum of the kidney [35]. These incidents can be prevented with the utilization of fluoroscopic guidance.

Drug Effects

Complications can occur from the use of either local anesthetics or neurolytic agents. Significant sympathetic blockade and postural hypotension may occur as a result of the

physiologic response to injection. Another possible undesirable effect is sexual dysfunction in male patients, although this may also be caused by vascular insufficiency, an indication for lumbar sympathetic block in the first place. There remains a possibility that sympathetic blockade of a limb where there is critical fixed stenosis of the arterial supply to one region may vasodilate only the normal vasculature. This will give rise to a "steal" syndrome—deterioration of perfusion to the ischemic area, if there is a fixed inflow.

The most common complication associated with lumbar chemical sympathectomy is genitofemoral neuralgia [36]. The genitofemoral nerve arises from the lumbar plexus at the first lumbar segmental level and passes on the ventral surface of the psoas muscle. It emerges from the anterior aspect to supply the groin and upper thigh. The incidence varies between 5 and 40 % and most cases are transient, lasting less than 6 weeks [37, 38]. A transdiscal approach to lumbar sympathetic block has been advocated to avoid genitofemoral neuralgia because the needle does not pass through the psoas muscle [39].

Ureteric injury is uncommon but can occur following chemical sympathectomy [40]. Whether injury is related to needle trauma or ureterolysis from the neurolytic agents is unclear. Most case reports claimed fluoroscopic confirmation of needle location and delayed presentation of urological symptoms, suggesting that injury is more likely related to the neurolytic agent. This highlights the importance of limiting the amount of neurolytic agents applied.

Intravenous Regional Sympathetic Block

The technique of intravenous sympathetic blockade has been used for treatment of sympathetically mediated pain in the upper limb. The technique is essentially one of perfusion of the isolated limb with a sympatholytic solution. After an interval of 20–30 min, when a significant portion of the drug is assumed to have become fixed to the tissues, the tourniquet is deflated. The block is repeated, often weekly, for three to six times. This method of sympathetic block is becoming unpopular due to the lack of support of efficacy from the literature [41].

Sympatholytic agents used for intravenous regional sympathetic block are guanethidine (not available for this use in the United States), bretylium, reserpine, phentolamine, and ketanserin. Guanethidine is an agent that blocks reuptake of noradrenaline in sympathetic nerve endings for up to 3 days, thus depleting the stores. It should not be used in patients on monoamine oxidase inhibitors for this reason, as there is an initial release of amine from the stores. Guanethidine is usually used in a dose of 10–20 mg in up to 40 mL of saline or dilute local anesthetic for the upper limb. The dose and the volume are generally higher for the lower limb. The rationale for using local anesthetic in the mixture is that there is less pain at the initiation of the injection. However, local anesthetics can reduce the sympatholytic actions of guanethidine [42].

Complications

Drug Effects

Despite the relative simplicity of the technique, there is a risk of unwanted systemic absorption if the drug bypasses the inflated tourniquet or following deflation. Transient decrease in blood pressure on tourniquet release is common [43], although Sharpe et al. reported prolonged hypotension (80 mmHg for 1 week) can occur after repeated blocks [44]. Autonomic denervation due to drug accumulation may be responsible for the prolonged hypotension.

Other adverse events following cuff deflation were transient apnea and syncope during an intravenous regional anesthesia using guanethidine and lidocaine [45]. Whether this neurologic event was due to hypotension or drug toxic reaction is unclear. Seizures following cuff deflation have been reported with a tourniquet time of as long as 60 min with a lidocaine dose as low as 1.5 mg/kg. Compartment syndrome has also been reported [46].

Visceral Nerve Blocks

Celiac Plexus Block

The celiac plexus innervates the upper abdominal viscera, including pancreas, diaphragm, liver, spleen, stomach, small bowel, ascending and proximal transverse colon, adrenal glands, kidneys, abdominal aorta, and mesentery. It contains preganglionic splanchnic afferent, postganglionic sympathetic fibers, and parasympathetic fibers (Fig. 16.6). Celiac plexus blockade may therefore be indicated in chronic or cancer pain involving one of these organs, the pancreas and stomach being the most common.

The greater (T5–10), lesser (T10–11), and least (T12) splanchnic nerves form the preganglionic sympathetic supply for celiac ganglia. These nerves lie on the thoracic paravertebral border, pierce the diaphragmatic crura, and form the plexus lying on the anterior and lateral aspects of the abdominal aorta, between the origins of the celiac arterial axis and the renal arteries. The celiac ganglia number between one and five and may be up to 4.5 cm in diameter.

Four techniques of blocking the splanchnic nerve and celiac plexus are commonly used. The first is the retrocrural splanchnic nerve block technique. The needles, one on each side, are placed posteriorly and paravertebrally below the 12th rib and advanced medially to make contact with the L1 vertebral body. With this approach, the aim is to position the needle tip close to the splanchnic nerves behind the aorta and the diaphragm. A modification of this classical retrocrural technique is to direct the needle more cephalad at the level of the anterolateral margin of T12 vertebra. Theoretical advantage of this modification is to block the visceral sympathetic pathway more effectively with a smaller volume of neurolytic solution. The second approach is the transcrural tech-

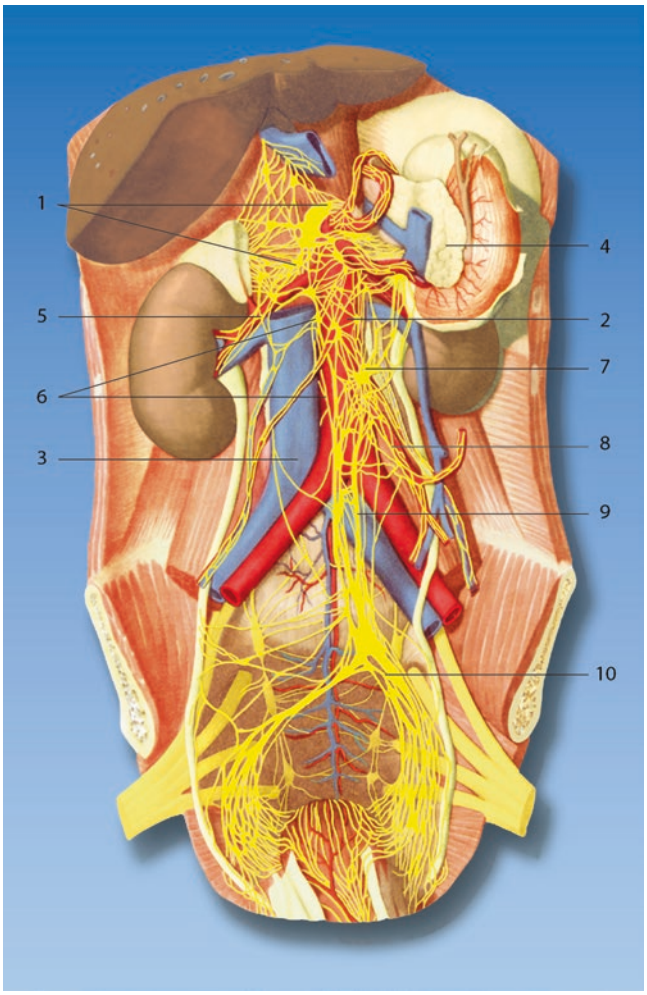

Fig. 16.6 Anatomy of the neural plexus to the visceral organ. (*1*) Celiac plexus, (*2*) aorta, (*3*) inferior vena cava, (*4*) pancreas, (*5*) renal plexus, (*6*) abdominal aortic plexus, (*7*) inferior mesenteric ganglion, (*8*) inferior mesenteric plexus, (*9*) superior hypogastric plexus, (*10*) inferior hypogastric plexus. Reproduced with permission from Dr. Danilo Jankovic

nique, which aims to block the celiac plexus proper by positioning the needles (one from each side) farther anterior and through the diaphragmatic crura. Under radiologic guidance, injectate is deposited anterior and caudal to the crura and posterior to the aorta. A smaller volume of drug is required, thus minimizing the risk of somatic block. The third approach is the transaortic approach developed by Ischia using a single needle from the left side of the back [47]. The advantages of this technique are a single needle insertion and a smaller dose requirement of local anesthetic or neurolytic agent, resulting in a lower risk of retrocrural somatic spread. However, there is a slightly higher risk of hematoma formation. The fourth approach is a percutaneous anterior approach. Fine needles guided by ultrasound may be used [48]. Visceral or vascular perforation can occur, but the sequelae of perforation may be minimized by antibiotic coverage and avoidance of the technique in "coagulopathic" patients. Celiac plexus block can also be performed under direct vision following a laparotomy. Alternatively, endoscopic ultrasound-guided (EUS) injection is a safe and cost-effective approach [49]. With an ultrasound transducer mounted in front of the viewing lens of the endoscope, the aorta and celiac artery can be easily identified as reference landmarks prior to injection.

Celiac plexus block is considered to be a relatively safe procedure; however, the possibility for serious complications exists. In many clinical contexts in which this block is offered (e.g., intra-abdominal malignancy), the analgesic benefit is considered to outweigh these risks.

Complications

Hypotension

Because of the sympathetic blockade of splanchnic vasculature, the most common complication of celiac plexus blockade is hypotension. Without adequate prehydration or vasopressor drugs, this may occur in 30–60 % of patients. There is some evidence that the incidence of hypotension is higher with a retrocrural approach [50]. In a meta-analysis of neurolytic celiac plexus blocks, Eisenberg et al. report 10 studies covering 571 patients of whom 217 (38 %) had hypotension [51]. Splanchnic vasodilatation and visceral blood pooling contribute to orthostatic hypotension. Providing an intravenous fluid bolus prior to the procedure can minimize the incidence of hypotension. It is recommended that blood pressure and an electrocardiogram (ECG) be monitored for 2 h after a block. Patients should remain supine or in the lateral position for at least 1 h postprocedure, or until they can stand unaided. In approximately 3 % of patients, orthostatic hypotension may persist for up to 5 days [52].

Diarrhea

Unopposed parasympathetic activity following celiac plexus block can lead to gastrointestinal hypermotility [53]. Additionally, after a successful celiac plexus block the patient will need smaller doses of opiate analgesics. Diarrhea is usually transient, but may sometimes develop a chronic pattern. The incidence of transient diarrhea is approximately 40 % [54]. When diarrhea occurs in the presence of preexisting dehydration and pooling of blood in the splanchnic circulation, life-threatening hypovolemia may appear if massive intestinal fluid loss is not replaced. Somatostatin has been suggested as therapy in this situation, and octreotide may have a role in treatment of persistent diarrhea.

Needle Trauma

Needle puncture and drug injection into the aorta, vena cava, renal vessels, and various viscera have been reported [55].

The anatomy may be distorted by tumor or other mass in the retroperitoneum or abdomen. One expects the risk of hematoma formation to be highest with Ischia's transaortic approach. Aortic puncture is more likely with needle placement on the left side than on the right side. A large retroperitoneal hematoma following vascular puncture may cause hypovolemia and must be differentiated from hypotension due to splanchnic vasodilatation. Limiting the size of the needle and ensuring normal patient coagulation status will reduce the risk of bleeding.

Aortic dissection after formation of an infected pseudo aneurysm has been reported after celiac plexus block, possibly related to the effect of neurolytic agent on the aortic wall [56]. Kaplan et al. report fatal aortic dissection, which extended to the superior mesenteric and hepatic artery, resulting in extensive liver and bowel infarction [57]. Other vascular complications include phlebitis, vessel thrombosis, and vasospasm.

Unintentional injection between vertebrae producing an incidental discogram was reported by Wilson [58]. Pneumothorax is another theoretical complication, even though the point of needle insertion is below the 12th rib. Chylothorax has been reported in association with tumor and after puncture of the cisterna chyli during celiac plexus block [59]. The cisterna chyli classically lies anterior to the first two lumbar vertebrae to the right of the aorta, but this is variable. The transdiaphragmatic movement of the retroperitoneal lymph collection is via lymphatic. Retroperitoneal fibrosis after multiple blocks has been reported [60].

Infection

Because of the proximity of the needle path to the bowel, especially with the anterior and EUS approach, infection is a concern. In a series of 90 patients, only 1 patient developed an infectious complication, a peripancreatic abscess, which resolved with a short course of antibiotics [61]. Retroperitoneal abscess has also been reported [62].

Neurologic and Neurovascular Sequelae

The most serious complications of celiac plexus block are neurologic; however, the overall incidence of major neurological adverse events is low [63, 64]. There are several mechanisms of injury. Drug misplacement and anomalous or excessive retrocrural spread can affect epidural and lumbar somatic nerve roots. Direct accidental intrathecal injection can also occur, which could lead to permanent paraplegia. Permanent and extensive autonomic blockade may cause male sexual dysfunction.

The arterial supply to the spinal cord may be damaged during celiac plexus block. The anatomy of the blood supply is variable, and the major radicular artery of Adamkiewicz may arise from T7 to L4. In 80 % of patients, this vessel lies on the left. It enters via a single intervertebral foramen to supply the anterior spinal artery of the lower two-thirds of the cord. Damage to this artery (either mechanical by a needle or chemical by neurolytic drug) may lead to paraplegia. Although radiologically guided techniques minimize the incidence of direct intravascular injection, neurolytic drugs deposited perivascularly may alter arterial reactivity and cause vasospasm. This has been demonstrated in isolated canine lumbar arteries in vitro [65]. Injury to artery of Adamkiewicz due to compression, spasm, or both can lead to anterior spinal artery syndrome [66]. There is a possibility that using only a right-sided approach might lessen the incidence, but it might also diminish the effectiveness.

The incidence of paraplegia is difficult to estimate, but a meta-analysis by Eisenberg shows that it may lie between 0.1 and 0.5 % [51]. Davies surveyed complications of all blocks done in a 5-year period (1986–1990) in England and found an incidence of paraplegia of 1 in 683 (0.15 %) [64].

Drug Effects

Phenol-induced cardiotoxicity may account for a report of cardiac arrest in a patient undergoing intraoperative splanchnic nerve block during laparotomy [67]. Ventricular fibrillation occurred 3 min after injection of 30 mL of 6.66 % phenol, after negative aspiration under direct vision. The authors cite other reports of cardiac toxicity of phenol, mostly arising from transdermal absorption in dermatologic and plastic surgical practice, where much higher doses are used. In the case of celiac plexus block, cephalic spread of the neurolytic agent may result in involvement of the cardiac nerves and plexus, which may in turn affect the heart and surrounding thoracic structures [68].

Systemic effects have been reported as a result of absorption of a large volume of alcohol administered for retrocrural celiac plexus block. Measured serum ethanol concentration was up to 39 mg/dL after injection of 25 mL of 50 % ethanol bilaterally and 29 mg/dL after 15 mL of 99.5 % ethanol [69, 70]. Although this will not cause any serious impairment and is below the legally defined limit for intoxication, the authors noted that all patients reported a feeling of mild euphoria. However, toxic alcohol levels may appear in patients who have a genetic deficiency of aldehyde dehydrogenase, which is relatively common in the Japanese population. There is also a possibility of interaction with drugs such as disulfiram or metronidazole, although this has not so far been reported.

In summary, the retrocrural technique has the lowest risk of visceral or vascular puncture, but a higher risk of somatic nerve block due to a larger volume of drug. Transcrural injection requires smaller volumes but has a slightly increased risk of perforation of vital visceral structures. Transaortic celiac plexus block, a single-needle technique, uses the least amount of drug but most likely causes vascular damage and hematoma formation even with a fine needle.

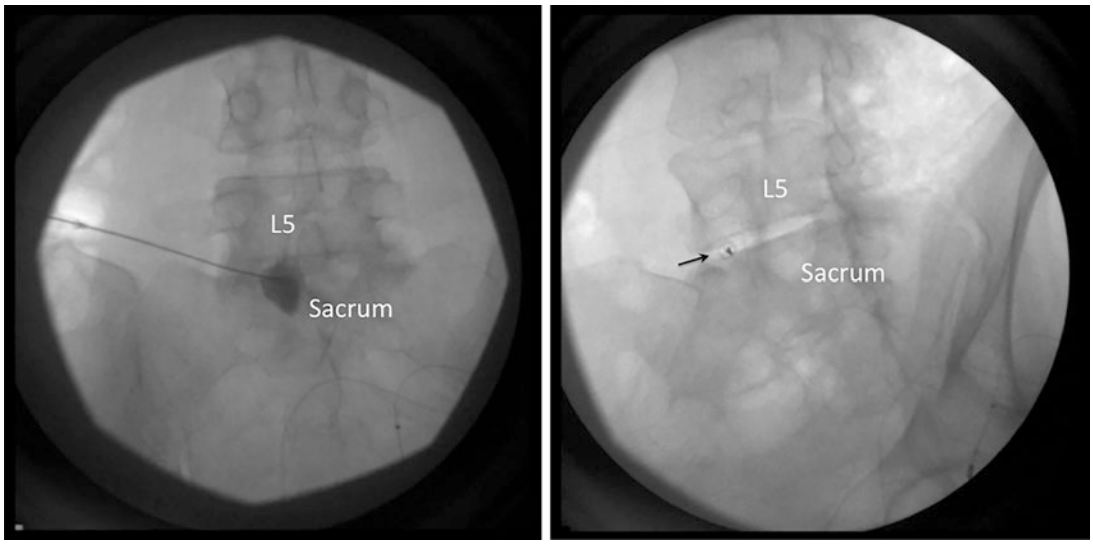

Fig. 16.7 (**a**) The image on the left is an anteroposterior radiograph of the lumbosacral junction. The needle was seen inserted to the anterior aspect of the lumbosacral junction with contrast confirmation. (**b**) The image on the right is an oblique radiograph of the lumbosacral junction. The spinal needle (indicated by the *arrow*) was inserted with transdiscal technique evident with the end-on view. Thus, only one needle inserted was required as this technique allowed the needle to reach the anterior aspect of lumbosacral junction. Reproduced with permission from Philip Peng Educational Series

Pelvic Visceral Nerve Blocks

The superior hypogastric nerve and the ganglion impar are two sites amenable to blockade for chronic or cancer pain of the lower abdominal or pelvic organs [71]. The superior hypogastric plexus is found on the anterior aspect of the sacrum, in the midline (Fig. 16.6). Approach to the superior hypogastric plexus is percutaneous, from a point between the sacral ala and the interspace between the L5 and S1. The needle passes anteromedially to the anteriolateral aspect of the L5–S1 area. A transdiscal technique has been described (Fig. 16.7) [72]. The ganglion impar (or ganglion of Walther) lies on the concavity of the sacrum and is blocked percutaneously using a specially bent needle inserted toward the sacrococcygeal junction. The transdiscal technique is gaining popularity because of easier access to the target site without bending the needle (Fig. 16.8) [73].

Despite the presence of a number of case series, there are no recent reports of complications from the superior hypogastric plexus block [74]. Intravascular injection can easily occur due to the close proximity of the iliac vessels. Although there are limited reports of complications with the transdiscal technique, careful technique should be used to minimize the risk of discitis, disc herniation, or disc rupture [75, 76]. Strict sterile technique should be used, and some practitioners advocate for the use of periprocedural antibiotic prophylaxis to minimize the risk of infectious complications.

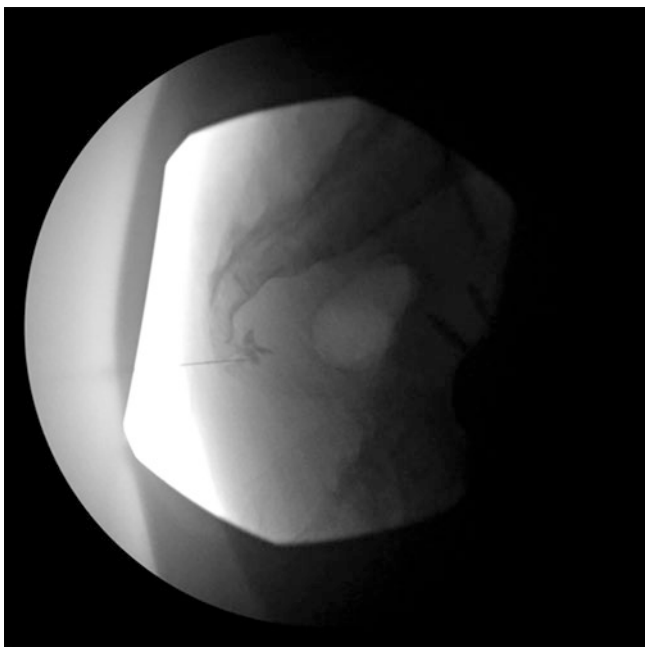

Fig. 16.8 Ganglion impar injection. The needle was inserted via the sacrococcygeal disc space. The puncture needle was initiated by the introducer needle through the skin and then a 25 G spinal (Whitacre) needle was inserted through the introduced needle to minimize the risk of discitis. The needle position was further confirmed, with contrast (with permission from Philip Peng)

Regarding the ganglion impar block, Plancarte et al. published a case report in which epidural spread of contrast material was demonstrated within the caudal canal [71].

However, no adverse effects resulted from this. Overall, the ganglion impar block is considered to be a safe procedure with no long-term complications being reported.

Somatic Nerve Blocks

Facet Joint Block

The lumbar facet (zygapophyseal) joint has long been considered by some to be a significant source of low back pain whereas cervical facet joint disease is linked to chronic neck pain [77]. The facet or zygapophyseal joints are true synovial joints with considerable sensory innervation and overlap. The medial branch of the posterior ramus supplies the lower pole of one facet joint and the upper pole of the adjoining facet joint.

A diagnostic facet joint injection or a medial branch block may be considered in patients with back or neck pain. Real-time fluoroscopic- or ultrasound-guidance is recommended to ensure accurate needle placement because off-target injection by a few millimeters can result in aberrant drug spread to intervertebral neural foramen or the epidural space, yielding false positive result of pain relief [78]. Injection of contrast material (0.3 mL) can enhance accuracy and injection of a small volume of local anesthetic (0.5–1 mL) will decrease the risk of spread to the epidural space or somatic nerves. In the neck, the vertebral artery lies just lateral to the facet joint, thus intravascular injection or damage is known risk.

Complications

Increased Pain

Transient increased pain is the most common side effect (2–20 %), which may last from 6 weeks to 8 months [79].

Infection

Infection is the most common serious complication following facet joint injection [80]. This includes case reports of iatrogenic septic arthritis [81, 82], epidural abscess [83], spondylodiscitis [84], and paraspinal abscess [85].

Intraspinal Injection

Configuration of the facet joints in the lumbar spine (oblique orientation with a curved shape) largely prevents needles from entering the vertebral canal; however, spinal anesthesia following attempted lumbar facet block has been reported [86]. These cases may be due to erroneous needle placement, possibly through a nerve root dural cuff.

Thomson et al. report chemical meningism after attempted facet joint block with local anesthetic and steroids, and this was presumably caused by inadvertent intrathecal injection, since there are very few reports of meningism associated with epidural injection of steroids [87]. Spinal cord injury during attempted cervical facet joint injection has also been reported [1].

Other Complications

Excessive local anesthetic injection and spread to the somatic roots can cause ipsilateral weakness, although we have found no recent reports of this obvious complication. This may be caused by needle placement too anterior or excess volume causing joint rupture. It should be remembered that the maximum volume of the facet joint is 1.0 mL. Pneumothorax during attempted thoracic facet joint injection has been reported [1]. Overall, the facet nerve block is a very safe procedure if one follows the recommended technique and aseptic protocol [80].

Facet Joint Radiofrequency Denervation

Radiofrequency (RF) neurotomy interrupts nociceptive pathways by applying heat (75–800 °C) from the tip of an electrode to denervate nerves. This technique is used for treatment of trigeminal neuralgia, dorsal rhizotomy, and dorsal root entry zone (DREZ) interruption for deafferentation syndromes [88]. Radiofrequency procedure can also be used for facet joint denervation in the lumbar and cervical regions. The complications are commonly secondary to direct needle trauma, needle misplacement during lesioning, and to low-level heat injury to the nerve.

Complications

Various side effects have been reported for cervical radiofrequency neurotomy, including postoperative pain, ataxia, denervation sensitivity, and vasovagal syncope [89, 90]. Ataxia is most common when the third occipital nerve is treated. The third occipital nerve carries a large proportion of fibers that provide cutaneous, innervation, and as a result postprocedural numbness can occur, which often leads to temporary dysesthesia and pruritus after 1–3 weeks. These side effects are relatively common and predictable outcomes that are attributed to destruction of the target nerve, hence these outcomes are not commonly referred to as complications [91].

More serious complications that arise from cervical RF neurotomy are rare but have been reported. Many of these complications have occurred during RF techniques that were performed under general anesthesia when the patient was unable to report adverse symptoms. These complications can be devastating and range from misplacing electrodes adjacent to the spinal cord during lesioning (leading to direct spinal cord injury) to thermocoagulation of reinforcing radicular vessels leading to spinal cord infarction [91].

Fluoroscopically guided percutaneous radiofrequency denervation of the lumbar facets is commonly used as a treatment for chronic low back pain. Adverse effects in this region of the spine are less common compared to cervical RF neurotomy. Complications occur in approximately 1 % of patients and present mostly as localized pain or neuritis pain in the first 2 weeks after treatment [92]. Cutaneous numbness and dysesthesia can also occur but usually resolve within 3 weeks [88]. Severe nerve injury, such as injury to the spinal nerve or ventral ramus, is rare but has been reported [91, 93]. This complication results in denervation of the entire associated dermatome and myotome of that segment in the lower limb. Other complications that have been reported include superficial burns due to insulation breaks in the electrodes, as well as burns at the site of the grounding pad adhesion due to generator malfunction [94, 95].

Pulsed radiofrequency is emerging as a popular technique in the management of neuropathic pain. This technique does not appear to be neurodestructive [96], and there is little published evidence demonstrating its efficacy [88]. Consideration for complications due to pulsed radiofrequency will not be addressed in this review.

Epidural Blockade

The epidural space may be approached in the cervical, thoracic, lumbar, or sacral regions (via the sacral hiatus). The most frequently injected agents are steroids and dilute local anesthetics, although opioid has been used in some circumstances [97, 98]. These injections are used with increasing frequency in the management of chronic spinal pain and radiculitis [99]. The transforminal approach to the epidural space has become popular in recent years because it has proven clinical efficacy over conventional techniques [100]. The major advantage of this approach is drug delivery directly to the site of nerve root impingement as opposed to only a fraction of the injected dose reaching target with the conventional interlaminar approach [101].

In 2004, the American Society of Anesthesiologists Closed Claims Study identified major complications associated with epidural steroid injections that resulted in malpractice claims [1]. Complications specific to steroid injections can relate to local or systemic drug effects. The mechanical and traumatic complications can also occur; however, these complications are similar to any epidural injection and will be discussed elsewhere. The Closed Claims Study did not specify complications that may occur according to the levels and techniques of needle insertion, and there has been a growing concern of neurological complications following the use of the transforaminal approach and injections performed at the cervical level [102]. The former will be discussed separately later, and the complications associated with cervical epidural steroid injection have been reviewed elsewhere [103]. A recent retrospective study examined 4265 ESIs performed in 1857 patients, over a 7-year period which included 161 cervical IL injections, 123 lumbar IL injections, 17 caudal injections, and 3964 lumbar TF injections [99]. While there were no major complications identified, there were 103 minor complications that resulted in an overall complication per injection rate of 2.4 %. In this review, the most common complications were increased pain (1.1 %), pain at the injection site (0.33 %), persistent numbness (0.14 %), and "other" (0.80 %). Complications were less common with a transforaminal technique (2.1 %) compared to an interlaminar approach (6 %). This section will provide an update regarding complications associated with epidural steroid injections.

Complications

Neurotoxicity

Arachnoiditis and aseptic meningitis are direct complications that may result from unintentional intrathecal (not epidural) injection of steroid. The symptoms of arachnoiditis can overlap with the symptoms for which many patients are receiving epidural steroid injections, as it most commonly occurs among patients who have had multiple spinal procedures. Recently, Lima et al. performed a randomized, double-blind controlled trial on dogs that demonstrated intrathecal administration of methylprednisolone was responsible for causing histological changes in the spinal cord and meninges [104]. Findings included meningeal thickening, adhesion of the pia, arachnoid, and dura mater, and nerve roots surrounded by fibrosis. Furthermore, a review by Abram and O'Connor identified 65 published series and 18 case reports in 6947 patients who received one or more epidural steroid injections and 368 patients who received one or more subarachnoid steroid injections [105]. There were no reports of arachnoiditis after epidural injection of steroids when intrathecal injection was excluded, highlighting the importance of using a local anesthetic test dose, and/or fluoroscopy with radiocontrast dye to help minimize the risk of inadvertent intrathecal injection of steroid. Nelson suggested that polyethylene glycol may be the offending agent [106]. However, Benzon et al. found that nerve conduction was affected by polyethylene glycol at concentrations seven times higher than clinically relevant concentrations [107]. Even at higher concentrations, the conduction defects were reversible. There is no definitive treatment for arachnoiditis or aseptic meningitis [108].

Neurologic Injury

Severe neurological injury following cervical, thoracic, or lumbar epidural steroid injections can occur due to direct

needle trauma to the spinal cord. This type of injury can occur with any epidural injection and will be discussed elsewhere. Another mechanism of injury relates to the injection of a steroid suspension that results in embolization of end arterioles supplying the spinal cord [109]. The blood supply to the spinal cord comes from a single anterior spinal artery and two posterior spinal arteries. At each vertebral level, radicular arteries from the aorta travel along with the segmental nerve roots into the neural foramen and supply the corresponding nerve roots. Some of these radicular branches contribute to the perfusion of anterior spinal cord by joining the anterior spinal artery. The most important radicular artery supplying the lumbar region is the artery of Adamkiewicz. At the cervical level, the important contributing radicular artery originates between C3 and C8. This type of embolic injury appears to be most commonly associated with injections performed at the cervical level. Following cervical transforaminal injections, fatal anterior spinal artery syndrome [110], massive cerebellar infarct [111], and bilateral complete cortical blindness [112] have all been reported. Transforminal injections performed in the lumbar region carry a lower risk; however, it has been determined that previous surgery at this level may increase the risk of spinal cord infarction [113]. All of the particulate-containing corticosteroid preparations available for use have been found to contain large enough particles to occlude capillaries and arterioles. Dexamethasone is a nonparticular steroid solution that minimizes this risk, however, theoretically may result in a shorter duration of effect due to increased solubility [114].

The rate of unintentional intravascular injection using the transforaminal approach is estimated to be 11 % [115]. It is important to note that the sensitivity of a positive blood aspirate in detecting intravascular injections is only 45 %. According to the Closed Claims Study, spinal cord injury due to infarction appears to be less common than injury due to direct spinal cord trauma [1].

Infection

Until recently, infectious complications following epidural steroid injections were considered to be extremely rare; however, the risk has been highlighted by recent catastrophic events [108]. In 2012 in the United States, an outbreak of fungal meningitis occurred among patients who received an injection containing contaminated preservative-free methylprednisolone acetate [116, 117]. In total, there were 751 cases of fungal infection, resulting in 64 deaths. The majority of these patients received the injection through an epidural or paraspinal route (89 %), with the remainder receiving peripheral joint or other nerve injections. Furthermore, in 2012 there was an outbreak of methicillin-sensitive *Staphylococcus aureus* (MSSA) infections in Toronto, Ontario, Canada following epidural steroid injections. An investigation concluded that nine patients developed serious infections (meningitis and/or abscesses) over a 4-month period [118].

In theory, the risks of neuraxial infection are increased when faulty aseptic technique or bacteremia is present, as for any spinal injection. However, as per the fungal outbreak in the United States in late 2012, contaminated medication at the time of injection can also be a contributing factor. In theory, the immunosuppressive effects of steroids may increase the risk of an infection. However, epidural abscesses can also occur on an idiopathic basis, in the absence of an intervention, and certain risk factors can increase this incidence. Tang et al. reviewed 46 cases of spontaneous epidural abscess and found that 46 % of these patients were diabetic [119]. In addition to fungal pathogens, common bacterial culprits would include *Staphylococcus aureus* (likely skin contaminant) [120, 121].

It would seem that, despite the theoretically increased risk of infection, clinical reports do not indicate that there is any greater incidence associated with epidural steroids than with local anesthetic agents alone, provided the same precautions and contraindications are noted. Even allowing for underreporting, the incidence just from published series and reports appears to be less than 0.01 %. With such a low incidence, routine prophylactic antibiotic use cannot be justified as this could lead to development of resistant antibiotic strains [108].

Dural Puncture

The frequency of inadvertent dural puncture in the laboring population ranges from 0.04 to 6 % [122]. However, the incidence of a headache is lower among patient undergoing ESI, likely due to the use of smaller gauge needles, an older patient population, and the use of contrast dye during fluoroscopic guidance. McGrath et al. analyzed 284 IL epidural injections and reported only 1 postdural puncture headache (incidence of 0.004 %) [99]. Proceduralists performing these techniques must be able to identify and recognize various patterns of contrast dye following administration to avoid the direct injection of medication into the intrathecal or subdural space.

Systemic Side Effects of Steroids

Suppression of adrenal cortical response has been reported after oral, nasal, inhaled, and parenteral as well as epidural steroid administration. Cushingoid side effects, including fluid retention, electrolyte imbalance, and fat redistribution, have been reported after epidural steroid injection. Stambough et al. [123] reported a case of hypercorticism after two injections a week apart totaling 160 mg of methylprednisolone acetate while Tuel et al. [124] reported one case following a single cervical epidural administration of 60 mg methylprednisolone acetate. In both cases, return of normal clinical and biochemical functions took weeks to months. Exogenous

steroid replacement should be considered for patients undergoing surgery who have had epidural steroids administered within the previous 3 months [125].

Steroid-induced myopathy is characterized by progressive proximal muscle weakness, increased levels of creatinine kinase, and myopathic evidence on electromyography. Iatrogenically induced steroid myopathy (proximal limb) was reported by Boonen et al. after epidural administration of triamcinolone diacetate [126].

The effects of steroids on glucose levels must also be considered. Steroid administration is known to reduce the hypoglycemic effect of interfere, leading to increased blood glucose levels in diabetic patients [127]. Diabetic patients can be warned about experiencing elevated blood glucose levels (and insulin requirements) for several days after administration of corticosteroids. Even et al. [128] assessed 30 diabetic patients who received an ESI and found elevated blood glucose levels which normalized within 2 days.

Although there is no consensus for the frequency or dose of steroid administration to prevent systemic side effects, it is prudent not to repeat injections within a 4-week interval and to limit the number of epidural steroid injections to three in 6 months, based on human and animal data.

Systemic Side Effects of Epidural Opioid

A review from 2005 found that only 2–10 % of anesthesiologists in North America add opioid to epidural steroid [97]. The addition of epidural morphine to steroid may further relieve low back pain but the associated benefits vary [129, 130]. Most of these early studies added 8 mg of epidural morphine to steroid. However, life-threatening ventilatory depression was noted in 3 of 14 patients who received an admixture of steroid and morphine (8 mg) [131]. While lower dose epidural opioid (e.g., morphine 5 mg) has been used, the effect produces analgesia up to 24 h [132]. The common side effects are pruritus (57–90 %), nausea and vomiting (40–64 %), and urinary retention (20–43 %) [129–132]. Clinicians must carefully weigh the limited benefit of epidural opioid against potential serious risks.

Other Complications

Various minor complications have been reported in different case series (Table 16.1). McGrath et al. identified the most common complications as being increased pain (1.1 %), pain at injection site (0.33 %), and persistent numbness (0.14 %) [99]. Overall, these complications were more common with the TF technique when compared to IL. Other complications identified include a decrease in bone marrow density in postmenopausal women who received a cumulative ESI dose of greater than 120 mg methylprednisolone [133]. A follow-up analysis did not identify an increased incidence of pathological fractures in this population [134]. Case reports exist describing delayed allergic reactions to epidural steroid/local anesthetic [135], persistent hiccup presumably due to systemic effect of steroid [136], and vision loss secondary to retinal hemorrhage [137].

Table 16.1 Complications and side effects of epidural steroid injection (interlaminar and caudal approach): aggregate data from published series

Injection type	Number reported	Complications or side effects	
Cervical epidural injections	1788	Neck stiffness, pain [138, 139]	40 (2.2 %)
		Facial flushing [138, 139]	24 (1.3 %)
		Headache [138]	16 (0.9 %)
		Nausea/vomiting [139, 140]	10 (0.6 %)
		Hypotension (inc. vagal) [138, 141]	9 (0.5 %)
		Dural tap [138, 139, 141, 142]	7 (0.4 %)
		Other (fever, insomnia) [138]	7 (0.4 %)
Cervical subtotal			123 (6.9 %)
Lumbar, thoracic and caudal epidural injections	13,233	Headache [95, 143–146]	45 (0.34 %)
		Dural tap [147–152]	35 (0.26 %)
		Hypotension (inc. vagal) [15, 138, 153, 154]	7 (0.13 %)
		Systemic steroid effects [147, 154, 155]	6 (0.05 %)
		Facial flushing [143]	6 (0.05 %)
		Other	26 (0.20 %)
			(fever [147], nausea, bloody tap [154], DVT [146], insomnia [143], increase back/leg pain [143])
Lumbar, thoracic and caudal subtotal			125 (0.94 %)
Total	15,021	All of the above	248 (1.65 %)

Several series reported no side effects or complications, but discussion was lacking. Data adapted and modified from Abram & O'Connor [105]

Neural Ablative Procedures

Nerve destruction is reserved mainly as a last resort for patients with debilitating pain related to cancer [156] and occasionally for noncancer conditions (e.g., postherpetic neuralgia [157] and bone graft donor site [158] that are refractory to conventional treatments). Neurolysis of peripheral nerves (e.g., sciatic, obturator nerves) has also been applied to relieve muscle spasticity following hemiplegic stroke [159]. Because neural ablative procedures are not commonly practiced, few clinical studies have documented their relative clinical effectiveness, leaving the practice of these procedures rather empirical. Neurolysis can be achieved in a number of ways: chemically induced with the use of alcohol or phenol, or by radiofrequency coagulation, cryoprobe, and surgery. This review will focus on complications associated with chemical neurolysis performed by regional anesthetic procedures.

Neurologic complications of chemical neurolysis are drug related and vary according to the site of injection. Injection sites will include peripheral application on a peripheral nerve or centrally in the epidural/subarachnoid space. Rarely, nonneurologic complications, e.g., bronchospasm secondary to accidental intrabronchial or intrapulmonary injection of phenol during an intercostal nerve block can occur [160]. As neurologic complications are potentially devastating, it is important to select patients appropriately and consider including only those with limited life expectancy (less than 6–12 months). Patients must have a clear understanding of the risk: benefit ratio of the proposed procedure. Here, we will highlight the use of peripheral and central neurolysis to treat malignant somatic pain. Neurolytic blocks for visceral and sympathetically mediated pain have been discussed earlier.

Neuropathic Effects of Neurolytic Agents

Neurolytic agents are applied to section a nerve and disrupt its transmission chemically rather than surgically. Commonly used agents include phenol, alcohol, and glycerol. Less commonly used ones are ammonium sulfate, hypertonic saline, chlorocresol, and butyl aminobenzoate (Butamben). Phenol is commonly prepared as an aqueous 5–7 % solution or as a concentrated 10–12 % solution in glycerin. Alcohol is used most often as a 95 % solution. Because of the nature of the vehicle solution, phenol in glycerin is hyperbaric while alcohol is hypobaric; this is an important consideration when performing central neurolysis.

The neuropathic effect of alcohol and phenol is nonselective. When applied to neural tissues, phenol coagulates proteins and injures perineural blood vessels, resulting in neural ischemia; ethyl alcohol extracts cholesterol, phospholipid, and cerebroside from neural membranes, leading to precipitation of lipoproteins and mucoproteins. There is no proof that small unmyelinated C fibers transmitting nociception are more vulnerable to neurolytic destruction than larger A beta sensory fibers for thermal and mechanical sensation.

Neurologic Complications

Neurolytic agents destroy sensory, sympathetic, and motor nerve fibers indiscriminately, especially when used in high concentrations and large volumes. To minimize the risk of neurologic deficit, needle placement should be accurate and aided by nerve stimulator or radiologic guidance. It is advisable to first perform a diagnostic local anesthetic block in the same target area prior to neurolysis. This allows both the patient and physician to assess the resultant pain relief and the extent of potential damage. Neurolytic agents can also destroy extra neural structures. Before needle withdrawal, flushing of the needle with saline or air is recommended to avoid skin slough and muscle necrosis.

Motor Paresis

Before a neurolytic agent is applied to peripheral mixed nerves supplying the upper or lower limb, patients must clearly understand that destruction of motor fibers can cause or increase limb weakness. For this reason, neurolysis is ideally reserved for patients with some degree of preexisting limb weakness. To preserve residual function, a dilute 3 % phenol solution has been used successfully in neurolytic brachial plexus block to alleviate arm pain from lung malignancy [161]. However, analgesia is short-lived with this approach. Another way to limit harm is lesioning more selectively and peripherally at the target site. For example, Kaplan et al. [162] performed a selective paravertebral C5–6 nerve root block, and Patt et al. [163] performed suprascapular block to treat malignant upper arm pain. The same risk-limiting measures apply when neurolytic block is performed in the lumbosacral plexus for lower extremity pain. On the contrary, while intercostal neurolysis to treat thoracic and abdominal wall pain can impair intercostal muscle function, the damage usually is of little physiologic consequence. However, proximal epidural spread has resulted in paraplegia following phenol intercostal neurolysis [164].

Central neurolysis performed in the epidural or subarachnoid space can also result in postblock motor paresis [165]. Well-executed, central neurolysis produces neural ablation more selectively, owing to greater separation of motor and sensory nerve roots at the spinal cord site of origin. The goal, therefore, is to execute a chemical dorsal rhizotomy (sensory) without ventral rhizotomy (motor) [156]. If poorly executed, a cervical and lumbosacral central neurolysis can result in

upper and lower limb paresis, respectively. Although rare, quadriplegia due to anterior spinal artery syndrome has been reported following cervical intrathecal phenol injection [166].

Subarachnoid phenol injection can cause motor paresis, in addition to sensory, bowel, and bladder dysfunction, as a result of posterior spinal artery thrombosis and spinal cord infarction [167]. Both anterior and posterior spinal syndromes can occur, presumably secondary to vasospasm and/or thrombosis.

To minimize risk, strict selection criteria and rules should be applied to limit central neurolysis to patients with limited life expectancy and whose pain is localized to two or three dermatomes. First, one must appropriately pick the lesion target. For example, malignant pain of soft tissue is treated by targeting specific dermatomes, but bony pain in the same area must be treated differently, by targeting the responsible sclerotomes, not dermatomes. Second, one must place the neurolytic agent as close to the targeted dorsal root as possible. It is important to recognize that the level at which a particular nerve root leaves the spinal cord is generally higher than the corresponding vertebral body. For example, L3 nerve root leaves the spinal cord at the level of T11–12 vertebral body. Thus, when doing a neurolysis of the L3 root, injection should be made at the T11–12 interspace and *not* L3.

When performing subarachnoid neurolysis, patient positioning is crucial in order to limit inadvertent drug diffusion to the ventral root. Positioning varies according to the choice of neurolytic agent. If hypobaric alcohol is used, the pain site should be positioned uppermost; the opposite is the case when hyperbaric phenol in glycerin is used [168]. Furthermore, to target the dorsal root specifically, the patient should be positioned at a 45-degree angle anteriorly when using hypobaric solution but should be angled posteriorly when a hyperbaric solution is used. Also, the patient should remain in this position for at least 30–45 min after injection, to limit spread elsewhere.

Similar to peripheral neurolysis, it is always advisable to first perform a local anesthetic prognostic block to determine adequacy of analgesia, the extent of motor blockade, and paresthesia. One should remember that local anesthetic is not as hypobaric as alcohol, so the resultant block area may be somewhat different. During injection, dose fractionation using 0.1 mL aliquots of alcohol should be used to improve accuracy. If several dermatomal levels are to be blocked, separate subarachnoid injections should be made at each level. One must remember that alcohol does not diffuse well in CSF and injecting a large volume of alcohol at a single spinal level does not reliably block neighboring levels but increase the risk of motor paresis.

When epidural neurolysis is performed, complication can be minimized if an indwelling catheter is used, so that repeated injections can be given in small increments over several days. Before neurolysis, catheter position should be checked with local anesthetic (no more than 5 mL) to document correct spread of drug and correct catheter tip position in relation to dermatomal pain site. Dosing of the neurolytic should be slow. For example, no more than 0.2 mL of alcohol is injected as a bolus and 3–5 mL is injected slowly over 20–30 min. Also, one must look for reports of tingling and numbness in nontarget areas (e.g., when doing a midthoracic neurolysis, paresthesia in the fifth finger or anterior thigh is indicative that spreading has gone to nontargeted T2 and L2–3 dermatomes) [169].

Loss of Bladder and Bowel Control

Destruction of the S2–4 parasympathetic fibers supplying the bladder, rectum, and colon can lead to urinary and fecal incontinence, respectively. Central neurolytic block performed in the lumbosacral region poses the greatest risk, although deficit following thoracic injection has also been reported [170]. Voiding is less likely to be affected after peripheral neurolysis even when performed in the sacral nerves [171]. There has been one report of bladder atony after an S3–4 alcohol block [172]. To minimize risk, it is advisable to perform a preneurolysis local anesthetic diagnostic block followed by a urodynamic study, to use radiologic guidance, and to limit injection volume (e.g., 1-mL aliquots at each sacral foramen).

Postblock Pain

Reactive neuritis, neuroma formation, and deafferentation pain are causes of postneurolytic pain in the denervated area after an initial period of pain relief. Painful paresthesia and neuritis develop in 2–28 % of patients after peripheral neurolysis with phenol or alcohol [173]. Raj suggested that this may be the result of incomplete lesioning and pointed out that when phenol intercostal nerve block was executed with precision under direct vision, neither neuritis pain nor deafferentation pain occurred [174, 175]. It is thought that alcohol may be more likely to cause neuritis than phenol, but this is unproven.

Pain, in form of mechanical hypersensitivity, can occur after peripheral neurolysis. This can be due to spontaneous firing of neuromas that were formed by sprouting of injured axons. Deafferentation pain can also appear as a new form of neuropathic pain. Dysesthesia and hyperalgesia may appear in an area of anesthesia, resembling the anesthesia dolorosa seen in gasserian ganglion neurolysis for trigeminal neuralgia.

Implantable Catheters and Drug Delivery System

Implantable catheters are placed in the epidural [176, 177] or subarachnoid (intrathecal) [178] space for long-term delivery of analgesics for treatment of debilitating pain from

malignancy [117, 179] and nonmalignant conditions [180–182]. Intrathecal analgesia may be preferred over the epidural route because of lower analgesic consumption, fewer drug refill, and fewer mechanical problems [177, 183]. Additionally, subarachnoid infusion of baclofen is sometimes used to treat lower limb spasticity from multiple sclerosis or quadriplegia [184].

There are three types of intraspinal drug delivery systems [182]. Implantable catheters can be connected to (1) an internalized subcutaneous programmable pump (e.g., Synchromed Infusion Pump, Medtronic Inc.) [185], (2) a subcutaneous port (e.g., the Port-a-Cath port system, Pharmacia-Deltac, Inc.), or (3) an externalized delivery system (e.g., Algoline catheter, Medtronic Inc.). The indwelling end of the catheter in the neuraxial space is sutured in place before it is tunneled subcutaneously from the back to the front. Complications of implantable catheter and drug delivery systems are either mechanical or drug related [186–188]. The safety of the externalized delivery system has notably improved in recent years through a change from bolus administration to continuous infusions and modification of line insertion techniques [189].

Complications

Neurological Injury

Neurologic injury, such as spinal cord and nerve trauma, is a devastating complication that can occur. This type of injury is most common during the placement of the implantable catheter [190]. Minimizing this risk involves utilizing fluoroscopic guidance during placement, and directing the needle below the level where the spinal cord terminates, when possible. This is especially important if one elects to use general anesthesia during placement. Surgical bleeding associated with implantation is rare but catheter-induced epidural hematoma has been reported [191, 192]. Caution must be exercised when the platelet count is below 60,000 or there is suspicious of tumor invasion into the epidural space. Catheter passage in this situation can provoke epidural bleeding.

Infection

Postimplantation infection is mostly localized but can become systemic. The risk of infection is higher in immunocompromised patients who had radiation, chemotherapy, and chronic systemic (HIV) or cutaneous infection. In patients with stomas (e.g., gastrostomy, enterostomy, or nephrostomy), it is important to direct the path of catheter away from these stoma sites, to avoid potential infection. Frequent change of bacterial filters can result in a higher incidence of catheter hub colonization [193].

Localized infection such as an abscess can be formed anywhere along the implanted catheter. It can be superficial at the catheter exit site or deep in the subcutaneous pocket housing the access port and internalized pump, along the catheter tract, and in the epidural space. Superficial infection often produces purulent exudate at the catheter entry site or localized skin inflammation. A wound or pocket infection often presents as inflammatory skin changes overlying the infected area. Fever and leukocytosis may not appear in immunocompromised patients. Needle aspirate from local seroma or wound hematoma showing white blood cells and positive Gram stain confirms the diagnosis.

Epidural or intrathecal space infection and abscess encapsulation [194] are often manifested in the following manner: pain during injection (not previously present), retrograde flow of infusate and pooling of infused fluid in the paravertebral region, and decreased analgesia despite increased dose of analgesics. Spinal epidural abscess can also manifest as back pain, radicular signs, and spinal cord compression [195]. Common pathogens are skin flora contaminants *S. aureus* and *S. epidermidis*; less common ones are *E. coli*, Pseudomonas, *Candida albicans* and Mycobacterium organisms. A localized infection can track along the catheter until it reaches the epidural space. Otherwise, the epidural space is infected through hematogenous spread or through contamination of the analgesic injectate. Diagnosis is confirmed by getting an epidural/subarachnoid aspirate sample for Gram stain and culture as well as a MRI or CT scan to look for abscess. Once detected, both infectious disease and neurosurgery consultants must be involved in patient care.

In the case of an exteriorized catheter, exit site infection can be prevented by regular site cleaning with hydrogen peroxide and chlorhexidine. The catheter and exit site should be protected (e.g., by a minibag) when showering. Bathing in a hot tub is to be avoided. Always the catheter must be handled by aseptic technique, and patient and patient's family are instructed to look for signs of inflammation. If an infection occurs, treatments are daily cleaning with chlorhexidine and topical or oral antibiotics. Complete resolution is expected without catheter removal.

On the other hand, deep track and epidural/subarachnoid space infections must be treated vigorously by removing the catheter and providing parenteral antibiotic therapy. If the catheter is not removed, deep catheter track infection will recur despite antibiotic treatment. Infection may be prevented with intravenous broad-spectrum antibiotics given 1 h preoperatively and two doses given after the procedure every 8 h. Other prophylactic measures include wound irrigation with solution containing antibiotic and using the same fluid to bathe implanted hardware before subcutaneous insertion. Epidural/subarachnoid catheter may be replaced once infection is cleared. Meningitis can occur but is uncommon.

Infection is less likely to occur with the internalized injection port system when implantable catheters are used over the long term. In De Jong's series of 250 epidural catheters, he found that the infection rate for patients with an internalized

injection port was half that for the patients with percutaneous catheters (tunneled or nontunneled) −2.86 infections versus 5.97 per 1000 catheter days, respectively [196]. Patients in the injection port group did not have infection during the first 70 days of use but those with percutaneous catheters did. In this study, catheter tunneling did not offer any protection from infection, most likely because the tunnel was too short (no more than 30 cm). Interestingly, a large prospective multicenter study only showed a small number of superficial infections with implantable intrathecal catheters [197].

Drug-Related Complications

Implantable catheters are most commonly infused with opioids and local anesthetic, less often with α_2-agonist (e.g., clonidine), ziconotide [198], and baclofen [184]. In general, drug-related complications arise when drugs are used in high concentrations and large doses leading to systemic and neurologic toxic sequelae.

Long-term spinal opioid administration can cause constipation, urinary retention especially in men with prostate enlargement, nausea, vomiting, nightmares, and pruritus, in descending frequency [199, 200]. These side effects are often transient in patients who are tolerant to opioids. Endocrine side effects associated with chronic administration include decreased libido and impotency in men and amenorrhea in premenopausal women due to a subnormal level of sex hormones [201]. Respiratory depression is rare, but extremely large doses of spinal opioid can cause central nervous system (CNS) hyperexcitability manifested as muscle twitching, myoclonus, and eventually seizure.

When switching a patient from systemic opioid to spinal opioid, it is important to remember slow tapering of the systemic opioid dose, to avoid opioid withdrawal syndrome. When side effects of one opioid persist because of large doses, switching to another opioid type is helpful (e.g., from morphine to fentanyl or sufentanil). Another recommendation is to lower opioid dose by adding a local anesthetic to maintain analgesic efficacy [202]. Endocrine side effects can also occur. A randomized controlled trial by Roberts et al. did demonstrate a decrease in testosterone production, which was associated with a decrease in libido and potency [203]. Other less common side effects are allodynia, paranoia, meniere-like symptoms, nystagmus, and polyarthralgia [188].

Potential complications of long-term high-dose local anesthetic administration are exaggerated sympathetic blockade, intolerable sensory loss, persistent motor block, CNS toxicity, and loss of bowel and bladder function (Table 16.2). Postural hypotension occurs in as many as 10 % of patients during the first 24 h but usually disappears [202]. This can be corrected easily with intravenous fluid hydration. In the final days of life, many terminally ill patients become dehydrated, and the local anesthetic dose should be reduced at this time. Local anesthetic change is recommended should intrathecal tachyphylaxis developed [204].

Intolerable paresthesia and motor paresis affecting ambulation are complications secondary to chronic epidural or intrathecal infusion of local anesthetics. They are dose-related neurologic events that must be balanced against analgesia. Du Pen noted that 50 % of the patients receiving epidural bupivacaine, 0.25 %, developed profound sensory anesthesia lasting more than 4 days; the figure reached 82 % when 0.3 % bupivacaine was used [202]. Similarly, persistent motor block is dose related; it happened in 60 % of patients who received 0.35 % bupivacaine and in 85 % of the patients when 0.4 % bupivacaine was used. Interestingly, all patients could ambulate freely and had no difficulty voiding when the infused bupivacaine solution was weaker than 0.15 %. Alternatively, motor impairment can be lessened by the technique of patient-controlled bolus administration on demand [205]. Breakthrough pain is relieved without reliance on high dose infused hourly.

Local anesthetic-induced CNS toxicity is rare, even with long-term epidural infusion. Many patients develop decreasing bupivacaine clearance during infusion [206]. It is not unusual to see rising plasma bupivacaine concentrations in the last days of life. Plasma levels may reach as high as 10.8 μg/mL (total, toxic level is 4 μg/mL) and 1.01 μg/mL (free, toxic level 0.24 μg/mL) but most patients are asymptomatic, without toxic symptoms. Du Pen [186] noted generalized tremors in 12 of 68 patients in the terminal stage, but this was not related to high bupivacaine plasma level. None of the patients showed signs of myoclonic activity, seizure, or cardio toxicity.

Device-Related Complications

This type of mechanical complication can be due to issues with the pump or the catheter. Pump-related complications, such as a "pump dump" in which the pump delivers the entire volume of medication in the CSF, are extremely rare with today's highly sophisticated devices [190]. More likely, drug under- or overdose is the result of human error in pump programming. Internalized access ports and permanent pumps are housed subcutaneously. If the subcutaneous pocket is too superficial, the device can impinge on ribs, iliac crest, or other bones. This produces discomfort, impairs skin healing of the wound, and increases the risk of skin erosion, especially in cachectic patients. On the other hand, if the pocket is created too deep, access and reservoir refilling will be difficult.

More commonly, device-related complications include a fracture or disconnection in the catheter system. In a recent study [184], technical incidents were noted in 37 % of patient who had implanted indwelling catheters. Catheters can dislodge, dislocate, rupture, kink, leak, occlude, thrombose, or migrate. When this happens, failure of spinal drug delivery

Table 16.2 Opioid and bupivacaine (*B*) and related complications

Investigators	Route of administration (total patients)	Drugs and duration of use (days)	Intolerable paresthesia % (no.)	Motor paresis % (no.)	Postural hypotension % (no.)	Bowel/bladder dysfunction % (no.)	Other % (no.)
Driessen [223]	Epidural (40)	Morphine (mean 81)	NR	? Spinal cord compression 5 % (2)	NR	Impaired micturition 5 % (2)	NR
						Constipation 10 % (4)	
Hogan [192]	Epidural (16)	Morphine alone (6) opioid and *B* (10) (median 32)	Hyperesthesia and allodynia during epidural morphine 6 % (1)	31 % (5)	NR	NR	NR
Erdine and Aldemir [191]	Epidural (225)	Morphine (mean 47)	NR	NR	Hypotension 0.8 % (2)	Urinary retention 4 % (8)	NR
						Constipation 7 % (16)	
Du Pen [202]	Epidural (68)	Opioid and *B* (mean 60–120)	50 % when $B > 0.25$ %	0 % when $B < 0.15$ %	9 % (6)	0 % when $B < 0.15$ %	NR
			82 % when>0.3 %	15 % when *B* is between 0.15 and 0.25 %			
				60 % when $B > 0.35$ %			
				85 % when >0.4 %			
Sjoberg [206]	Intrathecal (53 but 27 with normal neurologic function)	Morphine and *B* (mean 29)	Paresthesia, no allodynia 41 % (11/27)	Paresis 33 % (9/27)	2 % (1)	Late urinary retention 33 % (9/27)	NR
Nitescu [215]	Intrathecal (200)	Opioid and *B* (mean 33)	NR	4 % (7)	NR	NR	0
Baker [183]	Intrathecal (81)	Diamorphine and *B* (median 24)	Persistent 1 % (1)	Persistent 9 % (7)	Symptomatic 17 % (14)	Retention 12 % (10)/ incontinence 10 % (8)	Respiratory arrest 4 % (3)

NR not reported

will result in an acute loss of analgesia despite drug escalation. Leakage can present as a subcutaneous swelling at the insertion site or in the paravertebral region because drug is being infused subcutaneously. If not recognized, an opioid abstinence syndrome (fever, vomiting, anorexia, hallucinations) can occur that requires systemic opioid rescue [207]. Percutaneous catheters are more likely to dislodge. de Jong noted that 21 % of catheters became dislodged in the percutaneous group but none in the injection port group [196]. Suspicion of catheter misplacement can be confirmed by a radiocontrast study (e.g., an epidurogram). Catheter obstruction may be a result of filter failure or, less commonly, vertebral compression, tumor, fibrosis, or epidural infection. Occlusion occurs significantly more often in catheters connected to the injection port than in others [196].

Pain on injection is another mechanical problem. Chronic drug administration leads to tissue reaction around the epidural catheter and epidural fibrosis. Several remedies are useful: injection of opioid in smaller volume, injection of a small dose of local anesthetic prior to the opioid bolus, and intermittent steroid injections to relieve ongoing inflammation. If all these measures fail and symptoms persist, catheter replacement or change to a subarachnoid catheter is necessary.

Inflammatory Mass

One of the growing concerns with the implanted intrathecal delivery system is development of an inflammatory mass around the catheter tip [208–210]. Not only can the mass block effective drug delivery to the target neural site, but spinal cord compression has been reported [211]. The incidence of inflammatory mass formation is estimated to be 0.04 % after 1 year of therapy but up to 1.15 % after 6 years [210]. Recent animal studies demonstrate that inflammatory reaction and granuloma formation at the catheter tip is triggered by high morphine concentration in the infusate (12 mg/day equivalent to 36 mg/day in humans) [212, 213]. Although hydromorphone has also been implicated, a recent animal study fails to show such an association [214]. When clonidine (0.25–1 mg/day) is added to low-dose morphine (1.5 mg/day), clonidine was found to reduce granuloma formation in a dose-dependent manner [213]. Although this finding is intriguing, clonidine protective effect on larger doses of intrathecal morphine or on other opioids is largely unknown.

Given the current state of knowledge, it is recommended to keep the concentration and total daily dose of intrathecal opioid as low as possible. When a large dose of morphine is required for pain relief, a more potent drug such as hydromorphone should be considered as a substitute. Physicians should be vigilant in monitoring for early symptoms and signs of granuloma formation (e.g., loss of analgesic efficacy, unexplained thoracic or lumbar radicular pain, and recent change in bowel and bladder function). Imaging studies such as contrast-enhanced T1-weighted magnetic resonance imaging (MRI) or CT myelography should be performed to rule out any suspicious lesion [211]. The inflammatory mass may regress with cessation of the therapy or removal of the catheter [208].

Miscellaneous

With a subarachnoid catheter, the incidence of CSF leak and postdural puncture headache (PDPH) may be 10–15 %. Risks for headache include size of the needle, patient factors such as age and size, difficulty of insertion, previous spine surgery, among others. Those who develop PDPH usually become asymptomatic in 2–4 days; epidural blood patch is seldom required. Persistent CSF leakage externally can present as a CSF hygroma, a subcutaneous fluid collection under the back wound. A big hygroma can cause skin breakdown and lead to development of a CSF cutaneous fistula and increased risk of infection [215]. Finally, indwelling epidural catheters can migrate intravenously, subdurally [216], or intrathecally [217]. Reported cases of epidural catheter migration are limited to those used postoperatively. Drug toxicity due to catheter migration during long-term administration has not been reported.

Spinal Cord Stimulation

Spinal cord stimulation (SCS) is indicated for intractable limb or trunk pain that has failed conservative treatment. Common indications include failed back surgery syndrome, lumbar or cervical radiculitis, complex regional pain syndrome, postherpetic neuralgia, and ischemic pain (peripheral vascular disease or refractory angina). A few randomized controlled studies [218, 219] show modest degree of pain relief but no significant improvement in physical function, activities of daily living, or work capacity.

Prior to permanent SCS implantation, patient screening, psychological assessment, and a trial stimulation are required. The electrode can be inserted percutaneously or via laminectomy. An external power source is required, either in form of an implantable pulse generator with a built-in battery or an implantable device powered by an external power supply utilizing radiofrequency coupling with an antenna taped to the skin over the receiver.

Complications

In general, three categories of complications are seen: (a) neuraxial complications, (b) complications of extra neural tissues, and (c) complications involving the device itself [220]. Complications involving the neuraxis are the most feared and serious complications. These risks are similar to those associated with intraspinal catheter placement. These

include epidural hematoma (which can progress to paraplegia if untreated), infections (such as meningitis, epidural abscess, and discitis), as well as direct trauma to the spinal cord or nerve roots during needle or electrode placement. The most common neuraxial-related complication is inadvertent dural puncture. Kemler et al. found the incidence of postdural puncture headache to be 11 % [218]. Complications of extra neural tissues include infections of the pocket or paraspinous electrodes (approximate incidence of 4–5 %), which could lead to the need to revise or remove the system. A noninfectious process such as a seroma may also develop, which occurs when there is leakage of serum from the tissues of the pocket to the area surrounding the generator. Other extra neural complications include the risk of developing a hematoma at the generator site or developing postprocedure pain at the generator site, lead site, or connectors. Complications involving the device itself can be quite common. In 2005, Taylor et al. published a device complication rate up to 43 %, but this included minor complications such as pain at the pocket site [221].

One of the more common problems is loss of stimulation to the desired area, which may occur in the context of lead migration, epidural fibrosis, or disease progression. Painful stimulation can occur if there is a current leak or lead fracture. More recently, burning of the skin has been observed if there is overheating during recharging of the generator. Allergic reactions to SCS are rare but can occur due to a reaction with the components in the stimulator [222]. Similar to a pacemaker, SCS is composed of titanium (generator casing), platinum and iridium (electrodes), and polyurethane (lead covering); all can trigger an allergic reaction. Generalized swelling and hives are often transient, but stimulator removal may be required in severe cases.

Implanting and caring for a spinal cord stimulator can be a challenging process, involving serious risks that need to be discussed thoroughly with the patient. Maintaining vigilance to identify and treat common and serious adverse events is critical.

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Local and Regional Anesthesia in the Elderly

17

Ferrante S. Gragasin and Ban C.H. Tsui

Key Points

- Due to the physiological changes and relative increase in comorbidities that accompany aging, anesthesia for the elderly population presents special considerations and the potential for complications.
- Regional anesthesia is an attractive option for elderly patients; however, type and dosing of sedatives and local anesthetics must be selected carefully. Sensitivity to sedatives increases with age, and metabolism of local anesthetics may be compromised by age-related changes in organ and tissue function.
- Both central neuraxial and peripheral nerve blocks can be administered safely in the elderly, although anatomic and physiologic considerations (e.g., ability to position the patient, decreased nerve conduction) as well as drug effects (e.g., altered rates of absorption/clearance, risk of toxicity) must be kept in mind.
- Appropriate dosing and adequate monitoring are keys to safe and effective regional anesthesia and analgesia in the elderly population.

Introduction

Life expectancy has been steadily increasing worldwide, and as a result, there is an increased proportion of the elderly population that is presenting for medical care and surgical procedures. Therefore, anesthesia for the elderly has become an increasingly important topic. Because of age-related physiologic changes that accompany aging (including a decline in organ function as well as pharmacokinetic and pharmacodynamic alterations as people age), the methods of safely administering anesthesia in this patient population need to be approached in a different fashion compared to a younger counterpart. It is therefore very important for anesthesiologists to understand these changes in order to provide safe anesthesia and analgesia to the elderly population. The elderly population is commonly assumed to consist of people 65 years of age and older. However, it must be emphasized that this is a generalization, and heterogeneity in this age group is definitely very apparent (e.g., differences in functional capacity and variable rates of organ function decline). Thus, a patient's age is only one factor when devising plans for anesthesia.

Use of regional anesthesia in elderly patients can be safely used. This review focuses on useful and practical tips for successful regional anesthesia in the aging population. Here, different anesthetic agents used for sedation as well as the pharmacokinetic changes of local anesthetics will be discussed. In addition, the physiologic changes associated with aging will be touched upon in this review. A literature search was completed using MEDLINE© and PubMed from January 1966 through March 2015. The literature search entailed the term "elderly" in combination with the following terms: anesthesia, local anesthesia, regional anesthesia, spinal anesthesia, epidural anesthesia, and analgesia. Abstracts were selected based on relevance, and the corresponding publications were obtained. Unpublished works were not considered, and none of the corresponding authors were contacted.

Regional Anesthesia in the Elderly

One can ask: is regional anesthesia the preferred modality in this patient population, and does the choice of anesthetic influence patient outcome? Despite these questions, there are

F.S. Gragasin, MD, PhD, FRCPC (✉)
Department of Anesthesiology and Pain Medicine,
University of Alberta, Edmonton, AB, Canada
e-mail: gragasin@ualberta.ca

B.C.H. Tsui, MSc (Pharm), MD, FRCPC
Department of Anesthesiology, Perioperative and Pain Medicine,
Stanford University School of Medicine,
300 Pasteur Drive, Stanford, CA 94305-5640, USA
e-mail: btsui@ualberta.ca

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_17

no large prospective trials that support the use of regional versus general anesthesia in improving outcomes in elderly patients. Outcome studies suggest that a difference in morbidity and mortality between general and regional anesthesia does not exist in most populations [1]. It makes intuitive sense that elderly patients benefit from regional anesthesia due to a decreased exposure to general anesthetic agents (i.e., minimal sedation) and can stay awake during surgery. Postoperative cognitive dysfunction (POCD) is a common complication following major surgery in the elderly [2, 3]. However, the effects of general anesthesia versus regional anesthesia on POCD continue to be debated. Hole et al. found a higher incidence of cognitive dysfunction in elderly patients following elective hip surgery when general anesthesia was utilized [4], which was corroborated with another future study [5]. In contrast, a study which included 262 elderly patients demonstrated that there was no difference in POCD in patients who had general anesthesia with patient-controlled analgesia compared to patients who had epidural anesthesia [1]. In a study investigating POCD in elderly patients undergoing transurethral resection of the prostate also revealed that the anesthetic method did not have a meaningful impact on cognitive dysfunction [6]. To further corroborate this, a systematic review suggests the use of intravenous versus epidural methods for postoperative analgesia in the elderly population results in no difference in perioperative cognitive function [7]. Regional anesthesia, however, may offer superior postoperative pain control in this age group [8] and can result in decreased opioid use, which may be advantageous in the elderly that are already cognitively impaired [9]. Although regional anesthesia may be a better choice in regards to cognitive function in the elderly in the immediate postoperative period, there is no evidence that avoiding general anesthesia preserves later cognitive function [10, 11]. Nonetheless, clinical observations recommend regional anesthesia in elderly patients since the use of minimal sedation for the surgical procedure allows the patient to maintain orientation and return to baseline function quickly [4, 12]. Pain has been implicated as a risk factor for developing POCD, so regional anesthesia may be of benefit in this respect [13]. Other advantages exist favoring regional anesthesia over general anesthesia. For instance, the incidence of thromboembolic events is decreased [14, 15], as are blood loss [16] and the rate of deep venous thrombosis [17] following hip surgery in the elderly population when regional anesthesia is used. However, other studies have found no difference in 28-day mortality when regional anesthesia is used compared to general anesthesia for hip surgery [1]. Additionally, provision of excellent pain control with regional anesthesia can decrease the incidence of adverse cardiac events in the postoperative period [18, 19]. Indeed, a case report demonstrating the use of regional anesthesia (brachial plexus block) for surgery in an elderly patient with active cardiac symptoms proved successful [20], suggesting that utilizing regional anesthesia techniques may help avoid cardiovascular stress, which has ramifications because of the increased incidence of cardiovascular disease associated with the aging process. However, when perioperative hemodynamics is well controlled in patients undergoing vascular procedures of the lower extremity, there is no difference in cardiac morbidity and mortality [1, 21]. Other advantages conferred when techniques of regional anesthesia are utilized include a more rapid return of bowel function [22] as well as maintenance of the immune system postoperatively [23], which are especially important in the care of elderly patients.

Despite these potential benefits of utilizing regional anesthesia techniques, a clear improvement in patient outcomes over general anesthesia cannot be established, possibly because there are few clinical situations where one technique can fully establish unequivocal advantages over the other, in part because there are multiple factors that come into play. The type of surgery, duration of procedure, and invasiveness of the operation are important factors to consider. From a patient perspective, important factors include existing comorbidities and baseline cognitive function (including preexisting neurologic disease). Finally, the underlying skill and expertise not only of the anesthesiologist but also of the surgeon are important provider factors which can affect outcomes. For instance, a regional anesthetic that is poorly executed can be more deleterious for an elderly patient than a well-conducted general anesthetic [24]. Therefore, it would be best practice to optimize the conditions of the patient during the perioperative period, with an emphasis on quality of anesthetic administered rather than the type of anesthetic (regional versus general) which may be the more important factor rather than choice in type of anesthetic. For additional discussion of this topic, please refer to Chaps. 2 and 4.

Sedation for Regional Anesthesia

When preparing patients for a regional anesthesia procedure, sedation is an important aspect of the process. Elderly patients exhibit enhanced sensitivity to most centrally acting agents (sedatives and opioids), thus paying particular attention to dosing and appropriate titration of these medications is of utmost importance to obtain the most benefit with the least side effect profile.

In the elderly, the ideal sedative agents should have a quick onset, be short acting, be easily administered, and have a high safety margin with minimal side effects. Long-acting benzodiazepines should be avoided [25]. Effective agents used for sedation include propofol, dexmedetomidine, midazolam, fentanyl, remifentanil, or a combination of two or more of these drugs (with appropriate dose reductions for each one used). Ketamine can be used either by itself or can be used in combination with midazolam, propofol, fentanyl, or remifentanil, and can also be very useful in the elderly. Regardless of which agents are chosen for sedation, the

anesthesiologist must remain cognizant of the physiological changes associated with aging (which can affect the pharmacokinetics and pharmacodynamics of the agents). For instance, spinal anesthesia induces a sedative effect in elderly patients (in the absence of exogenous sedative agents) [26, 27], and given the physiologic changes associated with aging, significantly reduced quantities of sedative agents are prudent in this patient population when this anesthetic technique is used. Indeed, deep and profound sedation can be a frequent occurrence in this patient population [28].

Benzodiazepines

Midazolam

Midazolam is a short-acting water-soluble benzodiazepine, making it an excellent choice for sedation in elderly patients undergoing regional anesthesia procedures. In the elderly, midazolam has both a reduced clearance as well as an increased potency [29, 30]. Intravenous bolus injection doses should be reduced by as much as 75 % in this patient population [31]. The Canadian Compendium of Pharmaceuticals and Specialties (CPS) recommendation for an initial dose is 1–1.5 mg of midazolam, with the total dose not exceeding 3.5 mg or 0.07 mg/kg [32].

Lorazepam

Lorazepam is a short-acting benzodiazepine ($t_{1/2}$ ~8–12 h, with no active metabolites) and is one of the few sedative agents which can be administered sublingually with good effect. Although lorazepam has enhanced central nervous system effects in the elderly, its disposition is minimally affected by age [33]. Benzodiazepine premedication can cause hypoxemia due to respiratory depression; however, 1 mg of sublingual lorazepam can be safely used in elderly patients [34].

In addition, it is prudent to exercise caution when benzodiazepines are administered for sedation prior to spinal anesthesia with a local anesthetic and fentanyl because of the potential for oxygen desaturation [35].

Opioids

Use of low-dose opioids in combination with other agents can provide good sedation in the elderly patient undergoing a regional anesthesia procedure. Opioids have a synergistic effect with other sedatives; hence, the doses used for all agents used must be reduced [36, 37]. Appropriate patient monitoring must be employed when combinations of opioid and other sedative agents are utilized because of the danger of enhanced respiratory depression as a result of the synergy between the agents used. Nevertheless, remifentanil 0.5 μg/kg combined with propofol 0.5 mg/kg, as well as midazolam 0.015 mg/kg combined with alfentanil 5 μg/kg, has been used successfully in the elderly, specifically for sedation for cataract surgery utilizing retrobulbar block [38, 39]. In addition, single-dose fentanyl (0.7 μg/kg) has been used successfully in elderly patients undergoing cataract surgery, with minimal impact on cardiorespiratory function [40].

Remifentanil

Remifentanil is an ultra-short-acting opioid. Because of its favorable pharmacokinetic profile, it has become a popular sedative agent for regional anesthesia. The effects of age on the pharmacokinetics and pharmacodynamics of remifentanil have been documented [41]. It has been recommended that half of the bolus dose should be administered in the elderly patient (as compared to their younger counterpart), and the infusion rates to maintain an adequate sedative effect in the elderly should be approximately one-third the rate of that used in a younger patient [36]. Initial suggestions for a remifentanil infusion rate in elderly patients have been 3 μg/kg/h for the elderly patient, but even further reductions to 1.5–2 μg/kg/h have been proposed to minimize cardiovascular and respiratory complications in the elderly population [42, 43]. In regional anesthesia for carotid endarterectomy, a continuous intravenous remifentanil infusion at a rate of 0.04 μg/kg/min has also been used effectively [44].

Other Sedatives

Dexmedetomidine

Dexmedetomidine is a highly selective α_2-adrenoreceptor agonist which is approved for the purpose of sedation and analgesia in the intensive care unit in the United States and other countries [45]. It is administered as a continuous infusion (recommended dose of 0.2–0.7 μg/kg/h for up to 24 h). One major benefit of using dexmedetomidine as a sedative is that it does not induce respiratory depression; however, adverse effects include hypotension and dose-dependent bradycardia [45]. A recent case report documented successful use of dexmedetomidine (6 μg/kg/h load for 10 min followed by 0.7 μg/kg/h infusion) as a sedative in a 98-year-old patient undergoing hip fracture surgery with a spinal anesthetic [46]. Another study has also demonstrated success with the use of dexmedetomidine sedation in the elderly population [47].

Ketamine

Ketamine is phencyclidine derivative and is a nonbarbiturate intravenous anesthetic agent used principally for the induction and maintenance of anesthesia. Ketamine has potent analgesic properties at subanesthetic doses and does not negatively affect ventilation, airway patency, or cardiovascular stability [48, 49]. There is not a great deal of information regarding the pharmacokinetic and pharmacodynamic profiles of ketamine in the elderly, but studies implicate a decrease in clearance and prolonged duration of action in this patient population [50].

Frey et al. demonstrated that a mean dose of 13.2 mg of ketamine to supplement a mean dose of 44 mg of propofol provided a quicker onset with enhanced quality of sedation for retrobulbar anesthesia in patients aged >65 years old [51]. Likewise, combination sedation with midazolam (0.025 mg/kg intravenously infused over 5 min) followed by ketamine (0.2 mg/kg, up to 15 mg maximum) has been used to enhance quality of sedation for peribulbar anesthesia [52].

Propofol

Propofol is an alkyl phenol intravenous anesthetic agent with a rapid onset and short duration of action due to its rapid redistribution. As such, intermittent propofol bolus injections as well as low-dose propofol infusions are frequently used for sedation for surgical procedures using regional anesthesia. In regards to pharmacokinetics in the elderly, although the volume of distribution remains relatively unchanged and its rate of clearance is decreased, plasma propofol concentrations increase and decrease more rapidly than in younger patients [53–55]. Pharmacodynamics is also altered in the aging process, including an increased sensitivity to propofol's anesthetic effects. It has been shown that in 75-year-old patients when compared to 25-year-old patients, the EC_{50} for loss of consciousness was reduced by 50 % [54]. Additionally, the neurologic depressant effects of propofol as assessed by electroencephalography are increased with age, despite a lack of age-related changes in blood-effect site equilibrium half-life [54]. Propofol can also adversely affect hemodynamic function in the aging population [56]. The concentration of propofol that cause a 50 % decrease in blood pressure is lower in elderly patients (aged 70–85 years) compared to younger patients (aged 20–39 years) [57]. This is due, in part, to the decrease of physiologic reserve that occurs with the aging process [56]. Therefore, administered doses of propofol must be reduced to achieve hemodynamic stability in the aging population. For instance, it was suggested that doses should be reduced by 20–30 % in patients greater than 55 years of age, translating into 0.3–0.6 mg/kg intravenous injection for initial sedation followed by 0.9–2.7 mg/kg/h for maintaining sedation [58]. However, continuous infusion rates of up to 4 mg/kg/h have been successfully used in elderly males undergoing urologic surgical procedures [59]. Propofol therefore is a suitable agent for sedating elderly patients; however, caution must be advised for elderly patients with neurodegenerative disease such as Parkinson's disease, since it can induce spontaneous involuntary movements [59, 60].

Regardless of which sedation is chosen for the respective procedure, it is vital to ensure supplemental oxygen is delivered and vigilant monitoring of the patient ensues, and administration of the chosen agents(s) involves careful titration in order to reduce the occurrence of untoward side effects while ensuring patient comfort for the procedure.

Local Anesthetics

General Considerations

Aging is associated with a multitude of changes in tissues and organ systems, involving changes in both structure and function. These changes affect the pharmacokinetic profiles of local anesthetics that are used for regional anesthesia. As a result, increased plasma levels of local anesthetics can result, leading to a greater danger of toxicity of the cardiovascular or central nervous systems.

Systemic Absorption

It has been shown that epidural or intrathecal administration of local anesthetics results in a biphasic absorption consisting of a rapid initial phase followed by a slower phase [59, 61–68]. When administered epidurally, the initial rapid phase of absorption is due to the high concentration gradient in combination with the vascularity of this potential space. The slow absorption phase, on the other hand, is due to partitioning of the local anesthetic into epidural fat. When administered intrathecally, the initial rapid phase of absorption is actually slower than that seen when administered after epidural administration because of decreased perfusion of the subarachnoid space in combination with a lower concentration gradient. Aging does not affect absorption of bupivacaine following epidural injection [67]. Conversely, systemic absorption of bupivacaine following intrathecal injection increases with age due to a faster late absorption rate; despite this, the duration of action is not reduced in older patients [66]. Therefore, increased sensitivity of neuraxial anesthesia in the elderly population is not likely related to impairment of vascular absorption. In fact, the increased sensitivity more likely stems from a decrease in neuronal population in the central nervous system coupled with a decreased neuronal conduction velocity that occurs with the aging process [68].

It is often believed that cardiac output decreases as patients age. However, there is no clear consensus regarding this physiologic attribute. Although studies suggest that there is a strong negative correlation between increasing age and cardiac output, others exist that show no correlation when investigating only healthy patients of advanced age [69–71]. Even so, nearly all anesthetic agents decrease cardiac output to varying degrees, which may be affected by aging. This can result in decreased peak concentrations in concert with delaying the time to achieve peak concentration. Also, if there is decreased tissue perfusion, there will be a delay in transporting drugs to their tissue effect sites.

Distribution

Aging is associated with an increase in total body fat while there is a decrease in both total body water and lean body mass. These changes can result in a greater volume of distribution of local anesthetics [72]. Accordingly, patients of advanced aged may exhibit varying peak drug concentrations following rapid bolus injections or infusions; therefore, drug toxicity can be unpredictable in the elderly [73].

The most important plasma protein involved with local anesthetic binding is alpha 1-acid glycoprotein (α-1AG), with the free fraction of local anesthetics such as lidocaine and bupivacaine being inversely proportional to the plasma concentration of α-1AG [74–78]. In the absence of disease, the aging process minimally affects α-1AG concentration in the blood [79, 80]. However, many older patients have existing comorbidities or conditions that can decrease the free fractions of lidocaine and bupivacaine due to elevated levels of α-1AG [81]. For instance, α-1AG concentrations increase in response to different types of stress, including inflammation, infection, the presence of cancer, and surgery itself [81].

Clearance

Given that there is a decrease in hepatic enzymatic activity, hepatic blood flow, and hepatic mass as people age, it makes intuitive sense that the clearance of local anesthetics will be decreased in this patient population, particularly since hepatic microsomal metabolism is the primary means of clearance for amide local anesthetics such as lidocaine and bupivacaine. Plasma clearance of lidocaine and bupivacaine is indeed decreased primarily in elderly males, although a high degree of interindividual variation exists [81–83]. Specifically, it has been demonstrated that clearance of lidocaine was reduced by approximately 35 % in males >65 years of age, but there was a lack of age effect in females [83]. This observation may be due to hormonal differences and their influences on local anesthetic protein binding [84, 85]. Regardless, it would be prudent to accept that the rate of clearance of local anesthetics is reduced with aging, so the anesthesiologist should exercise caution when repeat doses or continuous infusions of local anesthetics are administered to the elderly population.

Clinical Implications

Based on the information presented, the aging population will exhibit an enhanced sensitivity to the effects of local anesthetic agents. A greater than expected sensory level of blockade (when compared to the younger population) occurs following spinal as well as epidural anesthesia. Pharmacokinetic changes cannot fully justify the age-related changes to neuraxial anesthesia; as such, it is likely that the changes are more likely due to changes in pharmacodynamic alterations [73, 86]. These pharmacodynamic alterations may be due to a decrease in neuronal number in the central nervous system, deterioration of myelin, decreased conduction velocity in neurons, as well as altered anatomy of the spinal and intervertebral foramina that occurs with the aging process [73, 86]. It was initially demonstrated that the local anesthetic dose required to achieve segmental dermatomal blockade with epidural anesthesia progressively declined with age [87]. However, a subsequent study revealed that age minimally affects the number of dermatomes anesthetized with epidural anesthesia (using 1.5 % lidocaine with 1:200,000 epinephrine) [88]. Although not linear, the number of spinal segments that get blocked is linked to the total dose of epidural anesthetic administered. This may be due, in part, to initial filling of the epidural space when local anesthetic is injected in the epidural space, where the pressure is low; when additional volume is introduced, the resulting pressure increase causes local anesthetic to escape through the intervertebral foramina. This leakage through the intervertebral foramina may be part of the reason for prolonged anesthesia with potentially greater intensity. Therefore, a doubling of the anesthetic dose administered through the epidural space does not equate to doubling the number of spinal segments/dermatomes anesthetized. Notwithstanding, it is recognized that epidural dosing (i.e., volume) should be reduced in patients over 40 years of age [89].

On the contrary, the primary determinant of level achieved with spinal anesthesia is the baricity of the solution [73]. In the elderly, hyperbaric solutions have quicker onset and greater degree of spread (3–4 spinal segments) compared to younger patients; this effect is minimized with the use of isobaric solutions [73]. The hypotensive effects of neuraxial anesthesia exhibit a higher incidence in the elderly when compared to young patients because of decreased physiologic reserve, underpinned by altered cardiac capacity, structural and functional changes in the vascular system, and changes in the autonomic nervous system [56]. Given the increase in neuronal sensitivity mentioned earlier coupled with the increased potential spread of neuraxial local anesthesia in the elderly, the prevalence of hypotension is increased [73]. In addition, spinal anesthesia in elderly patients also results in a decrease of cerebral blood flow in elderly patients [90], whose organs are accustomed to increased perfusion pressures which potentially leads to danger [56]. Moreover, it has been documented that spinal anesthesia may cause increased episodes of cerebral desaturation, further exacerbating the effects of decreased cerebral blood flow [91]. Thus, the overall dose of local anesthetics and judicious use of sedative medications, which can further impact hemodynamic status

of the aging population, should be decreased in the elderly in order to reduce the possibility of untoward effects.

From a pharmacokinetic standpoint, peak concentrations and protein binding of local anesthetics in plasma following a single injection are comparable in elderly and young patients [92–94]. However, following a single injection of local anesthetics in the epidural space, terminal half-lives are increased for bupivacaine and lidocaine, leading to a decrease in total plasma clearance as age increases [68]. This reduction in clearance plays an important role particularly during continuous infusions of local anesthetics, since increased plasma concentrations imply a need to reduce infusion rates and doses for top-ups in the elderly. Indeed, in elderly patients it has been previously shown that the concentration of free lidocaine was increased during continuous epidural anesthesia [95], necessitating the reduction and appropriate adjustment of epidural dosing in this age group. One would think that a reduction of epidural dose would affect the quality of anesthesia; however, this may not be the case since the increased neuronal sensitivity may compensate for the decreased dose [68]. The introduction of levobupivacaine (the isolated S(−)-enantiomer of a racemic mixture of bupivacaine) and ropivacaine into clinical practice has allowed for additional alternatives for regional (neuraxial) anesthesia. Notwithstanding the fact that levobupivacaine has a lower volume of distribution, marginally increased amount of protein binding, higher rate of clearance, and hence shorter half-life compared to the R(+)-enantiomer [96], it has similar potency and clinical attributes for neuraxial and peripheral nerve block techniques, but accomplishes this with a decreased risk of central nervous system toxicity and cardiovascular toxicity when compared to racemic bupivacaine [97, 98]. Similarly, ropivacaine also exhibits a high level of potency and lipid solubility, but decreases the risk of central nervous system toxicity and cardiovascular toxicity compared to bupivacaine. Basic science work has demonstrated that the doses of ropivacaine and levobupivacaine to cause seizures are higher than those required of bupivacaine [99]. In regards to cardiovascular toxicity, ropivacaine may demonstrate superiority since the doses of ropivacaine to cause arrhythmias and asystole in rats are larger than those required of both levobupivacaine and bupivacaine [99]. Hence, ropivacaine and levobupivacaine may be used for advantage in the elderly population. Again, it is important to remember that individual variability exists (particularly as patients get older, given the increased incidence of existing comorbid disease states), and thus it is necessary to carefully assess each patient prior to administering any anesthetic.

Peripheral Nerve Block

Peripheral nerve blocks can be used in the elderly to help reduce stresses of surgery and minimize the risks or POCD. As such, there are multiple options for peripheral nerve blocks that are appropriate for the elderly [100].

Anatomic and Physiologic Considerations

Landmarks requiring bony prominences are usually easily identified in elderly patients because of decreased lean mass and total body fat. However, arthritic changes can affect optimal positioning of the patient for regional anesthesia procedures, but this issue can often be overcome with proper padding and support of the head, pressure points, and extremities.

The primary concern regarding peripheral nerve blocks in the aging population is the effect of local anesthetics on neural structures. The changes to neural and perineural tissues associated with aging can affect the efficacy of the peripheral nerve block. For example, the number and diameter of myelinated fibers in both the ventral and dorsal roots decreases as age increases [101, 102]. Moreover, there are increased acceptor sites accessible to local anesthetics because of decreased distances between Schwann cells in myelinated nerves as a person gets older [101, 103, 104]. Furthermore, there is a decline of mucopolysaccharide composition in connective tissue sheaths that allows for increased local anesthetic infiltration of the nerves [101].

Neuronal sensitivity is also increased with age since there is a decrease in neuronal numbers as well as a slowing of peripheral nerve conduction velocity [103, 104]. Due to a decline in drug clearance, cumulative toxicity is a risk in elderly patients; thus, large doses as well as repeated doses should be administered with extreme caution if not avoided altogether. In addition, using ultrasound imaging, a reported reduction in minimum effective local anesthetic volume for supraclavicular brachial plexus block was observed in part due to smaller cross-sectional surface area of the brachial plexus in elderly patients [105].

As with any regional anesthesia technique, the local anesthetic agent of choice for a given peripheral nerve block is dependent on the length of time anticipated for surgery.

Clinical Observations

In a study by Paqueron et al., ropivacaine (20 mL of 0.75 %) utilized for brachial plexus block provided good analgesia in all patients (age range 27–81), but this dose had a faster onset and lasted longer in patients who were 70 years of age and older, demonstrating a relationship between age and drug sensitivity in peripheral nerve blocks [106]. Regional anesthesia for carotid endarterectomy may potentially avoid complications related to shunt use intraoperatively [107]. The effectiveness of comparable volumes (0.2 mL/kg of 0.75 % ropivacaine, 1 % ropivacaine, and 2 % mepivacaine) for cervical plexus anesthesia in the elderly undergoing carotid endarterectomy was studied [108]: all three local anesthetics are suitable choices, but both concentrations of ropivacaine provided longer postoperative pain relief than mepivacaine. In elderly patients administered femoral 3-in-1 nerve blocks, a 20 mL of bolus of 0.5 % of levobupivacaine

or bupivacaine has been used successfully; in addition, 20 mL of 0.2 % bupivacaine followed by an additional 10 mL of 0.2 % bupivacaine has been used with success [98, 109].

Adjuvant Epinephrine

Epinephrine, through its vasoconstrictor ability, can be combined with local anesthetics to prolong the duration of anesthetic action as well as improve hemostatic conditions. For example, the addition of 1:400,000 epinephrine to 0.375 % bupivacaine (at a dose of 2 mg/kg) for femoral nerve block provided successful and long-lasting analgesia for hip and knee surgery [110]. However, one must exercise caution since there is a potential for ischemic neurotoxicity with the use of epinephrine [111].

Central Neuraxial Block (Spinal and Epidural Analgesia)

General Pharmacokinetic Considerations

It is important to appreciate the normal physiologic changes as patients age, since these changes will affect the actions of drugs at point of uptake, site of action, and with clearance. Very little metabolism of local anesthetics takes place in the epidural and subarachnoid spaces, so essentially the entire administered dose is absorbed into the circulation. Therefore, the rise in plasma concentrations of local anesthetics is important for the possibility of systemic toxicity. As mentioned earlier, the early absorption of local anesthetics administered via the intrathecal route is far slower than for those administered through the epidural route because of poor perfusion of the former relative to the latter. Although the absorption of bupivacaine, along with the total duration of epidural anesthesia, is minimally altered with aging, the absorption of hyperbaric bupivacaine when administered via the intrathecal route is shorter in older patients compared to the young because of a rapid second phase of absorption in older patients [61–68]. One may thus expect a diminished duration of action of spinal anesthetics in the elderly; however, this has not been definitively established.

Although there is an increase in plasma half-life of lidocaine in the aging population, peak plasma concentration is minimally affected by advancing age after a single dose epidural injection [81, 83, 93, 112, 113], suggesting that the dose of lidocaine administered through a single epidural injection need not be reduced. However, given the prolonged terminal half-life of lidocaine in the elderly, in combination with decreased systemic clearance, the accumulation of systemic lidocaine can happen with multiple single injections or continuous infusions through the epidural space [81, 95].

In regards to bupivacaine, both peak plasma concentration and time to achieve peak concentration following epidural injection are minimally affected by age [67]. On the other hand, increasing age may affect early absorption kinetics [114]. There is a prolonged terminal half-life of bupivacaine in elderly patients, and total plasma clearance is also decreased [67]. Intrathecal administration reveals a slow initial phase of absorption of bupivacaine into the systemic circulation, resulting in low peak levels in conjunction with a protracted time to achieve peak concentrations [62]. A multitude of factors may affect the systemic clearance of bupivacaine. These include a decrease in hepatic enzymatic activity, hepatic blood flow, and hepatic mass as people age. However, since bupivacaine has a low hepatic extraction ratio and minimal age-related changes for protein binding [94], the decrease in total plasma most likely stems from an alteration in the hepatic enzyme metabolic activity [68].

Epidural Anesthesia

Anatomic and Physiologic Considerations

Epidural analgesia has been demonstrated to improve recovery and the rehabilitation process following major surgery when compared to other techniques for analgesia [115, 116]. The technical aspects of epidural anesthesia are often more difficult than spinal anesthesia and can cause additional duress since there is enhanced risk of nerve injury given the relatively larger size of epidural needle as well as attempting placement at higher intervertebral levels. Notwithstanding, a satisfactorily placed epidural catheter offers excellent perioperative analgesia [117–120].

An aging patient can affect the ability of the anesthesiologist to perform adequate epidural anesthesia. For example, patient positioning for regional anesthesia becomes progressively more challenging with increasing age. Although many would argue that landmarks requiring bony structures for neuraxial anesthesia are more prominent in the aging population, calcification of spinal ligaments and the existence of osteophytes can be problematic for the ease of needle entry into the epidural and intrathecal spaces. To assist in overcoming this issue, a paramedian or lateral approach has been advocated for epidural and spinal anesthesia in the aging population [89].

In addition, the structures outlining the intervertebral foramina develop an increased density and firmness with advancing age; this reduces the overall volume of the epidural space, which in turn results in a higher spread of local anesthetic in the cephalad direction following injection in the epidural space [101, 121, 122]. This consequence is worsened by certain comorbidities, such as atherosclerosis and diabetes, which can cause premature and accelerated aging [123]. Additionally, a rapid onset of epidural blockade with local

anesthetics can be seen with advanced age, which may be due in part to increased dura permeability as well as enlarged arachnoid villi [101, 124]. Although it has been suggested that age minimally affects the level of anesthesia with epidural blockade, it is still recommended to reduce overall dose of local anesthetics in the elderly, since this population is at increased risk of developing unwanted side effects such as hypotension [125]. Moreover, large volume injections of local anesthetics in the epidural space in elderly patients have been connected to cauda equina syndrome in the setting of spinal stenosis. As well, extended duration of epidural anesthesia in elderly patients has been linked to neurologic derangement from cauda equina syndrome [126, 127].

Clinical Observations

Local anesthetic choice for epidural anesthesia and analgesia usually depends on the duration and type of surgery. Short-acting agents, such as procaine and chloroprocaine are suitable for procedures of short duration (i.e., 30–90 min); lidocaine, prilocaine, and mepivacaine are appropriate for procedures of intermediate duration (i.e., 60–90 min); for more prolonged procedures (i.e., 180–360 min), tetracaine, bupivacaine, and ropivacaine are indicated [100]. A study investigating the onset and duration, as well as quality of postoperative analgesia, of epidural anesthesia administration has been completed in elderly patients undergoing total hip arthroplasty [97]. The authors compared 0.125 % levobupivacaine, 0.125 % racemic bupivacaine, and 0.2 % ropivacaine, and found that all three solutions provided sufficient analgesia necessitating similar volumes (5 mL/h baseline infusion rate) with the incidence of hypotension not differing between the groups. Another study investigated the extent of motor blockade with ropivacaine and the effects of age: with the same amount of local anesthetic administered, the extent of motor blockade increases as age increases [128]. Along those lines, an epidural saline washout technique has been described in elderly patients following transurethral surgery: epidural washout with 30 mL of saline facilitates the regression of both motor and sensory blockade without affecting postoperative analgesic benefit [129]. The pharmacologic properties of prilocaine and lidocaine are similar, and it has been suggested that 1 % prilocaine at a dose of 150 mg is a safe and reliable choice for epidural anesthesia for transurethral resection of the prostate in males over 60 years of age [130]. In addition to improving pain profiles, the use of epidural anesthesia in cardiac surgery has also been suggested to confer benefit, including improving cardiac performance, decreasing release of markers for cardiac damage, and shorter length of stay in the intensive care unit postoperatively [131, 132].

Adjuvant Epinephrine

Local anesthetic duration of action can be enhanced with the addition of 1:400,000 to 1:200,000 epinephrine, as has been documented with lidocaine and 2-chrloroprocaine [133]. Epinephrine also provides some additional analgesia to the local anesthetic mixture by activating central α_2-adrenoreceptors. Epinephrine can, however, augment the drop in blood pressure and rise in cardiac output that can be seen with lidocaine use for epidural anesthesia [134]. Fortunately, increasing age does not appear to exacerbate this consequence. Indeed, it has been suggested that the reduction in systolic blood pressure observed with the addition of epidural epinephrine is less prominent with advancing age, and there is also an increase in the dose necessary to cause a rise in heart rate [135, 136]. This may pose an issue when a test dose utilizing epinephrine is used to assess epidural catheter placement: the anesthesiologist should be aware that a small deviation in heart rate may indicate that the tip of the epidural catheter may still in fact have an intravascular placement, particularly since there is already an upregulation of the autonomic nervous system in the elderly (i.e., an overt increase in heart rate may not be readily observed) [56].

Adjuvant Opioids

Low-dose preservative-free opioids can be added to local anesthetic solutions used for epidural analgesia. Due to enhanced central nervous system depressant effects of opioids in the elderly, caution must be exercised with the use of opioids in epidural anesthesia, with a reduction in the total dose of opioid used [137, 138]. It has been suggested that up to a 50 % reduction in epidural bolus injection and continuous infusion rates would be sensible when epidural opioids are delivered to the elderly [73]. In total hip arthroplasty, ropivacaine 0.1 % combined with 0.5–1 μg/mL sufentanil has provided very good analgesia in the elderly [139–141]. Bupivacaine 0.125 % administered as a constant epidural infusion (4 mL/h) in combination with either 0.05 or 0.005 mg/ml has also been used successfully for postoperative analgesia following total hip arthroplasty [142]. Although not in the opioid class, epidural ketamine (40 mg bolus injection followed by 2 mg/mL) in combination with bupivacaine 0.125 % has been used successfully in the elderly population [143]. However, when compared to epidural morphine, the use of epidural ketamine resulted in less sedation and postoperative nausea and vomiting, pain scores were higher suggesting a possible need for increased amounts of ketamine to achieve a similar analgesic effect to epidural opioids [143].

Spinal Anesthesia

Anatomy and Physiological Considerations

Spinal anesthesia can be used for surgeries of the lower body, including gynecologic, vascular, orthopedic, and urologic procedures. Despite its technical straightforwardness and general effectiveness, risks and complications are still possibilities when this technique is used in the aging population.

As mentioned earlier, positioning of patients as well as spinal needle target localization can pose some difficulties in elderly patients. Changes to neural tissues, including anatomic changes to the spinal column, will affect the pharmacokinetic properties (absorption, distribution) and resultant duration of action of local anesthetics. Total cerebral spinal fluid volume is decreased, whereas cerebrospinal fluid specific gravity is increased [68]. With bupivacaine (both hyperbaric and isobaric), there may be a quicker onset and a greater degree of spread than in younger patients [89]. However, inconsistencies have been identified between studies correlating age with spread of anesthesia following subarachnoid injection of local anesthetic because of differences in the types of local anesthetic as well as the varying doses used and the baricity of the solution used [68]. Studies investigating the characteristics of blockade with hyperbaric tetracaine are inconsistent [144–146], while others suggest that subarachnoid administration of hyperbaric bupivacaine and mepivacaine has widespread distribution throughout the spinal levels in comparison to glucose-free bupivacaine [147–150]. These discrepancies can be attributed, in part, to the alteration of cerebrospinal fluid volume and baricity in combination with the altered anatomical configuration of the spine with advancing age. High spinal anesthesia can be problematic in the elderly, since large decreases in blood pressure of up to 30–40 mmHg and bradycardia can occur with this anesthetic technique [89]. Hence, the need for vigilant monitoring of this patient population is essential. Nevertheless, blockade of up to the $T_{10–12}$ dermatomes for operations on the lower abdominal or inguinal areas of patients of advanced age can be achieved with the use of hyperbaric as well as glucose-free bupivacaine.

Clinical Observations

Although spinal anesthesia results in hypotension, it may provide better hemodynamic stability compared to general anesthesia in American Society of Anesthesiologists Class III elderly patients [151]. Previous meta-analysis also suggests that spinal anesthesia has consistent evidence of benefit for elderly patients with hip fractures [152]. Despite this established benefit, the optimal effective and safe dose of glucose-free bupivacaine remains controversial [147, 149, 153]. Spinal anesthesia results in a biphasic response to changes in cardiac output, with an initial increase in cardiac output followed by a reduction below baseline [154]. Doses less than 10 mg have been suggested to be used in older patients to reduce the occurrence of hypotension [155] although moderate amounts of hypotension (37.5 and 25 % reduction in blood pressure) still occurred when 5 mg [156] and 7.5 mg [157] of bupivacaine were used. To combat hypotension, prophylactic intramuscular administration of glycopyrrolate has been shown to be beneficial in the elderly [158]. Ropivacaine administered at a 5 mg dose in the subarachnoid space has shown effectiveness for total hip replacement in both young and elderly patients [159]. Ropivacaine administered at other dosages and baricities has proved satisfactory in older patients undergoing total hip arthroplasty (isobaric ropivacaine 7.5 and 10 mg/mL) [160], transurethral resection of the bladder or prostate (isobaric ropivacaine 0.3 %, 15 mg) [161], and lower abdominal or lower limb surgery [162, 163]. Hyperbaric tetracaine (administered at a dose of 8 mg), with its long duration of action, has also been used for spinal anesthesia for transurethral resection of the prostate [164]. Lidocaine provides a quick onset as well as a quick regression of spinal blockade when administered in the subarachnoid space [165]. However, there is concern over intrathecal lidocaine and its association with transient neurological symptoms, which has influenced many anesthesiologists to utilize alternative local anesthetic agents as their primary choice. Prospective randomized trials have revealed an incidence of transient neurological symptoms with intrathecal lidocaine to be somewhere between 5 and 40 % [166–171], although the etiology behind this phenomenon remains uncertain [172, 173].

Small, incremental amounts of local anesthetics can be introduced if there is an intrathecal catheter in place. Moreover, continuous spinal anesthesia with an intrathecal catheter allows for the titration of local anesthetics to achieve the appropriate levels of blockade while minimizing hemodynamic fluctuations, which can be very useful in the aging population [174–176]. This technique and its safety in practice has been called into question because of reports of harmful neurologic effects, such as cauda equina syndrome, as the use of microcatheters has been associated with this untoward outcome. In elderly patients, hyperbaric solutions did not appear to be a factor in the development of poor distribution of the local anesthetic—what appeared to be the primary factor was the caudal orientation of the catheter tip rather than its

route of travel or position in regards to spinal level [177]. Therefore, the anesthesiologist should exercise caution if he or she plans to utilize continuous spinal anesthesia, since it would be difficult to predict and in fact control the manipulation of the catheter to ensure that the catheter tip is in an advantageous position (i.e., to avoid improper distribution of local anesthetic), even in the absence of microcatheter use or avoiding the use of hyperbaric local anesthetic solutions.

Adjuvant Epinephrine

Intrathecal adjuvants can provide additional analgesia and increase the duration and effectiveness of local anesthetic administration for spinal anesthesia. Although there is a lack of consistency regarding clinical benefit, epinephrine at typical doses ranging from 1:400,000 to 1:200,000 are often used [178–180]. Nonetheless, varying amounts of adjuvant intrathecal epinephrine have been demonstrated to be effective in prolonging the duration of isobaric bupivacaine (dose of 15 mg) anesthesia in elderly patients [181]. Alternatively, the α_2-adrenergic receptor agonist clonidine can prolong the duration of spinal anesthesia while decreasing the dose of local anesthetic required to achieve anesthesia and being able to provide some analgesia itself (given its α_2-adrenergic receptor agonism) [165, 182]. For instance, intrathecal clonidine (dose of 100 μg), when added to 40 mg of 2 % lidocaine, can provide adequate spinal anesthesia with minimal hemodynamic perturbations in patients aged 50–70 years for surgical procedures such as hysterectomies, open prostatectomies, or surgical correction of fractured hips [182].

Adjuvant Opioids

An alternative adjuvant for local anesthetic administered through the subarachnoid space is the use of an opioid. Opioids have a potent synergistic effect with local anesthetics, so the probability of achieving success with the spinal anesthetic is enhanced while reducing the risk of hypotension. Fentanyl, at a dose of 20–25 μg, when added to bupivacaine at low doses (i.e., 4 mg) can provide adequate anesthesia for older patients undergoing transurethral resection of the prostate as well as surgical repair of a hip fracture with fewer side effects when compared to bupivacaine if it alone was administered [157, 183]. Similar effects were achieved with the use of adjuvant sufentanil (5 μg) when administered intrathecally in combination with low-dose bupivacaine in the elderly undergoing repair of hip fractures [184]. Similarly, the addition of 10 μg of fentanyl to 4 mg of hyperbaric tetracaine provided adequate anesthesia with a decrease in side effects compared to a conventional tetracaine dose of 8 mg in elderly patients undergoing transurethral resection of the prostate [164]. In regards to longer acting opioids, an intrathecal dose of 0.1 mg of morphine has been safely used in elderly patients undergoing total hip arthroplasty, with excellent postoperative analgesia [185]. In addition, although not in the opioid family, intrathecal S(+) ketamine (0.1 mg/kg) has also been used successfully in transurethral resection of the prostate in elderly males [186].

Table 17.1 Commonly used sedatives

Bolus	Infusion
Midazolam 0.5–2 mg (titrated up to 0.07 mg/kg)	Remifentanil 0.05–0.0625 μg/kg/min
Fentanyl 0.25–0.5 μg/kg	Propofol 1.5–3 mg/kg/h (25–50 μg/kg/min)
Ketamine 0.1–0.2 mg/kg	Dexmedetomidine 0.2–0.7 μg/kg/h

Table 17.2 Suggested anesthetic doses for nerve block

Nerve block and drug	Bolus dose	Infusion	Useful adjunct
Spinal			
Isobaric bupivacaine	5–15 mg	N/A	Epinephrine 0.3 mg
			Morphine 0.1 mg
			Fentanyl 10–25 μg
Epidural			
Bupivacaine	0.5 %, 5–10 mL	0.125 %, 5–10 mL/h	Morphine 0.05–0.1 mg/mL
			Fentanyl 1–2 μg/mL
Levobupivacaine	0.5 %, 5–10 mL	0.125 %, 5–10 mL/h	Morphine 0.05–1 mg/mL
			Fentanyl 1–2 μg/mL
Ropivacaine	0.5 %, 5–10 mL	0.2 %, 5–10 mL/h	Morphine 0.05–1 mg/mL
			Fentanyl 1-2 μg/mL
Peripheral			
Bupivacaine	0.5 %, 20 mL	0.2 %, 5–10 mL	N/A
Levobupivacaine	0.5 %, 20 mL	0.2 %, 5–10 mL	N/A
Ropivacaine	0.5 %, 20 mL	0.2 %, 5–10 mL	N/A

Conclusion

Given the increasing life expectancy in today's society, it is no wonder that geriatric medicine is gaining importance in all disciplines of clinical medicine including anesthesiology. The normal processes of aging affects multiple organ systems, not only anatomically but also physiologically. The caveat is that safe practice of regional anesthesia for the aging population requires modification of regional anesthesia techniques as well as generalized reduction in dosing of many of the anesthetic agents used to achieve a good effect. Additionally, elderly patients are at risk for negative perioperative outcomes, so adequate monitoring (as dictated by their overall health) and vigilance in the care of these patients are mandatory. The information presented in Tables 17.1 and 17.2 are based on available literature as well as the authors' own experiences so the reader is cautioned when using these dosages in his or her own practice. The doses presented here are intended to be used as guidelines; therefore, the agents in question should be titrated by the anesthesiologist according to the patient's individual needs and conditions. Nonetheless, excellent regional anesthesia can certainly be provided to the elderly patient in efforts to optimize patient safety, comfort, and satisfaction during the perioperative period.

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Local and Regional Analgesia for Labor and Delivery

18

Yoo Kuen Chan and Peng Chiong Tan

Key Points

- Regional anesthesia is a safe, effective, and widely used modality for caesarean section delivery. In addition it is useful for controlling labor pain and postoperative pain. While severe complications are rare, common complications, such as hypotension, must be considered when using neuraxial anesthesia.
- Hypotension occurs in around half of individuals receiving central neuraxial block; coloading with crystalloid is a common method to prevent hypotension. Administration of vasopressors may be required to stabilize blood pressure.
- Local anesthetic toxicity is a potential complication, given the abundant vascularity of the epidural space; this presents concern for both parturient and fetus. Treating every epidural dose as a test dose can help avoid infusion of toxic doses.
- Paracervical and pudendal blocks are decreasing in popularity due to inadequate pain control and associated complications.
- Other complications to be considered in the obstetric population include neurologic dysfunction, infection, chronic adhesive arachnoiditis, postdural puncture headache, cauda equina lesion, damage to the spinal cord, transient neurologic symptoms, inadequate/extensive block, and rarely, respiratory and cardiac arrest.

Y.K. Chan, MD (✉)
Department of Anaesthesiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
e-mail: yookuen@gmail.com

P.C. Tan, MD
Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
e-mail: pctan@ummc.edu.my

Introduction

Most cesarean sections, whether elective or emergency are currently done under regional anesthesia worldwide [1, 2]. The reason for this predominance is because in the last 20–30 years the database shows that general anesthesia for cesarean section has greater risk as a cause of maternal mortality compared to regional anesthesia [3, 4]. There have been great strides in the development of regional analgesia and anesthesia in obstetrics to deliver to the varying needs of the population [5].

Regional anesthesia is deemed safer as the most common adverse event that comes with the technique—hypotension is easily managed by providers [6, 7]. This is in contrast to failure in airway and respiratory management seen with general anesthesia [8–11]. Airway difficulties occur approximately ten times more frequently in the obstetric population than with nonparturients and often lead to hypoxic complications in the parturient and the fetus if not handled properly [10–12].

Incidence of Adverse Events

Many providers opt for regional analgesia and anesthesia with the understanding that it provides the best analgesia for labor pain and regional anesthesia is extremely safe for the parturient during a cesarean section. While hypotension is the most common complication of regional anesthesia, affecting nearly half of those given central neural blockade, the other complications are rare [13, 14]. Several surveys and audits of central neural blockade attest to the rarity [13, 14]. This rarity is a result of great attention being paid to prevent the occurrence and further attention to treat any complications early before they can cause any permanent damage. There has been a further move to reduce the use of pudendal and paracervical blocks as the latter especially has been associated with fetal bradycardia due to the rapid absorption from the vascular site of administration [15]. Pudendal and

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_18

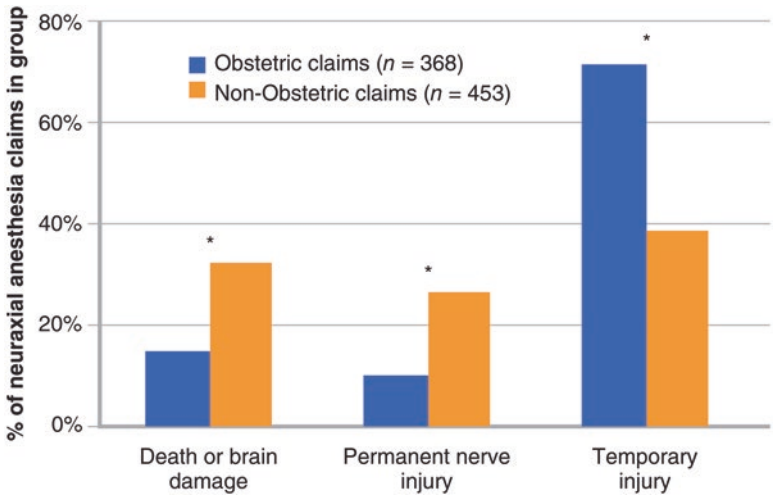

Fig. 18.1 This shows that a substantial portion of the claims against regional anesthesia complications are for temporary injury. *Reproduced with permission of Wolters Kluwer Health, Inc. Lee LA, Posner KL, Domino KB, Caplan RA, Cheney FW. Injuries associated with Regional Anesthesia in the 1980s and 1990s—a closed claims analysis. Anesthesiology 2004; 101:143–52* [16]

Table 18.1 The primary damaging events for neuraxial anesthesia claims 1980–1999, obstetric versus nonobstetric cases

	Obstetric (n = 368), no. (%)	Non-obstetric (n = 453), no. (%)
Block related	187 (51 %)*	186 (41 %)
Block technique	62 (17 %)	84 (19 %)
Neuraxial cardiac arrest	20 (5 %)*	61 (13 %)
Inadequate anesthesia/analgesia	40 (11 %)*	7 (2 %)
High spinal–epidural	21 (6 %)	19 (4 %)
Epidural–spinal catheter	27 (7 %)*	8 (2 %)
Unintentional intravenous injection	17(5 %)	7 (2 %)
Other anesthetic event	58 (16 %)	51 (11 %)
No event	55 (15 %)	75 (17 %)
Unknown	25 (7 %)	33 (7 %)
Surgical event	14 (4 %)	19 (4 %)
Cardiovascular event	9 (2 %)*	36 (8 %)
Respiratory event	9 (2 %)*	30 (7 %)
Wrong drug or dose	8 (2 %)	15 (3 %)
Equipment	3 (1 %)	5 (1 %)
Multiple events	0 (0 %)	3 (1 %)

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*$P \leq 0.01$ between obstetric and nonobstetric regional anesthesia groups. Surgical events include complications of surgical technique or patient condition, with no anesthetic contribution to the complication

paracervical blocks as a means of labor analgesia or a means of pain relief for instrumental delivery, have been superceded [15] by a greater preference for central neural blockade.

Every regional anesthesia/analgesia provider must be aware of the several adverse situations which can still have a grave impact on this population of patients if not managed properly. Fortunately, most of these situations affect the parturient transiently but they still amount to a substantial 71 % of the claims (Fig. 18.1) in a closed claims database [16]. The transient nature means these events do not get into the maternal mortality database. With the predominant use of regional anesthesia techniques for anesthesia or for labor pain, an emerging consideration is inadequate block for the parturient. This has become an issue involving 11 % of the complaints [16] (Table 18.1) in a closed claims study and providers should be aware of this pitfall in regional anesthesia. This deficiency can be compared to the problem of awareness under general anesthesia when complete loss of consciousness does not occur during the procedure. There has also been renewed interest in preventing adverse events associated with regional anesthesia in the light of two high profile cases of neurological dysfunction following central neural blockade during their deliveries [17–20].

Hypotension

Hypotension following central neural blockade in the obstetric patient occurs probably in more than 50 % of our patients [6, 7]. It may be due to several causes, chief of

which is vasodilatation below the site of the block and hence pooling of blood in the lower limbs [21]. When the venous return to the heart is decreased, the cardiac output will naturally fall. With the parturient placed in the supine position, venous pooling is made worse by the presence of the term fetus obstructing the venous return following the blockade.

The extent of the obstruction and the decreased venous return is rarely appreciated. I once had a provider who was advised to place the parturient in the left lateral tilt position following a supervised spinal done in the sitting position. The provider failed to follow the instruction. Help was requested when the blood pressure dropped to near 45 mmHg systolic after the spinal blockade. In spite of the administration of fluids and vasopressor agents to improve the situation, the blood pressure continued to be low. It only improved when the patient was properly positioned as initially advised.

Most patients who need central blockade for vaginal delivery or cesarean section are required to fast and not eat solids or liquids. While a short fast may be well tolerated, longer fasting periods in an active parturient or a parturient moving around in pain, often leads to dehydration that may not be recognized and this can have significant impact on the cardiovascular system.

There are strategies to overcome this problem. Coloading with crystalloids [6] during the insertion of the central neural blockade is now the preferred technique as opposed to preloading which was previously used. Crystalloids are frequently used although colloids are often thought to be a better option. McDonald et al. found in a randomized controlled trial that there was no significant difference in the maternal cardiac output when these fluid management strategies were compared [22]. The cardiac output in the colloid group was, however, more sustained.

Vasopressors are often administered when coloading of fluids and positioning fail to sustain the blood pressure. There are providers who also administer vasopressors prophylactically in an attempt to prevent hypotension from occurring so as to reduce its impact on the parturient and the fetus [23, 24]. Previously ephedrine in small boluses of 5–6 mg per dose was favored as it has both direct (alpha and beta agonist) and indirect (release of norepinephrine from presynaptic terminals) effects and the beta agonist property was thought to better maintain uterine blood flow [25]. Ngan Kee et al. showed that placental transfer of ephedrine causes a slightly lower pH value of the umbilical blood of the newborn at the time of birth, in those whose mothers received ephedrine compared to phenylephrine [26]. A systematic analysis of the data of several studies confirmed the consistent finding of a slightly higher pH in those patients who were treated with phenylephrine for hypotension but there was definitely no fetal acidosis even in those who were given ephedrine [27]. The jury may be out as to the significance of this but there is now a definite shift to the use of phenylephrine to manage hypotension as it appears to be more effective [28].

Phenylephrine is more expensive than ephedrine and is not so readily available [27]. It has a rapid onset but is short acting and causes reflex bradycardia when the blood pressure improves. Ngan Kee et al. are now looking at the use of norepinephrine which with its weak beta agonist property may have less effect on the heart rate and cardiac output [29]. We are unlikely to start using this vasopressor in obstetrics any time soon. There are still many unknowns in the causation of hypotension following spinal blockade in many of the parturients we see everyday [30].

Local Anesthetic Toxicity: Maternal Rescue with Lipid

Local anesthetic agents are administered in greater quantities during an epidural blockade compared to a spinal blockade. This is because significant quantities of the local anesthetic agents have to diffuse from the epidural space to the intrathecal space to block the nerve roots concerned. Large quantities of local anesthetic drugs are required to achieve an adequate level of epidural blockade in obstetric patients. These patients are at risk for systemic toxicity if the epidural catheter is inadvertently inserted into a vascular structure. Subsequent injections of local anesthetic through the catheter result in a rapid increase in blood concentration of the local anesthetic thereby causing systemic toxicity.

Systemic toxicity primarily targets the CNS and cardiovascular systems [31]. The initial symptoms usually involve the CNS and include dizziness, tinnitus, or convulsions but with bupivacaine where the neurological/cardiovascular risk ratio is narrowed [32, 33], toxic manifestations in the form of life-threatening cardiac arrhythmias, cardiac collapse, or even cardiac arrest may occur in the early phase of toxicity. Local anesthetic toxicity is of particular concern for the obstetric patient as convulsions or arrhythmias can be life threatening not only to the parturient but the fetus too.

In order to avoid local anesthetic toxicity, there are many strategies that can be used. Slowly aspirating the contents of the catheter before injection is part of the process to exclude the possibility of intravascular placement after the initial insertion of the epidural. Test dosing is used before the administration of the larger epidural doses. These include the administration of at least 15 μg of adrenaline with the local anesthetic [34], but parturients in labor may manifest false positive values especially if the labor pain coincides with the administration [35]. The best advice is to treat every epidural injection, whether it is the initial dose or the subsequent top-up doses, as a test dose. This essentially requires the provider to administer small aliquots of the local anesthetic agent and to refrain from the administration of a large bolus dose at any time.

While the use of adrenaline-containing local anesthesia agents may allow the safe administration of more local anesthetic agents in the nonpregnant situation, in the obstetric setting, there are concerns about the effects of systemic absorption of adrenaline on the fetus and the parturient, especially those in the high-risk category with either cardiac disease or those with severe preeclampsia [36].

When there are signs of a local anesthetic systemic toxicity (LAST) occurring, additional injection of local anesthetics should stop [31]. Airway management and cardiovascular support are important considerations in the event of the occurrence of LAST. These measures to reduce the accompanying risk of hypoxia and acidosis complicating and prolonging the often difficult resuscitation of these patients [37]. Seizures should also be terminated with judicious use of benzodiazepines.

Lipid rescue in local anesthetic toxicity has become the recommended strategy to provide a "lipid sink" for the rapid decrease of the blood levels of the local anesthetic. The ASRA practice advisory recommends the administration of 1.5 ml/kg of the 20 % lipid emulsion as a bolus, followed by 0.25 ml/kg per minute to be given until there is attainment of hemodynamic stability lasting for 10 min [37]. An upper limit of 10 ml/kg of lipid emulsion for the first 30 min is advised. Those who have recovered from LAST should also be observed closely for the subsequent 12 h in order to prevent an occurrence especially with the redistribution of the local anesthetics back to the circulation.

While propofol is prepared in lipid, the lipid concentration in propofol is 10 % and hence it is not recommended to be used for the "lipid rescue" of local anesthetic toxicity [37]. The dose required if propofol is used for the purpose of lipid rescue will also cause excessive hypotension.

For additional discussion on this topic, please refer to Chap. 3.

Local Anesthetic Toxicity: Fetal Bradycardia

Local anesthetic agents readily cross the placental barrier. It is possible to get direct fetal toxic effects from these agents in the fetal circulation exemplified by fetal bradycardia without clinically obvious maternal systemic toxicity [38].

Fetal bradycardia is most typically associated with the paracervical block [39]. The localized effects of vasoconstriction and myometrial hypercontractility from the local anesthetic agent infiltration of the cervical milieu, can have an impact on placental perfusion, resulting in fetal bradycardia. Placental perfusion should be maximized by moving the parturient into the left lateral tilt position which will most effectively alleviate aortocaval compression [40]. Maternal oxygen supplementation is probably better avoided if the intention is to alleviate fetal distress [41]. Fetal bradycardia is usually transient but if persistent and judged to be due to excessive uterine tone, 0.25–0.5 mg subcutaneous bolus dose of terbutaline could be used to initiate tocolysis [42].

The Use of Paracervical Blocks

Paracervical blocks with infiltration of local anesthetic agents typically into the inferior cervical periphery between the 3 to 9 o'clock positions [43], have largely been superseded in routine obstetric practice due to its relative ineffectiveness for relief of labor pain [15] and major concerns about fetal safety [44]. Correct infiltration can be challenging as the cervix undergoes dynamic changes of effacement and dilation in labor, altering landmarks and the cervical milieu. Paracervical blockade can cause local vasoconstriction and increase myometrial contractility resulting in diminished placental function culminating in fetal bradycardia, hypoxia, and even death [39, 44]. The incidence of fetal bradycardia following cervical block is about 15 % [45]. Such effects can also occur with the inadvertent intrauterine injection of local anesthetics [46]. Given the reliability and availability of neuraxial anesthesia, paracervical blockade is unlikely to make a comeback into routine obstetric practice for labor analgesia, though it retains a role in gynecological procedures restricted to the cervix [47], and to a more limited extent, transcervical intrauterine minor surgery [48].

Complications due to local anesthetic agent systemic toxicity to the mother caused by hypersensitivity, overdose, or inadvertent intravascular injection, should be treated accordingly as previously described, specific to the agent. Fetal bradycardia can be managed as outlined previously but if the response is insufficient, expedited delivery by emergency cesarean section is indicated, as paracervical block has been associated with fetal and neonatal mortality.

The Use of Pudendal Nerve Block

Pudendal nerve blockade is still in fairly common use but its use for obstetric analgesia is definitely declining [49]. An effective bilateral pudendal block is the minimum analgesia required for operative delivery [50, 51], but this is insufficient for mid-cavity or rotational forceps for which central neuraxial anesthesia should be used [52]. The pudendal block may also be used to augment inadequate local infiltration in postdelivery perineal tear or episiotomy repair [49, 53]; in this context, the total dose of local anesthetic agent infiltrated must be carefully accounted for to avoid toxicity from overdose. As the pudendal nerve supplies only part of the sensory innervation of the perineum, the pudendal block is less effective to relieve pain during

the late second stage of labor compared to subarachnoid anesthesia [54]. A successful pudendal block also inhibits maternal bearing down [55]. Recent data suggest that practicing obstetricians can misidentify the exact injection site for transvaginal pudendal nerve blockade in a mannequin pelvis setting and they typically overestimate the block's speed of action [56].

Potential complications in pudendal block are uncommon but include inadvertent maternal intravascular injections or overdose of local anesthetic agent. Hematomas can arise from injury to the pudendal artery. Large hematomas can extend to the ischiorectal fossa or into the retroperitoneal space [57, 58]. Ongoing pudendal artery bleeding may best be managed with embolization if interventional radiology expertise is available, as it is difficult to access surgically, it being close to important nerve bundles. Infection (retro-psoas and subgluteal abscess) can also occur [59], and suspicion should be aroused if there is severe hip or back pain associated with fever after delivery aided by a pudendal block. If not responsive to antibiotics, drainage of these abscesses may be required. Neonatal toxicity [60], from absorbed or inadvertent direct fetal injection of local anesthetic agent is rare but may be suspected if unexplained neonatal hypotonia, papillary mydriasis fixed to light, apnea, or seizures [49], occur in the newborn after delivery.

Neurological Dysfunction in the Obstetric Patient

Dysfunction can be the result of failed care by the obstetrician or the anesthesiologist. It is often difficult to differentiate among the many causes but what is useful to understand is that the earlier the dysfunction is recognized [61], and attended to by the correct care provider—usually the involvement of a neurologist under these circumstances, the lesser the damage in the long term.

Obstetric Palsies

Postpartum sensory or motor dysfunction in obstetrics has an incidence approaching 1 % [62]. This is often secondary to the mechanics of labor or fetal pressure on the nerves, which can be exacerbated by dense sensory blockade allowing persistent unawareness of the ongoing nerve damage as it occurs [63].

There are several sites where there is increased vulnerability to damage occurring:

1. The lumbosacral nerve trunks as they cross the posterior pelvic brim before descending anterior to the sacral ala. The trunks can be compressed by the fetal head resulting in unilateral foot drop on the opposite side to the fetal occiput and some sensory loss on the lateral lower leg and dorsum of the foot [64].
2. The lateral femoral cutaneous nerve (no motor component, damage resulting in meralgia paresthetica) [65], the femoral nerve or both can be compressed particularly by prolonged thigh flexion as they cross the anterior superior iliac spine or inguinal ligament, with the likelihood of neuropathy exacerbated by increased abdominal pressure (possibly even from external cardiotogram straps). Femoral neuropathy, which can be bilateral, may cause inability to climb stairs, decreased patellar reflex, and femoral distribution sensory loss [66, 67].
3. Obturator neuropathy causes decreased inner thigh sensation and weakness of hip adduction and rotation [68, 69].
4. The common peroneal nerve can be injured from even inappropriate positioning of the patient's hand against the distal posterior thigh under epidural anesthesia in labor [70], prolonged pushing in squatting [71], or lithotomy positions [62], causing foot drop and sensory loss, limited to a wedge-shaped area on the dorsal side and proximal to the big and second toe [63].

Fortunately, these nerve palsies are usually temporary with recovery expected in about 2 months [62]. The occurrence of these palsies may be minimized by frequent changes of lower extremity positions, particularly if the second stage of labor is prolonged. One should avoid prolonged thigh flexion and extreme thigh abduction and external rotation. One should also avoid dense motor and inappropriately dense sensory blockade of labor regional anesthesia [63]. Alpha-lipoic acid supplementation has shown some early promise if neuropathic pain is a prominent feature [72].

Preventing Spinal–Epidural Hematoma

Improvement in medical care has seen many high-risk patients, especially cardiac parturients, arrive at a stage of their lives where they can potentially become pregnant and deliver in spite of their medical conditions. In order to safely do that, many may be put on treatment or prophylactic doses of antithrombotic agents by their care providers to reduce the incidence of thrombosis. This is especially likely in those who have arrhythmias, those with prior correction of lesions in the heart, and those who need to have bed rest in order to reduce the strain on their heart. Equally important are those parturients on antithrombotic therapy due to thrombophilia, or patients with history of venous thromboembolism [73, 74].

These treatment or prophylactic doses of antithrombotic agents have an impact both on the outcome of the fetus as well as the way we handle our anesthetic technique, especially regional anesthesia for deliveries in the parturient [75]. To reduce the impact of the antithrombotic agents on the

fetus, most providers would opt for heparin or heparin products during the first trimester when organogenesis is taking place [73, 75]. This is to avoid the embryopathy associated with the use of warfarin. Heparin compared with warfarin, however, is a much less efficient antithrombotic agent to prevent thrombosis in the parturient [75]. Most obstetric/cardiac care providers opt for heparin in the first trimester, cover the parturient in the second and third trimester with warfarin, and then move on back to heparin products by 36 weeks of gestation, in order to allow greater flexibility with antithrombotic management of the parturient during the delivery process involving either surgery or anesthesia [73].

When a parturient presents at term or near term for delivery and is in need of a central blockade for analgesia or anesthesia, it is important to determine the actual antithrombotic status of a patient. The primary physician would be able to advise if the parturient is on treatment or prophylactic doses of the antithrombotic agents. If the patient is on a treatment regime, central blockade is best avoided and other options like patient-controlled analgesia for labor pain and general anesthesia for cesarean section are safer choices. If the patient is on a prophylactic dose of the agent, it is possible to time or readjust the administration of the agent, in such a way as to reduce the risk of a spinal–epidural hematoma occurring [73, 74].

The risk of a hematoma is smaller in an intrathecal injection compared to that of an epidural injection—estimated to be around 1 in 150,000 for epidurals and 1 in 220,000 for spinals [75], although there are concerns that these are underestimated [74]. Catheter utilization increases the risk of spinal hematoma in these patients. They must also be inserted and removed at a time when the effect of the antithrombotic agent is at a minimum. Guidelines do exist on this subject [74, 76]. An excellent guide as to how to adjust these drugs for the various procedures appears in Table 18.2.

While it is important to be guided by them, it is as important to weigh the options and consequences of each individual

Table 18.2 Guide to adjustment and administration of antithrombotic agents for regional anesthesia/analgesia

	Time[a] before puncture/catheter manipulation or removal	Time after puncture/catheter manipulation or removal	Laboratory tests
Unfractionated heparins (for prophylaxis, ≤15,000 IU per day)	4–6 h	1 h	Platelets during treatment for more than 5 days
Unfractionated heparins (for treatment)	i.v. 4–6 h	1 h	aPTT, ACT, platelets
	s.c. 8–12 h	1 h	
Low-molecular-weight heparins (for prophylaxis)	12 h	4 h	Platelets during treatment for more than 5 days
Low-molecular-weight heparins (for treatment)	24 h	4 h	Platelets during treatment for more than 5 days
Fondaparinux (for prophylaxis, 2.5 mg per day)	36–42 h	6–12 h	(anti-Xa, standardized for specific agent)
Rivaroxaban (for prophylaxis, 10 mg q.d.)	22–26 h	4–6 h	(PT, standardized for specific agent)
Apixaban (for prophylaxis, 2.5 mg b.i.d.)	26–30 h	4–6 h	?
Dabigatran (for prophylaxis, 150–220 mg)	Contraindicated according to the manufacturer	6 h	?
Coumarins	INR ≤ 1.4	After catheter removal	INR
Hirudins (lepirudin, desirudin)	8–10 h	2–4 h	aPTT, ECT
Argatroban[c]	4 h	2 h	aPTT, ECT, ACT
Acetylsalicylic acid	None	None	
Clopidogrel	7 days	After catheter removal	
Ticlopidine	10 days	After catheter removal	
Prasugrel	7–10 days	6 h after catheter removal	
Ticagrelor	5 days	6 h after catheter removal	
Cilostazol[b]	42 h	5 h after catheter removal	
NSAIDs	None	None	

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ACT activated clotting time, *aPTT* activated partial thromboplastin time, *b.i.d.* twice daily, *ECT* ecarin clotting time, *INR* international normalized ratio, *IU* international unit, *i.v.* intravenously, *NSAIDs* nonsteroidal anti-inflammatory drugs, *s.c* subcutaneously, *q.d.* daily

[a]All time intervals refer to patients with normal renal function

[b]Prolonged time interval in patients with hepatic insufficiency

patient and determine what is best for the patient concerned. A patient on antithrombotic agents may have had a previous cesarean section done under general anesthesia with a Grade 1 laryngeal view—this should be a license in an elective situation, to proceed with another general anesthetic, instead of proceeding with the potentially hazardous risk of a spinal hematoma no matter how remote the possibility.

All parturients who have delivered with a central blockade should have monitoring regular enough to pick up a spinal–epidural hematoma. This is especially so for those who are on antithrombotic agents, even those on prophylactic doses of the agent. Monitoring should include sensory/motor functions of the lower limb and the ability to pass urine or pass flatus, plus the state of recovery of the anal sphincter tone. In order to facilitate monitoring for spinal hematoma, it is imperative that continued analgesia should have reduced concentrations of local anesthetic agents in them and preferably only analgesic agents should be used in the catheter infusion to facilitate recognizing the signs of a hematoma. A spinal hematoma picked up and definitively evacuated within 8 h of occurrence of the event has a better prognosis compared to one which is evacuated much later [77].

Newer drugs are increasingly brought into the market and some of these drugs may be used by the parturients [76]. The collective experience of these drugs in the global arena is limited—one should preferably err on the side of caution and opt for the safer alternative of general anesthesia in a parturient already proven to have an easily controllable airway or for patient-controlled intravenous analgesia for labor requirements especially if in doubt about the antithrombotic status.

For additional discussion on this topic, please refer to Chaps. 8 and 14.

Infection (Meningitis/Epidural Abscess)

Anesthesiology providers globally have been able to provide a very high level of cleanliness/sterility during the process of delivering central blockade to parturients. Infectious complications in the form of epidural abscess and meningitis are rare events considering that over 90 % of obstetric anesthesia conducted worldwide is in the form of regional anesthesia [78, 79]. As it is a rare event, it is difficult to prove that our stringent standard of wearing masks, caps, and sterile caps/gowns during the process is responsible for this clean or almost clean record [80]. Baer et al., however, noted that nearly 50 % of the meningitis in his historical series of 179 cases was related to viridans streptococcus, a mouth commensal, so presumably the risk of infection may be related to the way the care provider wears his face mask [78]. Whether related or otherwise, it still behooves us to be vigilant and to keep the standard of cleanliness high as every case of abscess or meningitis has the potential of causing permanent harm [81].

There has been debate on the choice of the best skin disinfectant to decontaminate the skin prior to the procedure. Chlorhexidine and povidone iodine are available as aqueous or alcohol-based solutions and may have comparable antiseptic properties [82]. However, chlorhexidine-based solutions have been shown to be superior in antiseptic properties to aqueous or alcohol-based povidone solution in other studies [83, 84]. The better efficacy of one agent over another may have to be explored in the context of whether alcohol [85, 86] was part of the test solution or the concentration of the solution involved [87]. Chlorhexidine is cheaper, faster in onset, and provides sterility of longer duration, and so is often preferred [82, 88].

To further enhance the safety record, most of us use occlusive dressings after the epidural catheters are inserted and bacteria filters for epidural infusions. We may on most occasions avoid regional analgesia/anesthesia techniques in those who are febrile as there has always been an element of doubt whether it would be safe to conduct intrathecal and epidural insertions in patients who possibly may have septic foci elsewhere in the body. Goodman EJ et al. have shown that it is safe to perform spinal and epidural anesthesia in parturients with chorioamnionitis [89]. Their experience with 517 parturients with epidurals and 14 with spinals, whose placentas were found to be subsequently positive for chorioamnionitis, had no adverse events in the form of meningitis or epidural abscess. As many as 18 % of his patients were febrile and there were 14 % having leukocytosis. From this collection, it is possibly safe, even without prior antibiotic therapy, to conduct regional anesthesia in these parturients.

Infectious complications of central neuraxial blockade although rare can be life threatening when they occur. It is therefore important to be aware of the possible symptoms and signs these patients may reveal. Any parturient who presents with fever, headache, backache [80], following a regional blockade and especially associated with photophobia, neck stiffness with any neurological deficits following a central neuraxial blockade, should be viewed as likely to have infection in/around the spinal cord, unless proven otherwise.

Cultures from the blood and cerebrospinal fluid should be requested for and if the catheter is still in place, the catheter tip should be sent for culture. Imaging studies may provide further details about collections of abscesses [90]. Involvement of the neurologists and other appropriate experts in the management of the patient early is essential [80]. Correct antibiotic therapy, guided by cultures and with the hospital infection team involved, are urgent considerations. It might be useful to know that the most common isolate for meningitis related to central blockade, is alpha hemolytic streptococci due to the proceduralist [78, 79]. Abscesses as may need drainage and these can be done either by surgeons or through percutaneous drainage with the help of a radiologist [80].

For additional discussion on this topic, please refer to Chap. 9.

Chronic Adhesive Arachnoiditis

This condition although rare has generated a fair amount of interest in light of two parturients experiencing quadriparesis, following the administration of regional techniques during their deliveries. The first patient has been awarded compensation for chronic adhesive arachnoiditis following the spinal she received for her cesarean section [17, 91–93]. The condition has been judged as due to a minute amount of chlorhexidine contaminating the bupivacaine which was injected into the epidural space. In the second patient's situation, it was due to a mix up of the chlorhexidine meant for cleaning and the normal saline meant for determining the loss of resistance and the subsequent administration of 8 ml of the former into the epidural space [18–20].

In both these cases, the condition is characterized by an initial complaint of pain at the time of administration, the subsequent complaint of headache and backache with the MRI demonstration of clumping of the nerve roots and demyelination in the cord with the formation of syringomyelia and hydrocephalus which needed drainage [17–20, 91–93]. They both ended up with paralysis/paresis in all four limbs with impairment of micturition and bowel control. While there have been doubts whether minute amounts of chlorhexidine are neurotoxic, in the case of the second patient where chlorhexidine has been accidentally injected, the cleaning agent was implicated as being responsible for the signs and symptoms she had.

Our practice in the conduct of central blockade must be so meticulously well carried out that a repeat of these cases is not possible. Once the condition sets in, attempts to intervene have never been successful based on the experience of the several cases in the literature [94, 95]. Prevention is the only way to decrease the risk of this condition. Regardless of whether chlorhexidine or povidone is used in our practice, chlorhexidine [93], which has been strongly implicated, must now be viewed as potentially neurotoxic by care providers and if possible to be kept as far as possible from the agents which are to be injected into the intrathecal or epidural space. The drugs to be injected should preferably be syringed directly into the syringes and not be decanted into the galley pots with the intention of aspirating it when needed. The possibility of it being exposed to contamination and mixed up with the antiseptic agents, is great under the circumstances. Besides the galley pots are sterilized and so are bacterial free but need not necessarily be chemically free of the antiseptic agent from a previous use, where they are cleaned and sterilized. There is no provision for determining that the galley pots are chemically free unlike the determination of the bacteria-free status of the sterile pack.

Whether we use sprays or solutions to clean the area for regional anesthesia, these cleaning agents must not come into contact with the needles and agents that ultimately enter the intrathecal space. It is advisable to prepare the needles and intrathecal agents with clean uncontaminated gloves as the initial part of the preparation and the cleaning agent must never be allowed to contaminate any devices or agents entering the spinal or epidural space. We advise change of gloves if they become contaminated, before picking up the spinal needle again.

Postdural Puncture Headache

In the care of laboring parturients, most providers administer epidural or combined spinal epidural injections for the relief of pain. Epidural needles are usually 18 G or larger and there is a 1.5 % risk of entering the intrathecal space, especially if the technique of insertion is incorrect or the parturient moves at the critical moment [96]. The incidence of postdural puncture headaches occurring following an inadvertent intrathecal puncture with an epidural needle, may be as high as 50 % [96]. Patients with a known inadvertent intrathecal puncture should probably not be encouraged to push during the delivery process and should have assisted instrumental delivery, in order to reduce the risk of a headache [97].

These headaches must be differentiated from other more menacing headaches that can occur [98]. Any patient with headache following central blockade should have the nature of the headache thoroughly explored to determine if there are any lateralizing signs that may portend more serious life-threatening conditions, e.g., strokes, cerebral hematomas, raised intracranial pressures, and meningitis [98]. Postdural puncture headache is a diagnosis of exclusion [99], although it typically is described as a headache that follows a central blockade performed a day or more previously. Patients may complain of headaches that are usually frontal, frontoparietal, or even occipital, often occurring bilaterally, worse upon sitting upright and this may be accompanied by nausea, vomiting [98], tinnitus [98], or other hearing [100], or visual disturbances [101].

Bed rest does not reduce the incidence of postdural puncture headaches—it may just delay the occurrence [102]. Fluid hydration does not obviate the occurrence [103] but most who have headaches will feel better with adequate hydration. Caffeine has also been used but there have been questions about the methodology of the limited numbers of studies done [103]. In a more recent study [104], caffeine was administered intravenously in a randomized, double-blind, placebo-controlled, nonobstetric study after spinal anesthesia and the results indicated a reduced incidence of headache. Morphine and cosyntropin (tetracosactide) have been found to be of use in the management of spinal headache but their limited studies do not provide very strong evidence [105].

An autologous epidural blood patch [106] is the gold standard in therapy of this condition once other causes of headache have been excluded [98]. It involves the sterile administration of 15–20 ml of blood (taken under sterile condition from an accessible vein) into the epidural space over the site of the previous central blockade. In most situations it is claimed that the blood patch may relieve as many as 93 % of the headaches but in reality probably only about 75 % get complete relief from the procedure and hence need a second blood patch to do so [107].

Patients with spinal headache not properly treated may progress to cranial subdural hematomas [108, 109]. This is due to the persistent CSF leak with resultant sagging of the brain and rupture of the bridging cerebral veins.

Epidural blood patch does not impact future administration of local anesthetics into the epidural space in most patients [110], although there was one case report of limitation of spread of the anesthetics in a patient with a previous patch [111]. For further discussions of PDPH please refer to Chaps. 14 and 15.

Cauda Equina Lesion

Just as epidurals with catheters can be titrated to meet maternal needs whether for analgesia or anesthesia, there is a lot of attraction for using continuous spinals to allow similar maternal benefits. However, experiences with continuous spinals in the early 1990s with nonobstetric cases ended with a few cauda equina lesions [112, 113]. Cauda equina lesion refers to the entity [114, 115] where there is compression/damage of the nerve roots in the cauda equina region and patients complain of symptoms of anesthesia in the saddle region, bladder, and bowel dysfunction plus lower limb weakness [114, 116].

Continuous spinal anesthesia technique is believed to deliver higher than normal doses of local anesthetic to the nerve roots causing damage. Part of the mechanism could also be attributed to maldistribution of the local anesthetic through the catheter and the catheter allows for prolonged administration into the same site. Animal studies do confirm the neurologic nerve damage with large doses [115], intrathecally of bupivacaine, chloroprocaine, and lignocaine and the damage seems to be greater with longer duration [117], of drug administration. Lignocaine has been particularly implicated as neurotoxic [118], and it is important to avoid the administration especially if there is any possibility of it entering the intrathecal space in large amounts [119]. Imaging studies may be needed to distinguish other remediable conditions that may present with similar symptoms of cauda equina lesion and early surgical involvement is prudent [120].

Cord Damage

There is also concern of damage especially if the neuraxial blockade is sited at a level before the cord ends. Felicity Reynolds describes the occurrence of neurological damage in a series of 7 patients where the spinal anesthesia had caused pain to the patients during the initial intrathecal injections [121]. The damages to the cord were subsequently confirmed through CT scans and even a postmortem in her series. As there is variability in the termination of the conus and with it being extremely low in up to 20–30 % of the population it is advisable not to inject intrathecally above L3 [121].

Transient Neurological Symptoms

This is described as a dysesthesia occurring after spinal anesthesia lasting up to 1–2 days where patients complain of pain in the back and or lower extremities [122]. The incidence is highest with lidocaine and lidocaine in any concentration, is no longer recommended for spinal anesthesia [123, 124]. There have also been incidences of the condition described with the use of levobupivacaine [125]. For patients who present with TNS, it is important to exclude more ominous causes of the pain [126]. If the pain is mild, nonsteroidal agents may be used.

Inadequate Block for Vaginal Delivery and Cesarean Section

While regional blocks especially epidurals and combined spinal epidurals are deemed to provide the best form of analgesia for vaginal delivery, there are instances when the blocks fail to provide adequate analgesia for this purpose. Pan et al. describe an overall failure rate of 12 % in his series of 19,000 deliveries [127].

There are many reasons why epidurals fail. The failure can be right from the start or it may be a block that was working well but became inadequate subsequently. The failure can even be during the delivery itself when patients complain of pain during the repair of the episiotomy. An epidural that did not provide analgesia right from the beginning is due to the catheter not being placed correctly in the epidural space. Loss of resistance is an appreciation by the epiduralist through touch, a situation that may not truly reflect the entrance of the epidural needle into the epidural space. Sometimes the epidural needle is correctly placed but the catheter has gone out of the space [128] or is in an epidural vein [127]. Preferably 4 cm of catheter length should

be left in the epidural space. Providers may sometimes opt for a reduced length of the catheter to be left in the space, especially if they have been aspirating and withdrawing the catheter that has presumably gone into the vein. The distance from skin to the epidural space measured by a metal epidural needle, may not necessarily be the same as that measured with the epidural catheter, which tends to move in the space, especially when the patient moves from the flexed upright to the lateral position [129]. There is also a risk of the catheter being displaced from the epidural space when that happens.

An epidural that fails after working well initially can also be due to several reasons. It is likely the catheter has migrated from its original site [130, 131], if the catheter has not been secured properly [131]. The migration can be so extensive that the catheter has totally come out from the epidural space. When an epidural is no longer working, one should at least turn the patient over to inspect the site where the epidural has been placed. Not connecting the epidural infusion set to the catheter but to an intravenous infusion was the reason why an epidural (in one of my patients), previously working was no longer doing so, 1 h after the insertion. This error not only would not provide adequate labor pain relief but may potentially expose the parturient to the risk of local anesthetic toxicity. The NHS is now mandating that injections of regional anesthetic drugs must be made through non-Luer fit devices, to prevent the injection of local anesthetic agents into the cardiovascular system [20, 132].

In some units, obstetric colleagues still labor under the impression that as epidural infusions prevent parturients from feeling pain and they no longer sense the need to push with each contraction at the end of the first phase of labor, the infusion has to be stopped. Obviously epidural infusions stopped by uncooperative providers, may be responsible for failure of epidurals to provide analgesia during the critical stage of labor when pain is at its worst [133].

In our move to reduce the impact of labor analgesia on the progress of labor, we often resort to use lower concentrations of local anesthetics without realizing this may not be adequate. All epidurals must be titrated to meet patient's needs and there are many ways of doing so. Computer-integrated patient-controlled epidural analgesia has been designed to deliver exactly the required amount of local anesthetic to meet the patient's needs and ultimately provide optimal maternal satisfaction [134]. The hourly baseline delivery is readjusted by the computer delivery system based on boluses requested in the previous hour. While it is often assumed that position does not affect the delivery of epidural infusion, it does often impact the levels and intensity of pain [135]. When a parturient on epidural infusion complains of pain, it is important to determine exactly where the pain is. A patient propped up during the continued infusion may have adequate relief in the sacral roots but may complain of renewed pain in the abdominal dermatomes and this may have to be relieved with a top up in a more horizontal position.

Failure to relieve pain adequately can eventually lead is a law suit against the provider. Lee et al. showed that temporary injuries from a closed claims database, are a more extensive issue in parturients than the nonobstetric patients [16]. In their series of 260 patients claiming for temporary injuries, 17 % claimed for inadequate analgesia/anesthesia. It is important to make it a practice to get the parturients receiving central blockade to provide a pain score for the labor analgesia or anesthesia and record it into the notes.

While spinal anesthesia has a high density of block compared to epidurals for cesarean section, the increased density comes from the use of an adequate dose of local anesthetic. In high-risk parturients we use low-dose spinals in order to preserve hemodynamic stability; inadequate block during anesthesia can occur and cause as much discomfort to the parturient—enough to initiate a law suit against the provider.

Extensive Block

In order to enhance the intensity of nerve blockade with epidurals, more local anesthetic drug is administered. Local anesthetics in the epidural space have to traverse into the intrathecal space to produce the effect. There is always the possibility that all the local anesthetic intended for the epidural space is inadvertently injected into the intrathecal space. This will lead to what is often known as a total or high spinal.

In the event that a total spinal has occurred, the patient is likely to lose consciousness and to suffer a hemodynamic collapse because of the extensive blockade. The parturient needs to be placed in the left lateral tilt position and her airway needs to be managed appropriately. Vasopressors are needed to slowly bring the blood pressure up to an acceptable level. It is important to understand that the head down position is to be avoided in these cases as a massive intrathecal injection of local anesthetic, recently administered will gravitate to the upper cord further endangering the patient. However, every effort must be made to maintain the venous return to the heart and this may also require elevation of the lower extremities.

Intentional spinal blocks usually do not cause extensive blocks during labor or anesthesia but it can still occur [136]. Even epidural test dose has been described to cause extensive block especially if the dose is more than is needed by the patient to produce the required intrathecal block [137].

A spinal done after a parturient has been exposed to an epidural/epidural infusion for labor albeit an inadequate one can result in an extensive blockade [138, 139]. Epidural infusions previously administered compress the intrathecal space and when a spinal dose of drugs is introduced into a "narrowed"

space, an excessively high block can result. It is important to reduce the dose to about two-thirds of what is normally administered to contend with this reduction in capacity of the intrathecal space.

Respiratory and Cardiac Arrest

These are probably extremely rare events in obstetrics. Auroy capturing the regional anesthetic experience of 158,000 central neuraxial blocks in participating hospitals in France over a 10-month period from 1998 to 1999 had only one cardiac arrest following a spinal and three respiratory failures related to epidurals in their obstetric patients. The obstetric portion of the data recorded a total of 5640 spinals and 29,732 epidurals. Similarly the third National Audit Project of the Royal College of Anesthetists, United Kingdom [13] with over 700,000 central neuraxial blocks in the data collected in 2006 of undifferentiated patients, did not capture any of these events in the obstetric population. These events can still happen and every care provider in the obstetric scene must have a plan to manage these life-threatening events or to prevent its occurrence.

Respiratory depression in central neuraxial block due to the administration of lipophilic narcotics is rare but is more likely to occur in vulnerable patients especially those with morbid obesity, obstructive sleep apnea; those with cardiopulmonary disease; and those given preoperative narcotics [140, 141]. Single-dose sustained-release [142], or extended-release [140], epidural morphine has also been described as relatively safe in normal patients but one must exercise caution in those who are vulnerable. All patients who receive [142] neuraxial opioids should have monitoring to determine adequacy of oxygenation (including level of consciousness) and ventilation. Respiratory rate monitoring may not be adequate and a pulse oximeter is not a sensitive monitor of oxygenation in the ward setting [141].

It is more important to ensure that the care providers looking after a parturient given neuraxial narcotics are aware of this life-threatening complication and treat early signs of respiratory depression appropriately with naloxone [141]. Oxygen should also be administered if oxygenation is impaired, together with strategies to provide ventilation [143].

Cardiac arrest whether related to neuraxial block or otherwise, can also be life threatening not only to the mother but to the fetus as well [144]. If an arrest occurs after 20 weeks gestation the parturient should be tilted to the left to relieve pressure of the gravid uterus on the inferior vena cava and the aorta [145]. The resuscitation should follow the algorithm designed for a nonpregnant patient with regards to airway, breathing, circulation, and drug/defibrillation dosages [145, 146]. Delivery of the baby should be undertaken within 4 min of the arrest in those mothers who are experiencing no return of circulation and where the baby exceeds 20 weeks gestation [145, 146]. Perimortem delivery was described as beneficial to the mother in a third of the cases [144], and earlier delivery better for the fetus, with the survivors experiencing a mean arrest delivery time of 14 min compared to 22 min for the non survivors. The perimortem delivery must be carried out at the place of the resuscitation and the parturient should preferably not be moved [145].

Conclusion

While it may seem that regional anesthesia and analgesia is fraught with issues providers may have to be concerned about, it is still exceedingly safe. One is more likely to be hauled up for hypoxic brain damage following general anesthesia than damage from regional anesthesia in spite of the fact that regional anesthesia is used so much more often in obstetric practice.

There are attempts to capture the risk of complications in obstetric anesthesia regardless of whether it is conducted under general or regional anesthesia. The Serious Complication Repository Project of the Society for Obstetric Anaesthesia and Perinatology started in 2004, may ultimately provide a better picture of the risks of regional anesthesia/analgesia and determine where we should put our efforts to improve the hazards [147].

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Local and Regional Anesthesia in the Obese Patients

19

Hendrikus J.M. Lemmens

Key Points

- Obesity is the major epidemic of our generation, and anesthesiologists are confronted to manage obese patients and their associated comorbidities at an increasing rate.
- Regional anesthesia is an attractive option for obese individuals because it avoids the need for airway manipulation with general anesthesia and may reduce or eliminate the need for opioids and their associated side effects. However, obesity presents unique challenges to performing regional blocks and raises the risk of certain complications.
- Respiratory complications are a major consideration when anesthetizing an obese patient; sedation should be avoided if possible, and breathing function may be impaired by certain nerve blocks (e.g., local anesthetic spread to phrenic nerve following interscalene brachial plexus block).
- The pathophysiology associated with obesity such as obstructive sleep apnea and the metabolic syndrome places these patients at increased risk for perioperative complications.
- Central neuraxial blocks tend to be more complicated in obese individuals due to positioning difficulties, smaller target area (i.e., epidural space), dosing adjustments, intravascular puncture, and hemodynamic changes.
- The aim of this chapter is to provide the anesthesiologist with a practical approach to the problems associated with regional anesthesia in obese patients.

H.J.M. Lemmens, MD, PhD (✉)
Department of Anesthesiology, Pain and Perioperative Medicine, Stanford University School of Medicine, Stanford, CA, USA
e-mail: hlemmens@stanford.edu

Introduction

More than 35 % of the adult population of the United States is obese (BMI>30 kg/m^2), and obesity rates throughout the world continue to increase each year. Obese patients outnumber normal weight patients for certain surgical procedures such as joint replacements. The increased prevalence of obesity has impacted perioperative morbidity and mortality. Surgical procedures in obese patients are technically more challenging which may result in a longer duration of surgery and greater intraoperative blood loss. Comorbidities such as the metabolic syndrome and obstructive sleep apnea can increase the likelihood of cardiac, pulmonary, and other complications [1–3].

A major advantage of regional anesthesia techniques is that loss of sensation is achieved without impairing consciousness or central control of vital functions. Airway manipulation is not needed, opioid use is avoided or decreased, opioid-related side effects are minimized, and the stress response to surgery may be reduced. These potential benefits are particularly important for the morbidly obese patient who has a significant decreased cardiopulmonary reserve.

Regional techniques are more difficult to perform in the obese. Positioning for a regional block may be more difficult, anatomic landmarks may be obscured, and special equipment, such as longer needles, may be required. If during surgery the regional blockade becomes inadequate the need to induce general anesthesia and establish an airway, often in less than ideal conditions, may be problematic. In regional anesthesia, obesity is associated with an increased rate of complications, failed blocks being the most important component. Nielsen et al. have shown that obese patients were 1.6 times more likely to have failed regional anesthesia [4]. The following is a review of local and regional anesthesia in obese subjects with a focus on complications.

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_19

Table 19.1 Classification of obesity

Classification	BMI range	Health risk
Overweight	25–30	Mild
Class I	30–35	Moderate
Class II	35–40	Severe
Class III	>40	Very severe

Classification of Obesity

The World Health Organization and the U.S. National Institutes of Health (NIH) have classified obesity primarily on the basis of BMI, associated comorbid conditions, and mortality risk [5, 6]. Overweight and obesity can be divided into four levels of severity of comorbidity and mortality risk (Table 19.1). Class III obesity (BMI >40 kg/m^2) is also known as morbid obesity.

Respiratory Considerations

At baseline morbidly obese subjects may be mildly hypoxemic, with higher respiratory rates and lower tidal volumes. The compliance of the respiratory system is reduced resulting in increased work of breathing. Functional residual capacity (FRC) and expiratory reserve volume (ERV) decrease exponentially with increasing BMI, with the greatest rate of change in the overweight and mildly obese. In sitting subjects with a BMI of 30 kg/m^2, FRC and ERV are only 75 % and 47 % of the values for person with a BMI of 20 kg/m^2 [7]. In supine position, the effect of BMI on FRC is more pronounced and tidal volume may fall within closing capacity, promoting shunting.

The prevalence of sleep apnea in obese patients can be as high as 75 % [8]. Of those with sleep apnea and severe obesity up to 20 % may have the obesity hypoventilation syndrome (OHS), which is characterized by awake hypercapnia, hypoxemia, and elevated HCO_3^- [9]. It is important for anesthesiologists to recognize patients with OHS because it is associated with severe upper airway obstruction, restrictive lung disease, blunted central respiratory drive, and pulmonary hypertension.

High-volume injections of local anesthetics during neuraxial or brachial plexus blocks may further compromise the respiratory status. For example, an interscalene brachial plexus block may affect the phrenic nerve, leading to temporary paralysis of the ipsilateral hemidiaphragm. The use of low-volume ultrasound-guided interscalene block is associated with fewer respiratory complications with no change in postoperative analgesia compared with the standard-volume technique [10]. Spinal anesthesia in obese parturient scheduled for Caesarean section was associated with a BMI-dependent decrease of lung function, which persisted well into the recovery period, even longer than the actual presence of motor blockade [11]. In nonpregnant obese subjects, similar changes in lung function have been observed [12]. Intraoperative application of noninvasive positive pressure ventilation can improve respiratory function.

Cardiovascular Considerations

The increased tissue mass of the obese needs to be perfused leading to an increased total blood volume [13]. The increased total blood volume results in an increased cardiac output. Cardiac output increases from 4 L/min at a BMI of 20 kg/m^2 to more than 6 L/min at BMIs greater than 40 kg/m^2. Cardiac output affects the early pharmacokinetics, the front-end kinetics of drug distribution, and dilution in the first minutes after administration. An increased cardiac output decreases the fraction of drug distributed to the brain and increases the rate of redistribution, which may result in lower peak concentrations.

The most prevalent comorbidity in obese patients is hypertension. The increased cardiac output, the metabolic syndrome, diabetes, and physical inactivity all contribute to systolic and diastolic dysfunction even in otherwise healthy young obese subjects, which may eventually progress to left and/or right heart failure. The combination of super obesity (BMI>50 kg/m^2) with hypertension and diabetes is associated with a twofold increased risk of death and adverse cardiac events in the perioperative phase [14]. There is evidence that epidural analgesia can reduce cardiovascular and pulmonary morbidity and mortality in high-risk obese patients undergoing major thoracic and abdominal surgery [15].

Pharmacology

Effect of Obesity

Until recently, obese subjects have been routinely excluded from clinical trials to obtain regulatory approval for investigational drugs. This has resulted in package insert dosage recommendations valid for normal weight patients but not for the obese. Obesity is not only associated with an increase in tissue mass but also changes in body composition and tissue perfusion. Fat mass and lean body mass both increase, but the increase is not proportional. The percentage of lean body mass as a percentage of total body weight decreases (Fig. 19.1). The different ratio of lean body weight to fat weight at different BMIs will have a significant impact on drug distribution. Fat perfusion is also altered at different BMIs. At low BMIs fat is relatively well perfused, at high

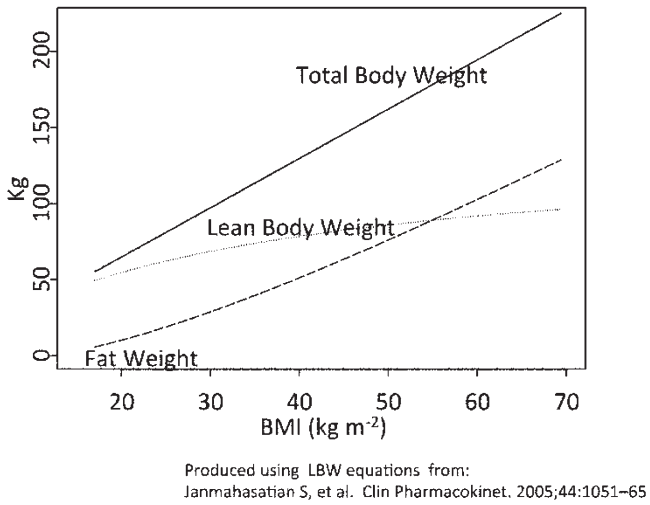

Fig. 19.1 Changes in body composition for a typical frame 167 cm tall female who increases her BMI. Lean body weight was calculated using the equations published by Janmahasatian, S., Duffull, S.B., Ash, S., Ward, L.C., Byrne, N.M. & Green, B. Quantification of lean bodyweight. Clin Pharmacokinet 44, 1051–65 (2005). Fat weigh was calculated by subtracting lean body weight from total body weight

BMIs fat is poorly perfused. Because of the different ratio of fat to lean body weight at different BMIs and changes in fat perfusion, the effect of obesity on drug distribution into the different tissues is poorly understood. The increased cardiac output of the obese decreases the fraction of drug distributed to the brain and increases the rate of redistribution, which may result in lower peak concentrations. In obese patients with normal cardiac function, cardiac output is highly correlated to lean body weight, more so than total body weight or other variables. Therefore, lean body weight and cardiac output are more appropriate dosing scalars than total body weight. Total body weight dosing will result in overdosing and side effects.

Numerous pharmacokinetic studies have shown that clearance, the most relevant pharmacokinetic parameter for maintenance dosing is linearly related to lean body weight but not total body weight. This implies that lean body weight is the appropriate dosing scalar, not only for determining loading doses, but also for maintenance doses.

Sedation

Ideally administration of sedatives should be minimized or avoided. Respiratory depression caused by benzodiazepines and opioids is more pronounced in the obese, especially in those with obstructive sleep apnea. Upper airway collapsibility and decreased arousal response to airway occlusion make these patients particularly sensitive to drug-induced respiratory depression. Benzodiazepines decrease upper airway muscle activity with consequent obstruction and cause central apnea during the initial postadministration minutes. If very anxious, patients need premedication. Small doses of midazolam and opioids can be administered under continued monitoring. Recommend dosing scalars for several anesthetic agents used for sedation during block placement are summarized in Table 19.2.

Local Anesthetics

Local anesthetics have a well-characterized side effect profile that includes the risk of CNS and cardiovascular toxicity and other adverse effects such as nerve injury and chondrolysis. There is no evidence that these side effects occur more often in the obese. In diabetic rats, an increase in nerve damage occurs after nerve block with traditional local anesthetics such as ropivacaine [16]. Some have

Table 19.2 Recommended dosing scalars for IV sedative agents and opioids during regional anesthesia in obese patients

Sedative agents:	Dosing scalar	Comments
Midazolam	LBW	Titrate very carefully, time to peak effect is 3 min
		Avoid in sleep apnea patients
		Synergistic respiratory depressant effect with opioids
		Cave airway obstruction
Dexmedetomidine	LBW	
Ketamine	LBW	Minimal respiratory depression
		Potent analgesic
Propofol	LBW	For continuous infusion or maintenance dosing TBW
		Cave airway obstruction
Opioids		
Fentanyl	LBW	Titrate to effect, time to peak effect is 3 min
Alfentanil	LBW	
Sufentanil	LBW	
Remifentanil	LBW	TBW dosing may result in significant hypotension and/or bradycardia

LBW lean body weight, *TBW* total body weight

suggested that patients with diabetes, a very common comorbidity associated with obesity, may increase the likelihood of nerve injury [17].

Studies specifically addressing the effect of obesity on local anesthetics are nonexisting, and consequently, the optimal dosing scalar for the administration of local anesthetics in obesity is not known. Because the clearance of many drugs in the obese is proportional to lean body weight, lean body weight dosing is probably more appropriate than total body weight dosing [18]. Continuous infusion regimens using total body weight may result in overdosing.

Lipid Rescue Therapy

The recommendation when a local anesthetic overdose is suspected is to administer 20 % lipid emulsion based on lean body weight: A dose of 1.5 mL/kg lean body weight of 20 % lipid emulsion delivered as a bolus over 1 min followed by a continuous infusion of 0.25 mL/kg/min for at least 10 min after return of spontaneous circulation. The bolus could be repeated once or the infusion doubled for continued hypotension, but the total dose, including both bolus and infusion, should not exceed 12 mL/kg [19].

Neuraxial Anesthesia

Epidural

Difficult Placement

Procedure times for epidural placement are longer in morbidly obese patients [20]. Anatomical landmarks may be difficult to identify and the depth from the skin to the epidural space is increased. Depth can increase from 3 cm at a BMI of 20 kg/m^2 to more than 8 cm at BMIs greater than 40 kg/m^2 [21]. Additionally, narrowed interspinous and interlaminar spaces as a result of degenerative spinal disease with ossification of the interspinous ligaments and hypertrophy of the facet joints may further complicate correct epidural placement.

Seventeen percent of morbidly obese parturients required a replacement epidural catheter due to inadequate pain control or failure to achieve adequate bilateral dermatomal sensory levels compared to 3 % in nonobese parturients [20]. Obese women are less able to identify the midline of their back accurately by touching with their finger compared with nonobese [22]. Half of the obese were accurate to within 5 mm in locating the middle of their back with their finger compared with 84 % nonobese women. Ultrasound can be used to identify the midline, the intervertebral space, and the distance from the skin to the epidural space. However, excess adipose tissue can impair identifying structures with ultrasound. Visualization of the spinous process and ligamentum flavum was estimated as "good" 70 % and 63 % of the time, respectively [23].

Accidental Dural Puncture

The incidence of complications with epidural anesthesia increases with increasing weight. In nonobese parturients, the incidence of accidental dural puncture, as a complication of epidural insertion for labor analgesia, has a reported incidence of 0.16–1.3 % [24]. In obese women, the incidence of accidental dural puncture has been reported to be as high as 4 % [25].

Postdural Puncture Headache

There is no evidence that obese women are less likely to develop a postdural puncture headache or that the characteristics of the headache and use of epidural blood patch are different [26].

Intravascular Puncture

Inadvertent epidural venous puncture occurs more frequently in the obese patient. One study reports a rate of 17 % vs. 3 % in nonobese [27].

Catheter Migration

Migration of catheters related to sliding of the skin and changes in position is more important in obese compared to nonobese patients [28]. Leaving epidural catheters 7 cm or more inside the epidural space is appropriate in morbidly obese patients. In addition, before taping the catheter the patient should return to a neutral, relaxed position [29].

Hypotension

Morbidly obese parturients given similar bolus doses of epidural anesthetic have more hypotension and prolonged fetal heart rate decelerations when compared with normal size parturients following labor epidural placement [30]. In the morbidly obese at term, the epidural space is smaller, and the epidural space pressure higher because of the enlarged epidural venous plexus. This is exacerbated by increased vena cava compression from higher intra-abdominal pressure.

Another contributing factor for the increased incidence of hypotension is that morbidly obese women may require greater volumes of intravenous fluid for adequate preloading because their circulating blood volume and cardiac output can be twice as high as a normal size parturient. Diastolic blood pressures decrease more than systolic blood pressures because decreasing systemic vascular resistance affects diastolic blood pressures to a greater extent.

Dose Selection

Hodgkinson and Hussain reported that increasing BMI and weight increase the cephalad spread of epidural anesthesia [31, 32]; however, Milligan et al. [33] found no relationship

between obesity and cephalad spread. In another study, local anesthetic requirements were reduced by a factor of 1.68 with significantly higher initial levels of block in an obese group of patients with a labor epidural when compared to a nonobese group [34]. The authors speculate the decreased epidural analgesic requirements when not taken into consideration may be a contributing factor to the more difficult labors of obese patients.

Spinal Anesthesia

Difficult Placement

Morbid obesity is associated with a significant increase in the time needed to administer spinal anesthesia [35]. In obese parturients, prepuncture ultrasound examination improves the success rate of block placement on the first attempt and reduces the number of puncture attempts and the need to puncture different levels [36].

Hypotension

A BMI ≥25 kg/m^2 was a risk factor for hypotension after spinal anesthesia in patients undergoing cesarean section when compared to a nonobese control group receiving the same dose [37].

Cerebrospinal Fluid Volume and Dose Selection

Cerebrospinal fluid (CSF) volume is widely variable between individuals. Obesity is associated with a decreased CSF volume as a result of increased intra-abdominal pressure. The increased abdominal pressure moves fat and other tissue in the intervertebral foramen, which decreases CSF volume. The reduction in CSF decreases dilution of injected anesthetic and may produce more extensive neuraxial blockade [38]. However, a dose-ranging study with single-shot intrathecal bupivacaine suggests that obese and nonobese patients do not respond differently [39]. Findings from this dose-ranging study show that doses less than 10 mg are not recommended when using a single-shot spinal technique in morbidly obese patients undergoing cesarean delivery, and that intrathecal bupivacaine dose reduction is not necessary. Morbidly obese patients did have a more variable response to intrathecal dosing than leaner patients and therefore may be better suited to a CSE, epidural, or continuous spinal anesthetic technique.

In another study in patients undergoing total knee arthroplasty, no difference was found between obese (BMI range 28–39 kg/m^2) and nonobese subjects regarding the dose of intrathecal hyperbaric bupivacaine required for successful block. However, analgesic duration and time to self-voiding was prolonged in obese patients [40].

Combined Spinal-Epidural

Some advocate the preferential use of a combined spinal-epidural (CSE) technique over a single-shot spinal technique in the morbidly obese. The epidural needle is more rigid, deviates less during placement, and serves as a long introducer for the spinal needle than the short introducer needle used for a single-shot spinal. An added benefit is the availability of an epidural catheter for supplemental anesthesia in the event of prolonged surgical duration or inadequate subarachnoid anesthesia. The median [interquartile range] time required for successful placement of single-shot spinal or CSE in morbidly obese parturient undergoing elective cesarean delivery was 210 [116–692] seconds and 180 [75–450] second, respectively [41].

Peripheral Nerve Blocks

For surgery on the extremities, peripheral nerve blocks have become a highly favorable anesthetic option when compared with general anesthesia.

Brachial Plexus

Using nerve stimulation to perform axillary brachial plexus block 91 % of obese and 98 % of nonobese patients did have a successful block. Supplementation, with nerve blocks at the elbow, was more frequently needed in obese (7 %) than in nonobese patients (2 %). Inadvertent vascular punctures were more frequent in obese than in nonobese patients (27 % vs. 9 %). Patient satisfaction was 87 % in the obese and 94 % in the nonobese patients [42]. In 1468 brachial plexus blocks at the humeral canal, it was shown that the failure rate was not associated with the patients' physical characteristics [43]. Similarly, supraclavicular block in the obese population resulted in a slight decrease in success rate without an apparent effect on complications. In an analysis of 2020 supraclavicular blocks, the overall success rate was 97.3 % in nonobese and 94.3 % in obese patients [44]. Besides the small decrease in success rate, obesity was associated with an increase in difficulty of block placement.

Interscalene block is one of the most efficient techniques for postoperative analgesia after shoulder surgery. Ultrasound-guided interscalene nerve blocks for perioperative analgesia can be safely and effectively performed in the obese patient but they may be more difficult to perform and analgesia may not be as complete [45]. Another study concluded ultrasound provides efficient depiction of the interscalene plexus structures in obese patients and, when

used for guidance of regional blockade, renders similar results as in patients of normal weight [46]. Low-volume ultrasound-guided interscalene block decreases the incidence of phrenic nerve paralysis and is associated with fewer respiratory complications with no change in postoperative analgesia compared with the standard-volume technique [10].

Lower Extremity Blocks

In overweight and obese patients, a sciatic nerve block may be performed 50 % faster with the ultrasound-guided subgluteal space technique. There are no detectable differences in block success and analgesic efficacy, compared with the infra-gluteal technique. The authors conclude that injection of local anesthetics along tissue planes may produce similar block characteristics to perineural injection for ultrasound-guided sciatic nerve block [47]. Ultrasound guidance for popliteal-sciatic nerve blocks in obese patients results in faster procedural performance, less pain during placement, and greater overall satisfaction while producing similar block characteristics when compared to electrical stimulation guidance [48]. In patients with a continuous femoral nerve block after total knee arthroplasty, obesity was an independent risk factor for a postoperative fall [49].

Transverse Abdominis Plane Block

Data regarding the analgesic efficacy of the transverse abdominis plane block in the obese are lacking. Bilateral transverse abdominal plane blocks do not provide additional analgesic benefit when added to trocar insertion site local anesthetic infiltration and systemic analgesia for laparoscopic gastric bypass surgery [50].

Catheter Site Infections

In a retrospective cohort study, obesity was associated with peripheral *but not neuraxial-related* catheter infections [51]. In obese persons fat tissue is poorly perfused [52], resulting in subcutaneous tissue hypoxia [53]. Because the risk of wound infection is inversely proportional to the partial pressure of oxygen in tissue [54], obesity not surprisingly is associated with an increased risk of catheter site infections.

Conclusion

There have been few studies describing regional anesthesia in the obese patient.

Regional anesthesia may avoid complications associated with general anesthesia such as cardiopulmonary depression and postoperative pulmonary complications. Performing regional blocks in the obese is technically more difficult and the failure rate is higher.

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Local and Regional Anesthesia in Pediatrics

20

Belen De Jose Maria

Key Points

- Over the past 30 years, practice of pediatric regional anesthesia and analgesia has expanded rapidly. There are now a substantial number of studies, publications, and chapters in textbooks regarding the techniques, pharmacokinetics, clinical outcomes, and dosing guidelines in children.
- Regional anesthesia in children requires special consideration due to generally smaller anatomy and the fact that the vast majority of blocks are administered under general anesthesia or heavy sedation.
- Multiple studies of data collected by regional anesthesia centers have found a low incidence of complications in pediatric patients receiving nerve blocks. Permanent or severe complications are extremely rare.
- Specific complications that may hinder pediatric nerve blocks include nerve injury, inadvertent dural puncture, improper catheter tip placement, high doses with risk of local anesthetic toxicity, infection, and compartment syndrome.
- Ultrasound-guided approaches increase efficacy of blocks and may reduce the risk of complications associated with injection of large volumes of local anesthetic.
- As with regional practice in adults, aseptic technique and use of appropriate equipment (e.g., needle size, ultrasound probes) are critical for performance of safe nerve blockade in the pediatric population.
- At the end of the chapter, the reader will find some personal suggestions and "pediatric common sense" safety considerations the present author considers necessary for the practice of safe pediatric regional anesthesia.

Abbreviations

ACS	Acute compartment syndrome
ADARPEF	French-Language Society of Pediatric Anesthesiologists
AGP	$Alpha_1$-acid glycoprotein
ASRA	American Society of Regional Anesthesia and Pain Medicine
ECG	Electrocardiogram
EIA	Epidural infusion analgesia
GAs	General anesthesia
ILE	Intravenous lipid emulsion
LAST	Local anesthetic systemic toxicity
PDPH	Postdural puncture headache
PRAN	Pediatric Regional Anesthesia Network
RCTs	Randomized controlled trials
TAP	Transversus abdominis plane
USG	Ultrasound guidance

Introduction

Evidence-Based Safety Records of Pediatric Regional Anesthesia

In the second edition of this text (Complications of regional anesthesia©), the authors Broadman and Holt reviewed the established safety records of pediatric regional anesthesia [1]. They analyzed the data from the following studies: the first French (ADARPEF) study [2], the ASA Closed Claims Review [3], the Australian Incident Monitoring Study [4], the 2001 Italian literature review on caudal block safety [5], and the experience of a single center in Finland with 1132 spinal anesthetics [6].

In the first study from the ADARPEF, Giaufre et al. collected data on the complications encountered by 164 of the 309 ADARPEF members (French-Language Society of

B. De Jose Maria, MD, PhD (✉)
Department of Pediatric Anesthesiology, Hospital Sant Joan de Déu, University of Barcelona, Barcelona, Spain
e-mail: bdejosemaria@gmail.com

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_20

Pediatric Anesthesia) during 1 year [2]. A total of 85,412 anesthetics were performed and 24,409 cases contained some element of regional anesthesia: neuraxial (**62 %**), local infiltration, and peripheral blocks (**38 %**). Eighty-nine percent of the blocks were placed under general anesthesia. The anesthesia records from cases in which a complication or adverse outcome occurred were analyzed. There were no complications with either the placement of any of the peripheral blocks or the local infiltration cases. All of the complications (23/24,409) occurred during the placement of central blocks and the use of an unsuitable needle was the blamed cause in 11/23 cases. The caudal block was the most common central block and only 12 adverse incidents were encountered (incident rate of 1/1000 blocks). There were no complications associated with any of the 372 thoracic epidural blocks. The lumbar epidural block was associated with the highest adverse outcome odds ratio of 5/1000. Among all the neuraxial blocks, the most common complication was dural puncture (a total of 8) (4 resulted in total spinals and 2 caused postdural puncture headache (PDPH)). There were six intravascular injections resulting in two seizures, two cardiac arrhythmias, and two that did not produce any adverse reactions. The seizures and arrhythmias took place despite there being a previous negative test dose in five of the six cases. Two complications were directly related to needle placement and management of a catheter. One rectal puncture and one kinked catheter were also reported. There were two sacral postoperative paresthesias attributed to positioning because they took place after lumbar epidurals and completely resolved very early in the recovery process. There were three overdoses: two of these occurred with local anesthetic solutions and one with morphine. Finally, there was one burn-related necrotic lesion over the gluteal region of a child after placement of a caudal catheter. This burn likely occurred secondary to cautery grounding pad placement over an area of skin that had been cleansed with surgical alcohol just before the placement of the caudal catheter. This first-degree burn resolved within 3 days and did not require any form of treatment. Two conclusions can be drawn from this study: (1) it is absolutely imperative to use appropriate needles (correct length, gauge, and bevel) for every pediatric block, and (2) one should use peripheral nerve blocks whenever possible as opposed to neuraxial blocks. The author of the present chapter believes that the absence of complications associated with thoracic epidurals might be due to the smallest number of reported cases in this study (372) or most probably because all of these blocks were placed by the most skilled pediatric anesthesiologists and under extreme vigilance. In addition, because caudal block is such a common block in pediatrics, even if the rate of complications was low, the same vigilance used during other central neuraxial blocks must be used when performing caudal blocks.

Neither the American Society of Anesthesiologists' Closed Claims Review nor the Australian Incident Monitoring Study reported any pediatric cases [3, 4]. The ASA Review included 2651 claims; 445 of these claims were the result of nerve injuries, however, *none of the claims involved pediatric patients.* There were 50 adult claims for spinal cord injury during regional anesthesia (mainly in anticoagulated patients) but there were no spinal, caudal, or epidural closed claims in children. The Australian Incident Monitoring Study (AIMS) reported the first 2000 incidents that occurred in the AIMS program and selected 160 cases in which regional anesthesia was associated with a complication but again *none of these cases involved pediatric patients* [4]. However, since LAST was one of the most common incidents in this study, the authors highlight the risks of failure to recognize intravascular injections because this could possibly be a risk of greater clinical relevance in children.

Puncuh et al. reported a series of 1132 spinal anesthetics in children aged from 6 months to 14 years with a very low incidence of complications [6]. Seventeen children had intraoperative hypotension (defined as a decrease in systolic blood pressure by 20 % or more from baseline) but this rarely occurred in children younger than 10 years of age. Five children developed a PDPH but none of them required an epidural blood patch. Nine children reported a transient self-limited backache. There were no neurologic deficits or mortalities in any patient in this study. However, all these cases were performed in a single center and there is no other group of authors with such a large reported experience. In 2012 Kokki H, the main author from this group, wrote the review paper about spinal anesthesia in the monographic number of the European journal *Pediatric Anesthesia* [7]. The fact that it is mainly the Finnish group that publishes about spinal anesthesia in children gives credit to their superb expertise, but this expertise might not necessarily be extrapolated elsewhere.

After the second edition of this book (Complications of regional anesthesia©), some other reviews have been published in the pediatric literature. In 2007, the study published by Llewellyn and Moriarty described a prospective audit of children receiving epidural infusion analgesia (EIA) in Great Britain and Ireland [8]. This was a multicenter study aiming to quantify the risks associated with this technique, where each participating center sent a monthly return of the numbers of EIA performed to the coordinating center. If an incident occurred then the referring center completed a more detailed form and the child was followed up for 1 year if possible. Incidents were graded by severity 1–3, serious to minor. Data were collected over the 5-year period (2001–2005). A total of 10,633 epidurals were performed and 96 incidents were reported. Fifty-six incidents were associated with the insertion or maintenance of EIA; most were of low severity, five incidents were graded as 1 (serious), nine inci-

dents were graded as 2, and only one child had residual effects from a grade 1 incident 12 months after surgery. Forty reported incidents were also felt to be associated with the use of EIA; 33 of these incidents were the development of pressures sores. Four incidents of compartment syndrome were reported, but in each of these cases the presence of EIA did not mask the condition. The authors concluded that (1) EIA is associated with the occurrence of adverse incidents; however, these are usually minor; (2) serious incidents that have the potential to cause severe or long-term harm are rare (only one child had persistent problems following EIA 1 year after catheter insertion); (3) the occurrence of compartment syndrome does not appear to be masked by the presence of working EIA; (4) the most common complications identified by the audit were infection and drug error. Because drug errors were higher in centers where a smaller number of epidurals were performed, the author of the present chapter recommends staff education programs and medical support to the ward personnel to safely use epidural catheters in a pediatric ward.

The largest more recent studies reviewing the overall safety of pediatric regional anesthesia are the second French-Language Society of Pediatric Anesthesiologists (ADARPEF) study [9], and the Pediatric Regional Anesthesia Network (PRAN) study from the United States [10], followed by other studies of this same group [11, 12].

The French-Language Society of Pediatric Anesthesiologists (ADARPEF) published in 2011 the results of their second 1-year prospective, multicenter, and anonymous study to update both epidemiology and morbidity of regional anesthesia in children [9]. Data from participating hospitals were recorded from November 2005 to October 2006. Data collected in 47 institutions included 104,612 pure general anesthesia (GAs), 29,870 GAs associated with regional blocks, and 1262 pure regional blocks. Central blocks accounted for 34 % of all regional anesthesia procedures. Peripheral blocks (66 %) were upper or lower limb blocks (29 %) and trunk and face blocks (71 %). In children aged ≤3 years, the percentage of central blocks was similar to the peripheral ones (45 % versus 55 %), while in older children peripheral blocks were more than four times used than central ones. Complications (41 involving 40 patients) were rare and usually minor. They did not result in any sequelae. The study revealed an overall complication rate of 0.12 %, CI 95 % [0.09–0.17], and of note, the complication rate for central blocks was six times higher than for peripheral blocks. Therefore, once again, the literature supports the low rate of complications in regional anesthesia techniques in children and recommends the use of peripheral nerve blocks instead of central blocks whenever possible.

The Pediatric Regional Anesthesia Network (PRAN) was formed to obtain audited data on practice patterns and complications in regional anesthesia techniques in children in the United States. Its first multicenter publication in 2012 reviewed 14,917 regional blocks performed in 13,725 patients from April 2007 through March 2010 [10]. There were no deaths or complications with sequelae lasting >3 months. Single-injection blocks had fewer adverse events than continuous blocks, although the most frequent events (33 % of all events) in the latter group were catheter-related problems. Ninety-five percent of blocks were placed while patients were under general anesthesia. Single-injection caudal blocks were the most frequently performed (40 %), but peripheral nerve blocks were also frequently used (35 %). The authors concluded that in the United States regional anesthesia in children was commonly performed, under general anesthesia and had a very low rate of complications. Those results were comparable to those of the latest ADARPEF study in Europe. Therefore, combining the most recent data reported by French, British, and American researchers, there were 9 transient neurological complications associated with 37,543 epidural blocks (2 per 10,000) and no permanent neurological injuries.

Finally, in 2014 Suresh et al. published several other observational studies using the Pediatric Regional Anesthesia Network (PRAN) database. They first reviewed 18,650 caudal blocks from the database and looked at complications and sequelae [12]. A complication after a caudal block was defined by the presence of at least 1 of the following: block failure, vascular puncture, intravascular test dose, dural puncture, seizure, cardiac arrest, sacral pain, or neurologic symptoms. In addition, if a complication was coded, the presence of temporary or permanent sequelae was evaluated. Additional exploratory analyses were performed to identify patterns of local anesthetic dosage. A total of 18,650 children who received a caudal block were included in this study. The overall estimated incidence (95 % confidence interval [CI]) of complications after caudal blocks was 1.9 % (1.7–2.1 %). Patients who developed complications were younger, median (interquartile range) age of 11 (5–24) months, compared to those who did not develop any complications, 14 (7–29) months, $P = 0.001$. The most common complications were block failure, blood aspiration, and intravascular injection. No cases of temporary or permanent sequelae were identified leading to an estimated incidence (95 % CI) of 0.005 % (− % to 0.03 %). Therefore, the authors concluded that safety concerns should not be a barrier to the use of caudal blocks in children.

The same group (PRAN) then reviewed the transversus abdominis plane (TAP) blocks in children [11]. One thousand nine hundred ninety-four children receiving a TAP block were included in this analysis. Only two complications were reported—a vascular aspiration of blood before local anesthetic injection and a peritoneal puncture—resulting in an overall incidence of complications (95 % CI) of 0.1 % (0.02–0.3 %) and a specific incidence of

complications (vascular aspiration or peritoneal puncture) of 0.05 % (0.0054–0.2000 %). Neither of these complications resulted in additional interventions or sequelae. The median (95 % range) for the local anesthetic dose per weight for bilateral TAP blocks was 1.0 (0.47–2.29) mg of bupivacaine equivalents per kilogram; however, subjects' weights were not sufficient to explain much of the variability in dose. The authors of this study concluded that the upper incidence of overall complications associated with the TAP block in children was 0.3 % and that complications were very minor and did not require any additional interventions.

Specific Complications of Regional Anesthesia in Children

Neural Injury

Despite these encouraging large database studies showing the lack of major complications in pediatric regional anesthesia, sporadic case reports on complications attributed to regional techniques continue to be published. Eh et al. reported in 2011 the delayed occurrence of spinal arachnoiditis following a caudal block [13], and Symons et al. reported in 2008 a case of neuropathic pain after a caudal block [14]. However, most of the serious complications in children still involve continuous epidural techniques. In adults, possible mechanisms of injury to the spinal cord can be mechanical injury from needle or catheter trauma to neural or vascular structures, compression from masses as in hematoma or abscess formation, spinal cord infarction due to hypotension [15], or prothrombotic states, and toxicity from medications injected into the epidural space [16]. The most recent paper on serious complications in regional techniques in children is that of Meyer et al. in 2012, where a series of four cases of long-term or permanent neurologic complications after epidural catheter placements were reported and their possible mechanisms of injury and implications were discussed [17]. All four epidural catheters were placed by experienced pediatric anesthesiologists and neither of the cases had clinical or radiographic evidence of direct trauma, abscess, or hematoma in the spinal cord. The first case was definitely the most frightening of the four because there was no apparent cause: the patient (23 months old) was healthy and uncomplicated, the epidural catheter placement proceeded uneventfully at a lumbar level below the terminus of the spinal cord, the duration of general anesthesia was short, and there were no intraoperative hemodynamic clues to raise any concerns. However, the patient developed postoperative flaccid paralysis of both lower limbs. The MRIs revealed no hematoma, abscess, mass, or trauma to the spinal cord or dura, but there was an increased signal abnormality of the conus medullaris consistent with ischemia or venous hypertension. Despite rehabilitation, 12 months after the injury there was no further recovery of motor function and the paralysis persisted. Possible mechanisms of this very rare and unfortunate case report are: spinal cord ischemia due to either a low-lying arterial variant supplying an anterior spinal artery, unrecognized intravascular injection of air, or epinephrine-induced anterior spinal artery spasm [18]. The other three cases reported by Meyer et al. happened in older children (12 and 11 years old) and were definitely more complicated in technique, patients' comorbidity, and/or surgical procedures. All three cases finished without proof of medical negligence too, but some of the possible mechanisms of injury to the spinal cord may have played a role: reduced spinal cord perfusion pressure, prolonged surgery, extreme surgical positioning, and decreases in arterial blood pressure. None of these mechanisms of injury on its own were considered the direct cause of the morbidity, but in combination some may perhaps have played a role in the outcomes. In addition, one should not forget that especially in young children, cord perfusion may be impaired after transient increases in epidural space hydrostatic pressure due to big boluses, fast injections, or excessively large infusions of drugs into the epidural space [18].

The author of the present chapter is of the opinion that these complications should not be linked to the fact the children were under sedation or general anesthesia. Despite the fact that regional anesthesia is most often performed in awake adults, but both neuraxial and peripheral techniques are most frequently performed in pediatric patients under general anesthesia. This difference in adult and pediatric practice was considered in the past a potential risk factor for the development of neurological complications in children but all the large epidemiologic studies have proved that it is safer to perform a block in an anesthetized patient than in an uncooperative one [8–10]. Regarding central blocks, one should nevertheless avoid repeating doses of epidural drugs in an anesthetized patient when the previous doses are not having the expected outcomes. Nowadays, an ultrasound should at least be used to assess the spread of drugs through the epidural catheters especially if any difficulties are encountered. Moreover, if the catheter is not clinically working as expected one should consider removing the catheter or, in selected cases, using a low-volume contrast epidurography prior to repeating local anesthetic doses. Peripheral nerve blocks are no different. Interscalene blocks are not the most common peripheral nerve blocks in children because shoulder pathology is not as common as in adults. However, were complications to occur, they would certainly be compromising. Nevertheless, a recent review by the PRAN group concluded that the placement of interscalene blocks under general anesthesia in children is as safe as the placement of these blocks in awake adults [19].

Epidural Hematoma

Epidural hematoma associated with epidural analgesia is extremely rare in children. This may be because anticoagulation protocols are rarely indicated during the perioperative period in pediatric patients. Nonetheless, epidural analgesia should be avoided in patients with clinically significant coagulopathy or thrombocytopenia. The guidelines for use of epidural anesthesia in anticoagulated adult patients should probably also be applied in pediatric patients.

Dural Puncture

Because of the lower extension of the dural sac, the risk of dural puncture is higher in infants and small children than in adults or older children**.** Inadvertent dural puncture with subsequent intrathecal injection of an epidural dose of local anesthetic may result in total spinal anesthesia, the clinical expression of which is almost immediate respiratory arrest requiring rapid control of ventilation. If this complication occurs in adolescents the result would be cardiovascular collapse and respiratory compromise.

This complication is technique dependent and recognized by gentle aspiration previous to injection of drug**.** However, a negative aspiration of blood or cerebrospinal fluid should not be considered as an absolute indicator of proper needle and catheter placement in very small children because veins are so small that can collapse easily on aspiration. Therefore, the present author recommends using a 2 mL syringe, aspirate slowly, and consider opening to air to look for free flow. If a dural puncture is noted, further attempts at caudal/epidural blockade should be abandoned because of the risk of total spinal block.

The incidence of PDPH in children following spinal anesthesia or an inadvertent "wet tap" during placement of an epidural block is quite low, and Wee et al. suggest that the problem rarely occurs in children younger than 10 years of age [20]. However, these authors point out that PDPH is quite common in older pediatric patients and the incidence increases with age. Adolescent girls have headaches twice as frequently as boys do. The reason for the low incidence of PDPH in children younger than 10 years of age is unknown, but it may be related to the lower cerebrospinal fluid pressures found in this age group [21]**.**

Janssens et al. reviewed the literature concerning definition, etiology, incidence, risk factors, prevention, and treatment in order to provide recommendations not only in anesthetic spinal anesthesia but in oncology lumbar punctures too [22]. Conservative treatment for postdural puncture headache (PDPH) includes bed rest, oral or intravenous hydration, acetaminophen, nonsteroidal anti-inflammatory agents, and antiemetics. Caffeine is not frequently used in children for relief of PDPH, and an optimal dose is not known. PDPHs that fail to respond to conservative therapy have been treated with an epidural blood patch in pediatric patients too [23]. Sedation and EMLA® cream may be beneficial adjuncts to reduce the pain and emotional trauma of blood patch therapy. Practitioners should consider the child's age and level of maturity when determining whether conscious or deep sedation will be required. The volume of autologous blood recommended varies from 0.2 to 0.5 mL/kg and should be injected slowly [24].

Assessment of Catheter Tip Placement

Major upper abdominal and thoracic surgical procedures need targeting local anesthetic solutions at the site of surgery by placing lumbar or thoracic epidural catheters. However, some authors have considered these blocks hazardous to perform in small infants and children and prefer to thread caudal catheters cephalad to the lumbar level. This has been described as easy in infants under 1 year of age [25], but more difficult in older children [26], probably because older children have less loose epidural fat and more exaggerated lumbar lordosis. The group by Gunter and Eng used wire styletted microcatheters to solve this problem in older infants and children [27].

If a caudal catheter is threaded cephalad, then there is a need to determine where the tip of the catheter is finally placed. Tsui et al. described the Epidural Stimulation Test, a low-current electrical stimulation test used to monitor and guide the position of the epidural catheter during insertion [28]. In this test, the spinal nerve roots are stimulated with a low electrical current conducted through normal saline in the epidural space via an electrically conducting catheter (metal stylet). Correct placement of the epidural catheter tip (1–2 cm from the nerve roots) is indicated by a motor response elicited with a current between 1 and 10 mA [29]. A motor response observed with a significantly lower threshold current (<1 mA) suggests that the catheter is in the subarachnoid or subdural space or is in close proximity to a nerve root [30, 31]. One disadvantage of the epidural stimulation technique is that it cannot be performed reliably if any significant clinical neuromuscular blockade is present or local anesthetics have been administered in the epidural space. To overcome this limitation, an alternative monitoring technique using ECG monitoring has been suggested [32]. A reference ECG is monitored at the required spinal level for surgery; this is compared to the ECG formed from the epidural catheter tip as it is threaded cephalad. Unfortunately, this technique cannot easily differentiate subtle QRS complexes where the catheter is threaded a short distance; neither does it recognize intravascular or intrathecal catheter positioning.

All these problems may have become less relevant in the last decade with the widespread use of ultrasound guidance in regional anesthesia (see "Impact of Ultrasound Guidance on Complications in Regional Anesthesia in Children" section).

Local Anesthetic Systemic Toxicity (LAST)

On the one side, emphasis should be made to keep local anesthetics dosages as safe as possible in pediatric regional anesthesia. Plasma levels that are less than 2.0 μg/mL are thought to be safe in children. Metabolism of local anesthetics is greatly reduced in the neonate, because of both decreased plasma pseudocholinesterase and decreased hepatic microsomal activity. Alpha$_1$-acid glycoprotein (AGP) concentrations are quite low in infants younger than 2 months of age and they do not reach adult levels until after the first year of life. Reduced levels of AGP allow more local anesthetic to remain unbound and it is this free form of drug that crosses membranes and can precipitate seizure activity and myocardial depression. Lower AGP plasma concentration is to some degree compensated by a higher binding of local anesthetic to albumin, but acidosis and hypoxia will reduce global protein binding and therefore increase the proportion of free drug.

Local anesthetic systemic toxicity (LAST) is not only the most common complication in regional anesthesia in children but it should be largely preventable by using appropriate dosages and careful techniques. The largest study from PRAN detected a large variation in clinical practice among the centers regarding the doses of local anesthetics for caudal block [12]. Moreover, 4106 of 17,867 (24.6 %; 95 % CI, 24–25.2 %) subjects received doses that could be potentially unsafe (>2 mg of bupivacaine equivalents/kg). Therefore, the authors suggested that optimal dose regimens should be determined. In the next study from PRAN about the TAP block, the authors found that 135 of 1944 (6.9 %; 95 % CI, 5.8–8.1 %) subjects received doses that could be potentially toxic [11]. Subjects who received potentially toxic doses were younger than those who did not receive potentially toxic doses, 64 (19–100) months and 108 (45–158) months, respectively ($P < 0.001$). The large variability of local anesthetic dosage used could not only minimize potential analgesic benefits of the TAP block but also result in local anesthetic toxicity.

On the other side, in the unfortunate case that LAST occurs, resuscitation with 20 % intravenous lipid emulsion (ILE) should be used. The American Society of Regional Anesthesia and Pain Medicine (ASRA) first published in 2010 the guidelines for resuscitation of LAST with 20 % intravenous lipid emulsion [33].

The first case report in a child who was successfully rescued from LAST is that published by Lin et al. [34]. It is a case report of bupivacaine-induced cardio toxicity in a neonate following caudal epidural block under general anesthesia for urologic surgery. Prompt recognition of the complication allowed early intervention with both standard resuscitative measures and administration of 1 mL/kg of 20 % Intralipid® (Baxter Healthcare, Deerfield, IL, USA) resulting in a good outcome.

Then in 2012 the ASRA published the effective dosing of lipid emulsion [35]. However, before the 2012 guidelines recommending an upper limit of 10 mL/kg were available another child was resuscitated with ILE [36]. In this report, a child was successfully resuscitated after a suspected LAST immediately after a caudal block, but the child ended presenting a V/Q mismatch following what was later known as an inadvertent overdose of lipid emulsion. Fat overload syndrome is a known complication of rapid intravenous lipid emulsion therapy in children. It is characterized by headaches, fever, jaundice, hepatosplenomegaly, respiratory distress, and spontaneous hemorrhage [37]. The authors blamed a total dose of epinephrine greater than 10 μg/kg that may have impaired lipid resuscitation from bupivacaine overdose, possibly by inducing hyperlactatemia. Even though it is important to avoid high doses of epinephrine if ILE is going to be used it is also important to remember that ILE is not a substitute for normal resuscitation measures [38]. Lipid emulsion is a novel and effective method to reverse serious systemic toxicity of local anesthetics and should be administered as soon as it is available, but normal resuscitation measures should be continued simultaneously.

Infection

Despite an aseptic technique and the use of interposed bacterial filters, many grades of infections can occur following central blocks (epidural abscess, meningitis, arachnoiditis, radiculopathies, discitis, vertebral osteitis) [39].

Compared with lumbar epidural catheters, there is some concern regarding catheter infection with the prolonged use of caudally placed catheters owing to the proximity of the sacral hiatus to the rectum. Although studies have not found clinical evidence of higher infection rates with the caudal approach, bacterial colonization has been reported as higher. *Staphylococcus epidermidis* is the predominant microorganism colonized on the skin and catheters of lumbar and caudal epidurals. Gram-negative bacteria have also been demonstrated on the tips of the caudal catheter [40]. Although the overall infection rate associated with caudal epidural catheters appears to be low, isolated case reports exist of infection related to epidural catheters in children. Even with widely used single-shot caudal blocks, infection such as sacral osteomyelitis can still occur [41]. To reduce the risk of contamination by stool and urine, techniques such as catheter tunneling and fixation with occlusive transparent dressing in a cephalad direction can be used [42].

A strict aseptic technique including the use of a sterile closed-infusion system should always be used, and care should be taken to avoid local tissue trauma. A transparent dressing of choice and daily inspection of the dressing and entry site are recommended, although the dressing should not be changed unless strictly necessary. If the child develops a fever >38 °C of unknown origin the catheter must be removed and the tip sent for culture.

Compartment Syndrome

The incidence of acute compartment syndrome (ACS) is lower in children than in adults, but children may be at greater risk of developing ACS because the normal compartment pressures in the lower leg (13–16 mmHg) are significantly higher than those of adults (0–10 mmHg). This discrepancy between adults and children may be explained by the fact that children are in a stage of muscle growth and, hence, the increasing volume owing to muscle hypertrophy may cause a higher intracompartmental baseline pressure [43]. The prompt diagnosis of ACS is the key for adequate treatment of this syndrome, but no gold standard currently exists for diagnosing ACS. The classic warning signs of limb ischemia (e.g., pain, pallor, paresthesia, paralysis, and pulselessness) are relatively unreliable, and in children, particularly in preverbal children, the diagnosis is not easy. Patient history (pain out of proportion to the associated injury) and physical examination are central to the diagnosis. The degree of pain experienced and, particularly, the discrepancy between the seriousness of pain in comparison with the extent of the trauma can indicate an existing or developing ACS. Despite the lack of a general consensus, an absolute intramuscular pressure measurement of >30 mmHg in the compartment is commonly viewed as an absolute indication to perform a fasciotomy. The existing controversy is whether regional blocks may mask the signs and symptoms of a developing ACS. Some published case reports infer that the presence of a central or peripheral block may have delayed the appropriate diagnosis of ACS [44]. However, the latest pediatric anesthesiology review of the 12 published cases of ACS did not find any clear evidence that the presence of an epidural delayed the diagnosis [45].

Impact of Ultrasound Guidance on Complications in Regional Anesthesia in Children

The use of ultrasound assistance has been shown to minimize complications and/or improve efficacy of peripheral nerve blocks and catheter placement in adults when compared to nerve stimulation [46–48]. Large epidemiologic studies and meta-analysis in adult populations have documented improved safety, reliability, and efficacy with the addition of ultrasound guidance for neural blockade [49, 50]. Several recent large adult studies show a reduction in the incidence of local anesthetic systemic toxicity (LAST) when ultrasound guidance is used [51, 52]. The effect of using ultrasound on the incidence of neurologic injuries in adults shows promising trends [53]. The largest series to date (27,031 patients) attributing safety advantages to the use of ultrasound when performing regional anesthesia is that of Ecoffey [54]. This study sets risk of nerve injury at 1.5/10,000 and LAST at 0.37/10,000.

The literature contains no specific pediatric data on the effects of ultrasound guidance on the incidence of LAST or long-term neurologic injuries. Large, appropriately powered studies are probably still needed in children to determine the benefits of ultrasound, but existing pediatric studies demonstrate a trend towards a faster onset, a decrease in anesthetic dose requirement, and lower block failure rates [55, 56].

In 2009, Rubin et al. already published the first review article in children comparing ultrasound-guided (USG) regional anesthesia to nerve stimulation or landmark-based techniques [57]. They not only identified all suitable studies in MEDLINE, EMBASE Drugs, and Cochrane Evidence Based Medicine Reviews but also carried out a hand search of pediatric anesthesia and surgical journals. All randomized controlled trials (RCTs) comparing USG peripheral and neuraxial blocks with other techniques in children were included. The results of this study showed that ultrasound guidance improves block characteristics in children (including shorter block performance time, higher success rates, shorter onset time, longer block duration), needs less volume of local anesthetic, and enhances visibility of neuraxial structures. Moreover, the advantage of USG on safety over traditional landmark technique was demonstrated for ilioinguinal nerve blocks in children. Most of the pediatric updates and evidence reviews confirm that ultrasound technology confers additional safety and efficacy benefits [58–60].

Neuraxial ultrasound imaging is easier in small infants than in adults and a number of papers confirming this observation have already been published [56, 61–64]. Since the epidural space is still found by loss of resistance technique it is more an ultrasound-“assisted” technique than an ultrasound-“guided” technique. However, ultrasound assistance for neuraxial blocks in children offers at least two great advantages. First, it allows to accurately measure the depth to the epidural space in all patients decreasing the risk of spinal cord damage in lumbar or thoracic approaches. Preprocedural ultrasound imaging should always be carried out before a thoracic epidural block is performed in a child. The ultrasound probe is placed in a transverse, a median sagittal, and a paramedian oblique sagittal plane, and the depth to the epidural space is measured. The Tuohy needle is then

inserted at a similar angle as the ultrasound probe was held when the depth to the epidural space was measured. The epidural space is found by the loss of resistance technique but the depth of the needle insertion must never overcome the estimated depth of the epidural space under the ultrasound preprocedural imaging. This offers an additional safety measure regarding a possible damage to the spinal cord. The second advantage is that, by moving the probe cephalad up the spine, ultrasound assistance allows real-time visualization of the spread of local anesthetic, and this can be used as a surrogate of the catheter's tip placement [65]. Moreover, the study of the spread of local anesthetic under ultrasound assistance during caudal blockade in infants and children has proven that the speed of injection of local anesthetic does not affect its cranial spread [66]. The volume of local anesthetic injected affects the level reached but is not correlated to the classical formulas of skin dermatomes [67]. The final level reached by the local anesthetic is determined by a horizontal intrasegmental redistribution and a longitudinal cranial spread. The observed bidirectional movement of cerebrospinal fluid during a caudal block explains a major part of the difference between the initial ultrasound-assessed cranial level and the final level determined by cutaneous testing [68].

Author's "Pediatric Common Sense" Safety Considerations

The following are a few "pediatric common sense" safety considerations that the present author of this chapter believes should be followed in all possible cases in order to safely carry out pediatric regional anesthesia.

A significant problem in regional anesthesia was that techniques did not always achieve a success rate close to 100 % [69]. Indeed, the key to successful regional anesthesia has always depended on the accuracy of needle and local anesthetic placement in relation to the nerve or structures to be blocked. Ultrasound guidance allows real-time visualization of the target (nerve, fascial plane, or anatomical space) and monitoring of the spread of local anesthetic. Because serious complications luckily are very rare following pediatric regional anesthesia it is unlikely that even large-scale studies will prove ultrasound guidance to be superior to other approaches with regards to the rate of complications. However, at the time of writing this chapter and in this author's personal opinion, ultrasound guidance or assistance is the method of choice to guide regional anesthesia in children.

The present author believes that regional anesthesia should be performed under general anesthesia in all those children who cooperate as such: if a child is young but cooperates well and refuses general anesthesia, then a light sedation may be enough; however, if a child is old but cannot cooperate appropriately, then a general anesthesia may be required. Conventional monitoring is always required. Children are more easily kept anesthetized under spontaneous ventilation than adults are. Whenever possible, keeping the child under spontaneous ventilation, at least while doing the block is recommended. With the aid of a laryngeal mask this is easily achieved in most children and the visualization of the capnogram provides information about the absence of acute complications while doing the block. Should neural damage or LAST occur acutely, the first sign to be seen would be a change in the child's respiratory pattern. This would not prevent the complication from happening but would enable earlier diagnosis and treatment. Once the block has been established the child may be kept under spontaneous ventilation with pressure support or the trachea can be intubated if the surgery requires so.

Hypothermia occurs more rapidly in children in the operating room than in adults and for that reason they should always be kept covered. The covering blanket should be transparent to allow visual monitoring of any movement or abnormal breathing pattern. Moreover, the child should be covered not only during induction of general anesthesia (Fig. 20.1) but also while performing the block (Fig. 20.2). If ultrasound guidance is going to be used, the ultrasound gel should be warmed in advance (Fig. 20.3).

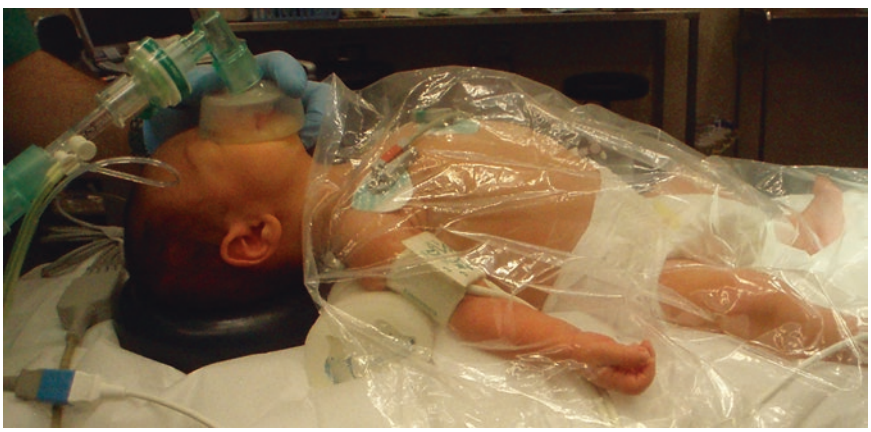

Fig. 20.1 Transparent blanket covering an infant during induction of general anesthesia previous to the regional block

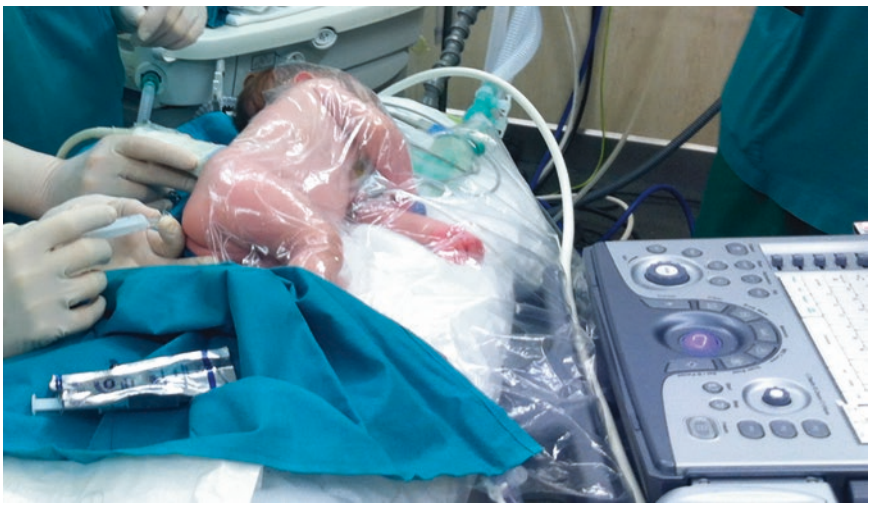

Fig. 20.2 Transparent blanket covering an infant during an ultrasound-assisted caudal block

Fig. 20.3 Warming of ultrasound gel previous to its use in ultrasound-guided pediatric regional anesthesia

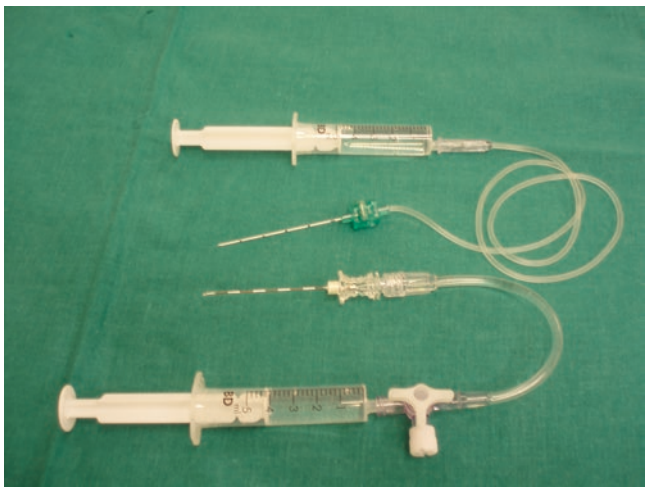

Fig. 20.4 Needles should be of appropriate tip, gauge, and length, and injection extension tubes are recommended

Appropriate pediatric regional equipment should always be used. Needles should be marked (1 or 0.5 cm); have an appropriate tip, gauge, and length; and injection extension tubes are recommended (Fig. 20.4). All local anesthetics used in adults may be used in children. The most commonly used local anesthetics are ropivacaine, levobupivacaine, and bupivacaine. Nevertheless, it is now recommended that *L*-enantiomers are used due to their lower cardiac toxicity compared with bupivacaine. After extravascular injection, the plasma concentration of ropivacaine peaks later than that of bupivacaine, sometimes up to more than 2 h after injection. This delay in the peak plasma concentration of ropivacaine usually reduces the maximum plasma concentration, providing some security in terms of toxicity [70, 71]. Even if the plasma concentration of free and total ropivacaine is higher in the youngest groups of children, plasma concentrations of ropivacaine and its main metabolite (2,6-pipecoloxylidide) are not influenced by the duration of infusion of local anesthetic. The clearance of ropivacaine increases with age but remains unchanged throughout the infusion in each age category. Therefore, ropivacaine seems to be more appropriate, more predictable and safer during continuous infusion for 48–72 h compared with bupivacaine [72].

It is the present author's opinion that regional blocks are indicated in all children without a formal contraindication. True contraindications include coagulopathy, sepsis, or infection at the needle insertion site, true local anesthetic allergy, and refusal by the child or parents. For central blocks, relative contraindications are myelomeningocele, ventriculoperitoneal shunt, and progressive neurologic disease. Risks

and benefits in these patients should be carefully considered on an individual basis. For peripheral nerve blocks, a relative contraindication may be the risk of compartment syndrome. In this author's personal opinion, analgesic regional blocks may be performed only if the surgical team agrees and provided that a dense motor block is not achieved. In these cases, if the surgery has been done with a block, it is imperative to wait for a partial recovery of the motor block (if any) before starting a continuous infusion of local anesthetic in the postoperative period. Any breakthrough or pain out of proportion to that expected should be carefully assessed before increasing the local anesthetic infusion or adding systemic analgesia. Early intramuscular pressure measurement should be available in the facility if regional blocks are to be performed in higher risk patients.

Both central and peripheral blocks should be performed under strict aseptic conditions. Anesthesiologists should follow their hospital's protocols regarding the use of chlorhexidine or povidone.

In a caudal block, direct visualization of the location of the needle tip with ultrasound is recommended. The spread of the local anesthetic while injected should then be assessed. In an epidural blockade, air loss of resistance techniques should be avoided in pediatric patients because children can develop a life-threatening venous air embolism from small quantities of air, especially in presence of patent foramen ovale (up to 50 % in children younger than 5 years of age). An ultrasound-assisted technique is recommended: the epidural space is found by loss of resistance to saline and subsequently incremental doses of local anesthetic are administered through the catheter while the spread is assessed under ultrasound imaging. As no method of test dosing is infallible, incremental and slow injection is a critical safety measure whenever large volumes of local anesthetics are injected in children. Fixation is to be done with a specific transparent fixation device to allow observation of the catheter or possible signs of infection. Fixation should only be changed if strictly necessary. Catheters should be removed and the tip cultured if the child develops fever >38 °C. Most epidural catheters for postoperative pain relief can be removed after 48–72 h but if the catheter is to be kept in place for more than 48 h tunneling is recommended.

Placement of peripheral nerve catheters is now common in pediatric regional anesthesia [73–77]. Continuous peripheral nerve blocks should be done under strict aseptic conditions and in this author's opinion mainly for major surgery or pain/rehabilitation therapy. Complications consequence of the technique should be avoided by a very careful procedure performed by skilled pediatric anesthesiologists. Complications derived from infusions and catheter's care need extensive team training. Personnel from the anesthesia pain team should inspect the catheter daily through a transparent fixation dressing (but only change the dressing if strictly necessary) and control the infusions.

Because drug errors are higher in centers where fewer catheters are managed in the wards, the author of the present chapter recommends thorough staff education programs and medical support to the ward personnel before catheters are managed in a the ward. Intravenous lipid emulsion resuscitation guidelines and intramuscular pressure measurement devices should be available in all locations where continuous local anesthetics are used.

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Part V

Special Environments: Safe Practice and Management of Adverse Events

Local and Regional Anesthesia in Dental and Oral Surgery

21

Stanley F. Malamed, Kenneth L. Reed,
Amanda Okundaye, and Andrea Fonner

Key Points

- Local anesthesia is the standard of care for dental surgery. While effective at controlling pain, regional procedures in dentistry are associated with rare but unique complications.
- A variety of local anesthetics and nerve block approaches are used for dental procedures. Lidocaine represents the gold standard for dental local anesthesia.
- Local complications related to dental regional anesthesia include risk of needle breakage, paresthesia, transient facial paralysis, and self-inflicted injury of still-insensate soft tissues. Local anesthetic toxicity and allergic reaction represent potential systemic complications.
- New developments, including computer-controlled local anesthetic delivery systems, agents to reverse local anesthesia (e.g., phentolamine mesylate), and intranasal delivery of local anesthetic mist, may help to reduce complications going forward.

S.F. Malamed, DDS (✉)
Herman Ostrow School of Dentistry of U.S.C.,
Los Angeles, CA, USA
e-mail: malamed@usc.edu

K.L. Reed, DMD
New York University College of Dentistry, New York, NY, USA
e-mail: kr@klrdmd.com

A. Okundaye, DDS
Department of Hospital Dentistry, UCLA, Los Angeles, CA, USA
e-mail: ddsanesthesia@gmail.com

A. Fonner, DDS
The Herman Ostrow School of Dentistry of the University of Southern California, Los Angeles, CA, USA
e-mail: afonnerdds@gmail.com

Introduction

Local anesthesia forms the backbone of pain control techniques in dentistry. Local anesthetics represent the safest (when used properly) and most effective drugs for the prevention and management of perioperative and postoperative pain. The first known injection of a local anesthetic (1885) was an inferior alveolar nerve block administered by the famed medical surgeon Dr. William Stewart Halsted (1852–1922) [1]. The drugs injected were the combination of cocaine and epinephrine. The dental profession quickly adopted local anesthesia as its primary means of controlling pain eschewing general anesthesia, which had been, along with no anesthesia, the techniques of choice prior to 1885.

The introduction in 1905 of procaine (2 % with epinephrine 1:50,000) led to a rapid increase in the use of local anesthesia by dentists and to the burgeoning of access to dentistry for millions of people worldwide. Known everywhere by its primary proprietary name 'Novocain,' procaine is synonymous, to most people, as the 'shot' you receive at the dentist's office. The amino-esters (primarily procaine, propoxycaine and tetracaine) were the drugs used from 1906 until the mid-1940s when Astra Pharmaceuticals, in Sweden, synthesized and introduced the first amino-amide local anesthetic, lidocaine (Xylocaine) in 1948 [2]. The demonstrably superior clinical characteristics of lidocaine compared to the most commonly used amino-esters in dentistry led to its rapid adoption and to the development of other drugs in this same category. The amino-amide local anesthetics mepivacaine (1960), prilocaine (1965), bupivacaine (1972), and etidocaine (1976), were 'borrowed' from medicine for use in the dental profession [3]. The amino-ester local anesthetics are rarely, if ever, employed for pain control in the dental profession, worldwide.

The local anesthetic articaine was synthesized in Germany in 1973 and introduced into clinical use in dentistry in 1976 [4]. Articaine was approved for use in Canada in 1984 and in the United States in 2000. It represented the first, and still only, local anesthetic developed specifically

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_21

for use in dentistry. Articaine, though classified as an amino-amide, possesses chemical characteristics of both the amino-amide and amino-ester groups of local anesthetics. It has become an extremely popular local anesthetic wherever it has been made available. The use of articaine by the medical profession is increasing [5].

The dental profession uses prefilled local anesthetic cartridges (Fig. 21.1) as well as syringes designed specifically for these cartridges (Fig. 21.2), unlike the medical profession which uses multidose vials of local anesthetics and plastic disposable syringes (Fig. 21.3). In most of the world, the standard glass (or plastic) dental cartridge contains 1.8 mL of solution, though 2.2 mL and 1.0 mL cartridges represent the standard in some countries (Fig. 21.1). As most dental treatments involve cutting soft tissue and/or vital tooth structure they are associated with the propagation of painful impulses. The administration of local anesthetics has become the standard of care in the dental profession.

Local anesthetic techniques vary according to the site of the planned treatment. In the maxilla, the cortical plate of bone overlying the teeth is usually quite thin, permitting the use of 'infiltration' anesthesia (also known as 'supraperiosteal'). Infiltration of a small volume of local anesthetic (0.6 mL) at or above the apex of the tooth to be treated effectively blocks nerve conduction. Infiltration is the most common dental injection and is recommended when one maxillary tooth is to be treated. Nerve blocks, such as the anterior superior alveolar and posterior superior alveolar, may be administered when multiple maxillary teeth are to be treated. A local anesthetic nasal mist often tracaine and oxymetazoline (Kovanaze) allows for treatment of maxillary anterior teeth (preolars, canine and incisors) without the need for injection [6].

The adult mandible presents a different situation. The cortical plate of bone overlying the mandibular teeth in the adult is usually quite dense, preventing the simple infiltration injection from proving effective. Nerve block administration is the 'norm.' The traditional inferior alveolar nerve block (IANB), as described by Halsted in 1885, remains the most commonly used mandibular technique, providing anesthesia to all eight teeth in the quadrant. The incisive (mental) nerve block may be used when treating teeth anterior to the mental foramen (premolars, canine, and incisors). Other techniques include the Gow-Gates mandibular nerve block [7], Akinosi–Vazirani (closed mouth) nerve block [8, 9], periodontal ligament (PDL) injection [10], and intraosseous (IO) [11].

As with any technique, complications—though rare—can and do occur. Within dentistry localized complications associated with intraoral injections include needle breakage, paresthesia, facial nerve paralysis, and self-inflicted soft tissue injury, among others. Systemic complications include allergy and overdose (toxic reaction). Fortunately, the incidence of true, documented, and reproducible allergy to amino-amide local anesthetics is exceedingly rare. However, overdose is a potential problem seen most often in the younger, lighter weight (<30 kg) patients undergoing multiple quadrants of treatment in a single visit [12]. The following sections of this chapter will discuss these topics in greater detail.

Fig. 21.1 Prefilled dental local anesthetic cartridges. 2.2 mL, 1.8 mL, 1.0 mL

Fig. 21.2 Dental local anesthetic syringes

Fig. 21.3 (**a**) Lidocaine 2 % with epinephrine 1–100,000 multidose vial. (**b**) Plastic disposable syringe

Dental Local Anesthetic Formulations

In the United States, there are five different local anesthetic formulations available in a total of nine preparations which are used in dentistry and packaged in single use, disposable dental cartridges [13]. They are as follows:

1. Articaine
2. Bupivacaine
3. Lidocaine
4. Mepivacaine
5. Prilocaine

Articaine

It is available as a 4 % solution in dental cartridges with 1:100,000 epinephrine and 1:200,000 epinephrine. This drug is an amide-ester hybrid unlike all other local anesthetics used in dentistry that are pure amides. As such, articaine possesses a degree of hepatic biotransformation which leads to a beta (elimination) half-life that is significantly shorter (27 min) than other amide anesthetics (≥90 min) [14]. Since local anesthetic manufacturers have adjusted the concentration of each local anesthetic such that 1 mL of drug "A" is equipotent to 1 mL of drug "B," articaine represents the least potent local anesthetic available in dental cartridges as it is available as a 4 % concentration [13]. Articaine provides pulpal anesthesia of about 1 h and soft tissue anesthesia of 3–5 h duration, making it a reasonable choice for most dental procedures [15]. Articaine is approved for use in patients age 4 years and older [16].

Bupivacaine

It is available in dental cartridges as a 0.5 % solution with 1:200,000 epinephrine [17]. As a 0.5 % solution, bupivacaine is the most potent local anesthetic routinely used in dentistry. Being 95 % protein bound, it is a long-acting local anesthetic with pulpal anesthesia, following nerve block, in the 4–6 h range and soft tissue anesthesia that may exceed 12 h. Bupivacaine has the highest p*K*a of all of the local anesthetics used in dentistry making it the local anesthetic with the slowest onset of action [14]. While it is true that bupivacaine is four times as toxic as lidocaine, as packaged in dental cartridges they are equitoxic and equipotent per mL injected [17, 18]. Because the maximum recommended dose of bupivacaine in dentistry is significantly less than in medicine (Table 21.1) and because local anesthetics in dentistry are never intentionally injected into a vein (careful aspiration should always be performed), the cardiotoxic concerns that are present in medicine are not an issue in dentistry.

Lidocaine

It is the most used local anesthetic in dentistry and since its introduction in 1948 has remained the "gold standard" for dental local anesthetics [19]. It was this drug that displaced the mighty "Novocain®" (procaine) almost 70 years ago. As a side note, no formulation containing procaine has been available in dental cartridges since the 1990s [20]. In the United States, lidocaine is available in dental cartridges as a 2 % solution with 1:100,000 epinephrine and 1:50,000 epinephrine. Lidocaine without a vasoconstrictor ("plain") was

Table 21.1 Maximum dosages for local anesthetics

Maximum dosages for local anesthetics (all local anesthetic data derived from the associated package insert and FDA approved)			
Agent	MG/cartridge	Maximum dose (mg/kg)	Maximum dose (mg)
2 % lidocaine (Xylocaine®) with 1:100,000 or 1:50,000 epinephrine	36	7	500
2 % mepivacaine with 1:20,000 levonordefrin (Carbocaine®, Polocaine, Scandanest, Isocaine®)	36	6.6	400
3 % mepivacaine plain (Carbocaine®, Polocaine, Scandanest, Isocaine®)	54	6.6	400
0.5 % bupivacaine with 1:200,000 epinephrine (Marcaine®, Vivacaine®)[a]	9	–	90
4 % articaine with 1:100,000 or 1:200,000 epinephrine (Septocaine®, Zorcaine®, Articadent®, Orabloc®)[b]	72	7	–
4 % prilocaine with 1:200,000 epinephrine (Citanest Forte®)	72	8	600
4 % prilocaine plain (Citanest®)	72	8	600

[a]Bupivacaine is not FDA approved for use in children under the age of 12
[b]Articaine is not FDA approved for use in children under the age of 4

manufactured for quite some time but has not been available in dental cartridges for a number of years. Lidocaine is intermediate in both potency and duration of action; it provides pulpal anesthesia for about 1 h and soft tissue anesthesia of 3–5 h making it very similar in duration to articaine but twice as potent [18].

Mepivacaine

It is different than all other local anesthetics used in dentistry for two significant reasons. First, it is the only local anesthetic available in two different concentrations, 2 and 3 %. Second, it is the only local anesthetic marketed in the United States in dental cartridges with a vasoconstrictor other than epinephrine. Two percent mepivacaine is available with 1:20,000 levonordefrin (NeoCobefrin®) [21]. Levonordefrin has a different profile than epinephrine with respect to receptor pharmacology. Epinephrine has roughly a 50:50 affinity between alpha (α) and beta (β) receptors. Levonordefrin is roughly 75:25 weighted toward alpha with significantly less beta effect. Additionally, levonordefrin is roughly 1/6 as potent as epinephrine [14]. Three percent mepivacaine is only available without a vasoconstrictor ("plain"). Mepivacaine plain is a short duration drug where mepivacaine with vasoconstrictor is intermediate, similar to articaine and lidocaine. Mepivacaine has the lowest p*K*a of all local anesthetics used in dentistry making it the local anesthetic with the fastest onset of action [21].

Prilocaine

It is available as a 4 % solution in dental cartridges, either with 1:200,000 epinephrine or plain (without vasoconstrictor). Prilocaine plain competes with mepivacaine plain with respect to duration of action, albeit with a slightly slower onset of action, though this is not clinically significant. Prilocaine with vasoconstrictor has a similar onset of action and duration of action of articaine, lidocaine, and mepivacaine [22].

Techniques of Dental Local Anesthesia

Maxillary Injection Techniques

Supraperiosteal (Infiltration) Injection

The supraperiosteal (or infiltration) technique can be used to anesthetize teeth and the surrounding soft tissue adjacent to the injection site. Penetration is the height of the mucobuccal fold parallel to the tooth to be treated. The depth of penetration is approximately 2–5 mm (the needle tip is located at or above the apex of the tooth). After careful aspiration, 0.6 mL of solution is slowly deposited. This technique is recommended for procedures limited to the treatment of one or two teeth [23].

Anterior Superior Alveolar Nerve Block

The anterior superior alveolar (ASA) nerve block (NB) will anesthetize the buccal soft tissue and teeth from the canine to the midline [24] (Fig. 21.4). The depth of penetration is about 16 mm in the mucobuccal fold over the maxillary first premolar. Slow deposition of 1.0 mL of solution after aspiration is generally sufficient [23–26]. Crossover innervation must always be considered in case of inadequate anesthesia near the midline.

Middle Superior Alveolar Nerve Block

The middle superior alveolar (MSA) NB will anesthetize the mesiobuccal aspect of the maxillary first molar, both premolars, along with the soft tissue lateral to this area [24] (Fig. 21.5). Penetration for the MSA NB is at the height of the buccal vestibule lateral to the maxillary second premolar. The needle tip should approximate the apex of the

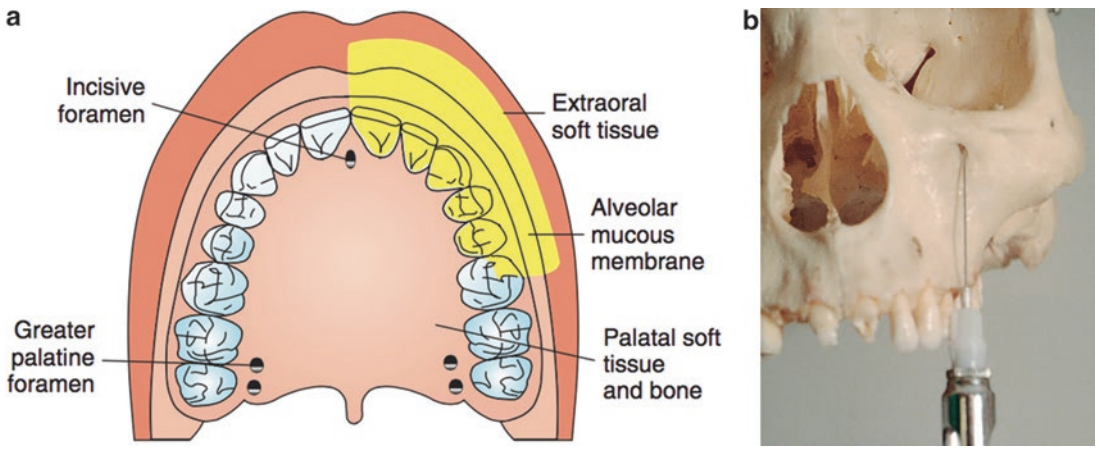

Fig. 21.4 Anterior superior alveolar nerve block ((**a**) area anesthetized; (**b**) needle placement)

tooth, which usually requires a penetration of about 5 mm. After careful aspiration, 1.0 mL of anesthetic solution is slowly deposited [23–26]. Note: The MSA nerve is absent in approximately 28 % of patients. If this is the case, the anterior superior alveolar (ASA) NB will anesthetize the premolar region.

Posterior Superior Alveolar Nerve Block

The posterior superior alveolar (PSA) NB will anesthetize the three maxillary molars except for the mesiobuccal aspect of the first molar (Fig. 21.6) and the buccal soft tissue adjacent to these teeth [24]. The PSA NB is administered with the insertion point at the height of the buccal vestibule at a point just distal to the malar process. The needle is inserted distally and superiorly at approximately 45° to the mesiodistal and buccolingual planes. The depth of insertion is approximately 15 mm, and following careful aspiration, 1.0 mL of solution is slowly deposited [23, 26].

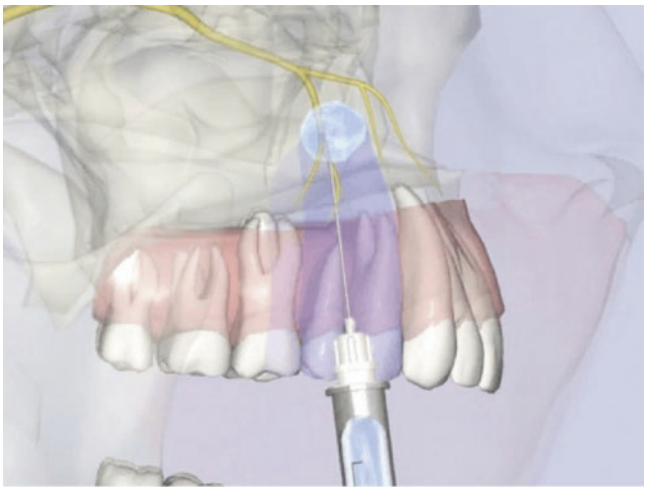

Fig. 21.5 Middle superior alveolar nerve block

Greater Palatine Nerve Block

The greater palatine (GP) NB will anesthetize the tissues of the hard palate anteriorly to the distal of the canine and laterally to the midline (Fig. 21.7) [24]. The entrance to the greater palatine foramen may be palpated as a depression or soft spot in the posterior area of the hard palate. It is usually located halfway between the gingival margin and the midline of the palate, approximately opposite the distal of the maxillary second molar [23–26]. Anatomically, this is generally 5 mm anterior to the junction of the hard and soft palates. The most comfortable way to perform this injection is to first deposit 0.3 mL of local anesthetic in the soft tissue around the location of the greater palatine foramen. Penetration will occur through the epithelium, and the needle will appear to "fall into" a space of less resistance. The needle should be inserted until bone is contacted. The depth of penetration is variable, but usually less than 5 mm is sufficient. After aspiration, 0.5 mL of anesthetic solution is very slowly deposited.

Nasopalatine Nerve Block

The nasopalatine (NP) NB will anesthetize the tissues of the palatal aspect of the upper anterior teeth [24] (Fig. 21.8). The entrance to the nasopalatine foramen is at the incisive papilla, which may be visualized posterior to the maxillary central incisors. The needle tip should contact soft tissue at the lateral aspect of the incisive papilla with a depth of penetration of <5 mm and bony endpoint. Approximately 0.25 mL may be very slowly introduced after aspiration [22–24, 26]. Note: Some patients also have a contribution from this nerve to the pulpal tissue of the maxillary incisors.

Maxillary (V_2) Nerve Block

The entire maxillary (second) division of the trigeminal nerve (cranial nerve V) is anesthetized most frequently via the greater palatine canal (Fig. 21.9). The V_2 nerve block

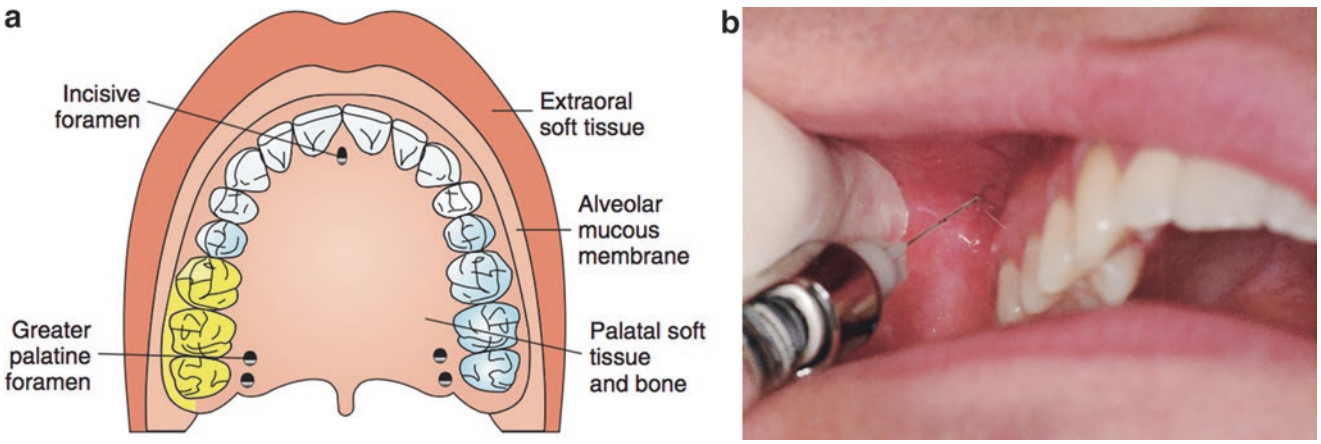

Fig. 21.6 Posterior superior alveolar nerve block ((**a**) area anesthetized; (**b**) technique)

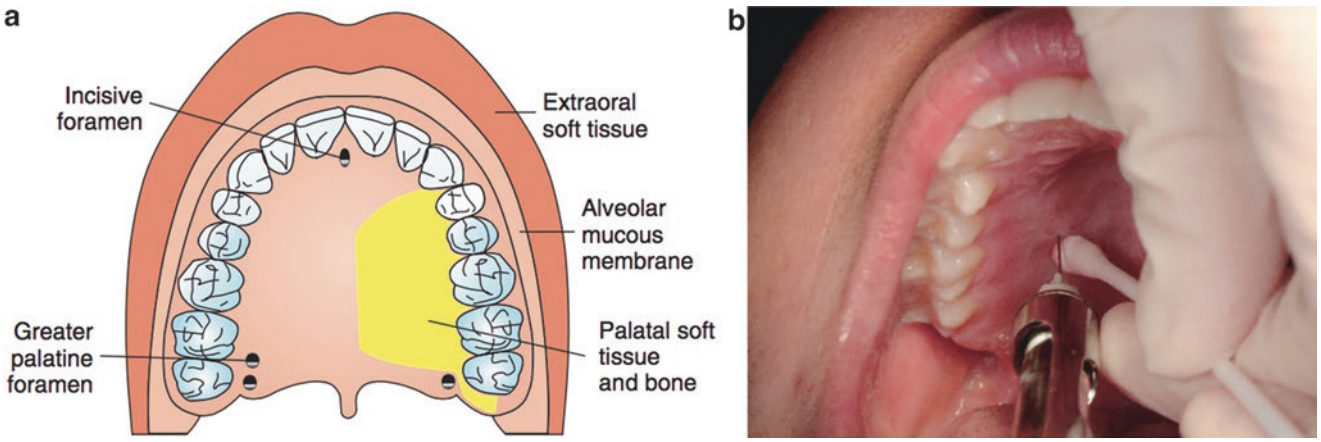

Fig. 21.7 Greater (anterior) palatine nerve block ((**a**) area anesthetized; (**b**) technique)

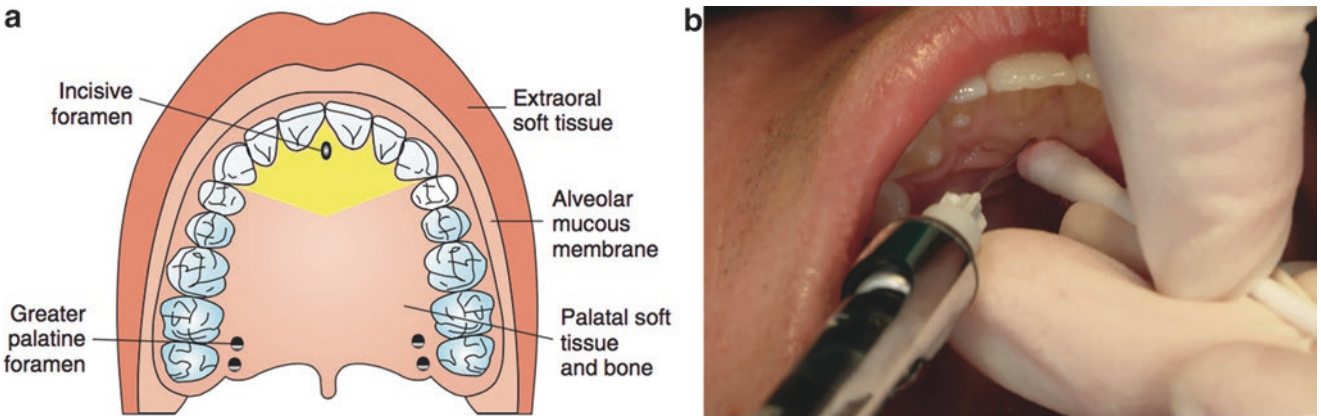

Fig. 21.8 Nasopalatine nerve block ((**a**) area anesthetized; (**b**) technique)

anesthetizes the maxillary teeth and periodontium, hard and soft palates, sinuses, and portions of the nose, orbit, upper cheek, lower eyelid, and side of the face on the ipsilateral side [24]. The entrance to the foramen is located at the distolateral aspect of the same depression felt during palpation before the greater palatine injection. This foramen generally is located halfway between the gingival margin and the midline of the palate, approximately 5 mm anterior to the junction of the hard and soft palates. After 0.3 mL of local anesthetic is given in the soft tissue, a long needle is used to probe the canal entrance gently. Angulation is mostly superior, with slight distal and lateral components [23–26]. The most effective position of the needle for administration of the V2 block injection generally is such that a 45-degree angle exists between the needle and the soft tissue. The needle is inserted to a depth of approximately 30 mm. After aspiration, the contents of the cartridge (1.8 mL) are slowly deposited [27]. Up to 15 % of patients have anatomical deviations that make this approach ineffective, because the needle cannot physically be manipulated up the canal to the proper depth.

Mandibular Injection Techniques

Inferior Alveolar Nerve Block

The inferior alveolar (IA) NB will anesthetize the mandibular teeth from the third molar to the midline, the buccal soft tissue from the premolars anteriorly, the body of the mandible, the periosteum, the PDL, and the skin and subcutaneous tissues of the chin and lower lip, all on the ipsilateral side (Fig. 21.10) [28]. In an IA block, a long needle is positioned parallel to the mandibular occlusal plane from the contralateral premolar area to a point on the soft tissue approximately 1.5 cm above the mandibular occlusal plane. Traditionally, the IA injection is described with an insertion point 1.0 cm above the mandibular occlusal plane. The use of a 1.5 cm puncture point should increase the success rate from approximately 84 % to 96 % [29]. The mucosa is pierced at a point between the pterygomandibular raphe and the deep tendon of the temporalis muscle, and the needle is advanced until bone is contacted, usually about 25 mm [24–26, 28]. The best way to visualize the lateral positioning of the needle prior to penetrating soft tissue is to look for the

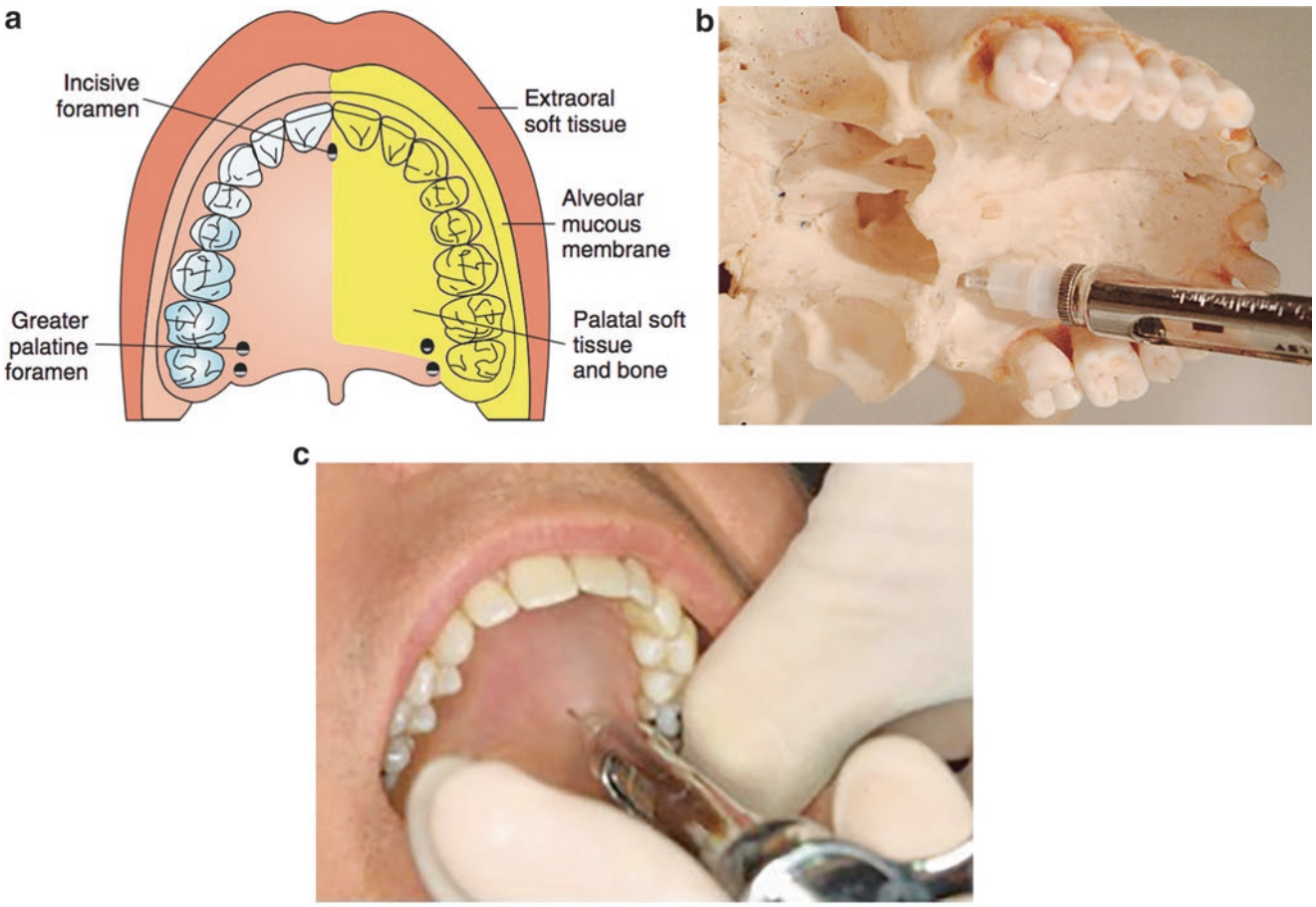

Fig. 21.9 Maxillary (V2) nerve block. Greater palatine canal approach ((**a**) area anesthetized; (**b**) anatomy; (**c**) technique)

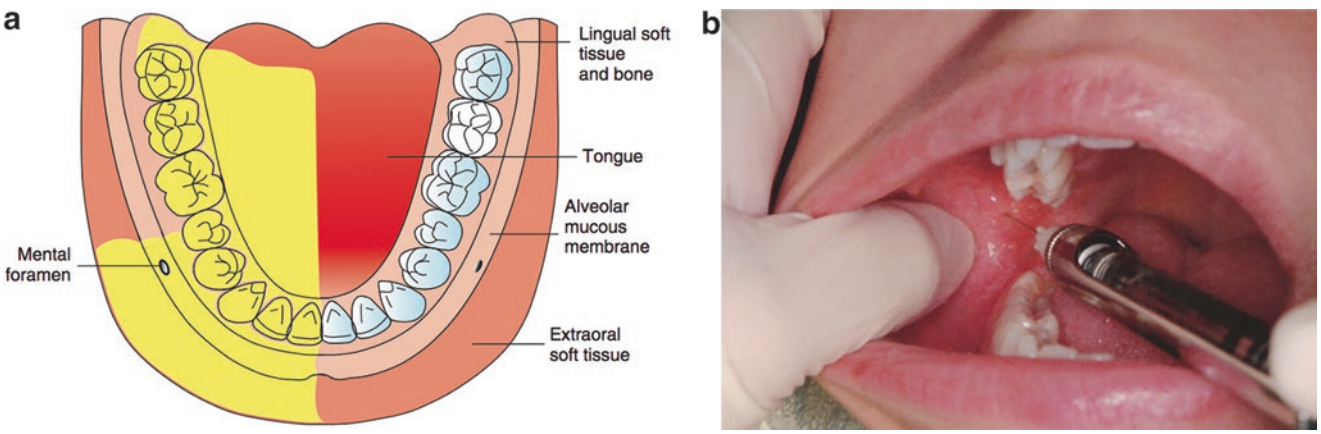

Fig. 21.10 Inferior alveolar nerve block ((**a**) area anesthetized; (**b**) technique)

depression seen on the immediate lateral aspect of the pterygomandibular raphe. This is sometimes termed the "poke me line" (Fig. 21.11). Once the needle is advanced and bone contacted, the tip should now be located just superior to the lingula. The needle should be withdrawn 1–2 mm so it is no longer in contact with periosteum. After careful aspiration, 1.5 mL of solution is deposited. As the needle is being removed, when it is approximately halfway out, the lingual nerve is injected with the remaining solution, unless a buccal nerve block needs to be done. In that case, a few drops of local anesthetic should be reserved. Frequently, even without this last step, the lingual nerve will be anesthetized.

A potential complication of this nerve block is an intravascular injection because it has the highest frequency of positive aspiration of all intraoral injections (10 %-15 %). Careful aspiration can avoid this complication.

Gow-Gates Mandibular Nerve Block

George A. E. Gow-Gates first published this technique in 1973 (Fig. 21.12) [7]. Significant advantages of the Gow-Gates mandibular NB over the IA NB include its higher success rate, its lower incidence of positive aspiration (2 %), and the absence of problems with accessory sensory innervation to the mandibular teeth. The Gow-Gates mandibular NB anesthetizes the inferior alveolar, lingual, auriculotemporal, buccal (75 % of the time), and mylohyoid nerves. The injection blocks the nerves at a point that is proximal to their division into inferior alveolar, buccal, and lingual nerves. The needle endpoint is the lateral aspect of the anterior portion of the condyle, just inferior to the insertion of the lateral pterygoid muscle. The injection is administered by having the patient open their mouth as widely as possible to rotate and translate the condyle forward. The condyle is palpated with the fingers of the nondominant hand while the cheek is retracted with the thumb. Beginning from the contralateral canine, the needle is positioned so that a puncture point is made approximately at the location of the distobuccal cusp of the maxillary second molar. A 25-gauge long needle is inserted slowly to a depth of 25–30 mm; the endpoint is inferior and lateral to the condylar head. The injection must not be performed unless bone is contacted to ensure proper needle placement. After the needle is withdrawn 1–2 mm, the clinician aspirates and injects the contents of the cartridge. This injection is unique among intraoral injections because the operator does not attempt to get as close as possible to the nerve to be anesthetized. In fact, the needle tip should be approximately 1.0 cm directly superior to the nerve, in the superior aspect of the pterygomandibular space.

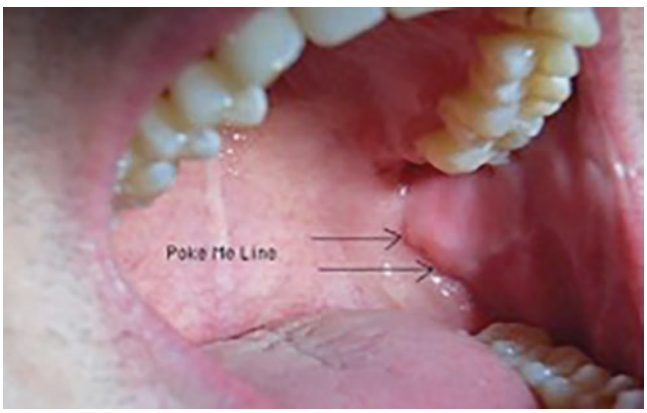

Fig. 21.11 'Poke Me Line" for inferior alveolar (mandibular) nerve block

Vazirani–Akinosi Nerve Block

This form of injection, also known as the closed-mouth mandibular block, anesthetizes the inferior alveolar, lingual, buccal, and mylohyoid nerves (Fig. 21.13) [8, 9]. This injection is useful for patients with trismus because it is performed while the jaw is in its physiologic rest position. A 25-gauge long needle is inserted parallel to the maxillary occlusal plane at the height of the maxillary buccal vestibule. The bevel should be oriented away from the bone of the mandibular ramus so that deflection occurs toward the ramus. The depth of penetration is approximately half the mesiodistal length of the ramus, which is about 25 mm in adults (measured from the maxillary tuberosity). The depth of insertion will vary with the antero-posterior size of the patient's ramus. The Vazirani–Akinosi injection is performed "blindly" because no bony endpoint exists. However, in adult patients, a rule of thumb is that the hub of the needle should be opposite the mesial aspect of the maxillary second molar. After aspiration, the contents of the cartridge (1.8 mL) can be deposited slowly.

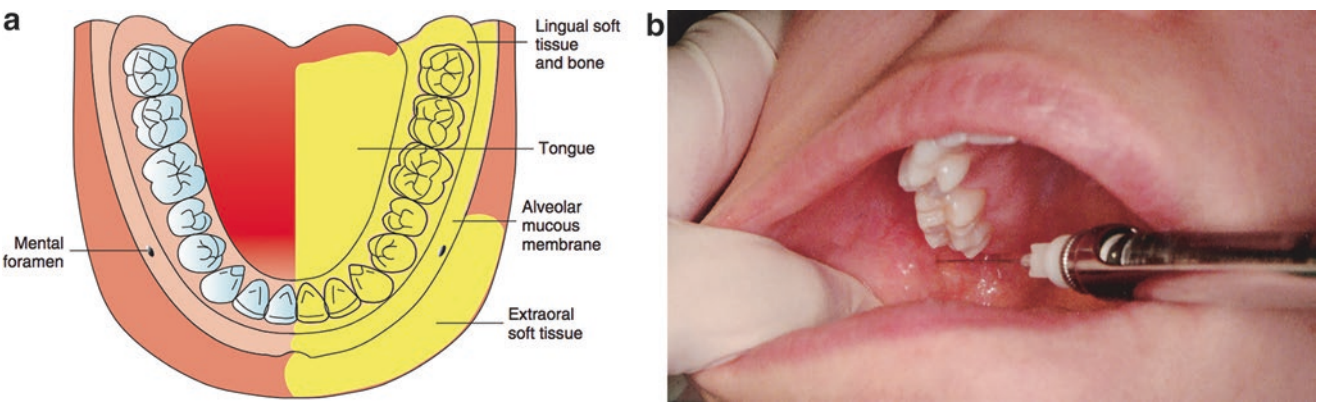

Fig. 21.12 Gow-Gates mandibular nerve block ((**a**) area anesthetized; (**b**) technique

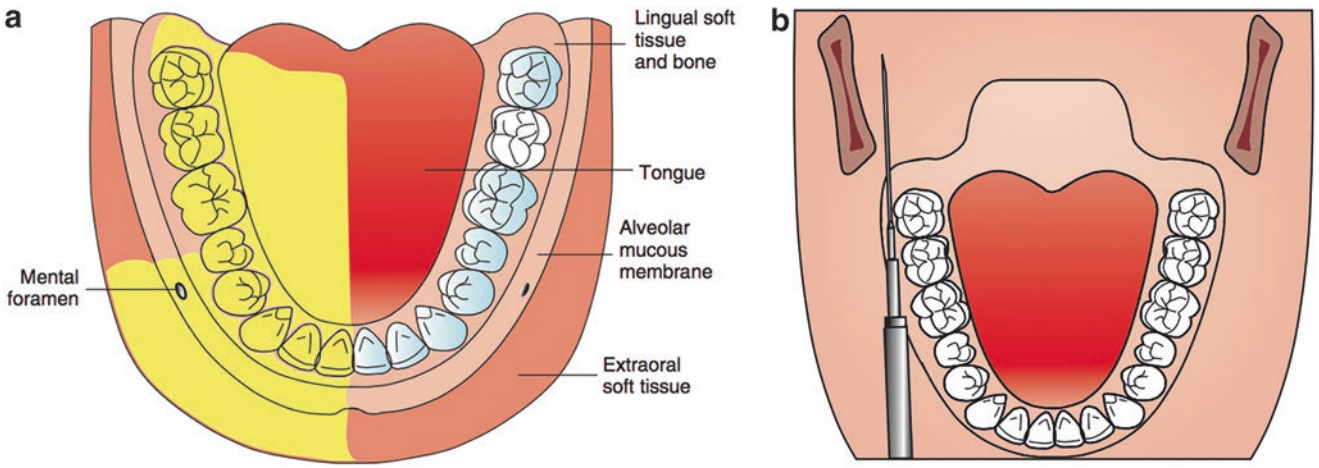

Fig. 21.13 Vazirani–Akinosi (closed mouth) nerve block ((**a**) area anesthetized; (**b**) technique)

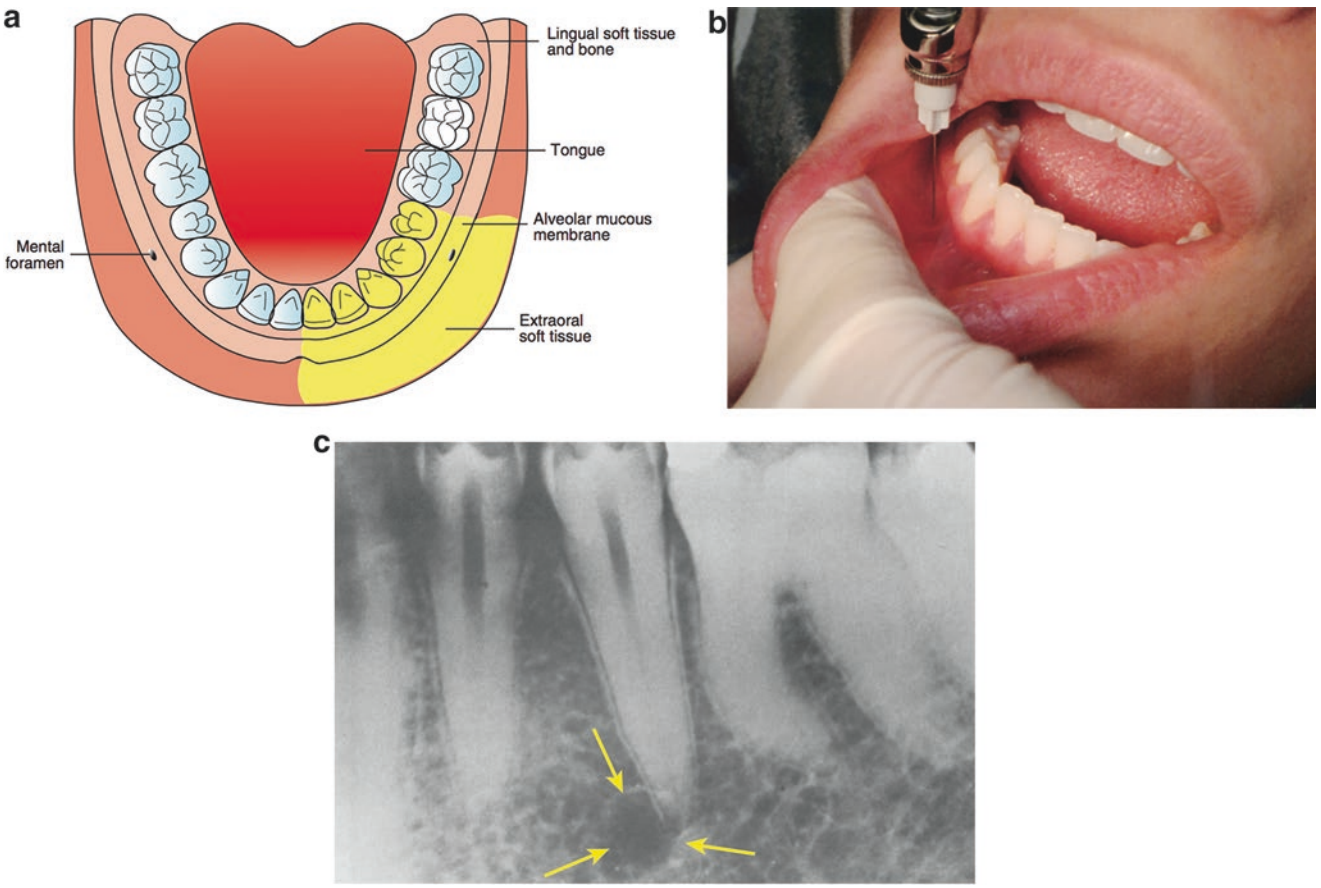

Fig. 21.14 Incisive (mental) nerve block ((**a**) area anesthetized; (**b**) technique; (**c**) radiographs can aid in locating mental foramen)

Incisive (Mental) Nerve Block

The mental and incisive nerves are terminal branches of the IA nerve. The mental nerve exits the mental foramen at or near the apices of the mandibular premolars. The incisive nerve continues anteriorly in the incisive canal. Both nerves will be anesthetized after a successful inferior alveolar nerve block, but this injection technique can be useful when bilateral anesthesia is desired for procedures on premolars and anterior teeth [28] (Fig. 21.14). The lingual tissues are not anesthetized with this block. The initial

technique for the mental and incisive nerve blocks is the same. A 25- or 27-gauge short needle is inserted at the mucobuccal fold at or just anterior to the mental foramen, which is typically located between the apices of the two premolars. The bevel of the needle should be oriented toward the bone and the tissue penetrated to a depth of 5–6 mm. After aspiration, approximately one-third to one half of the cartridge (0.6–0.9 mL) should be deposited. The difference between the mental nerve block and the incisive nerve block is that the incisive nerve block requires pressure to direct local anesthetic solution into the mental foramen. This can be accomplished by maintaining gentle pressure at the injection site for approximately 2 min following deposition of the solution [28].

Supplemental Injection Techniques

Periodontal Ligament Injection

The periodontal ligament (PDL) injection anesthetizes a single tooth and is utilized to avoid the undesirable consequences of regional block anesthesia [30]. A 27-gauge short needle with the bevel toward the tooth is inserted through the gingival sulcus on the mesial of the tooth to be anesthetized and advanced as far apically as possible (Fig. 21.15). Approximately 0.2 mL of anesthetic solution is deposited over a minimum of 20 s. Then the same technique is performed on the distal of the tooth [31]. The PDL injection may be uncomfortable if the rate of injection is too rapid or the tissues are inflamed. The duration of pulpal anesthesia is extremely variable, so repeated PDL injections may be necessary to complete a procedure.

Intraosseous

When conventional block and infiltration injections are ineffective, an intraosseous injection may be used to anesthetize a single tooth or multiple teeth in one quadrant [31] (Fig. 21.16). Originally, intraosseous anesthesia required the use of a round bur to provide entry into interseptal bone, which is still an acceptable technique [27]. Once the hole had been made, a needle would be inserted into this hole and local anesthetic deposited. Today, specialized devices help to ease this injection technique. The Stabident® System (Fairfax Dental Inc.) (Fig. 21.17) comprises a slow-speed handpiece-driven perforator and a solid 27-gauge wire with a beveled end that, when activated, drills a small hole through the cortical plate of bone. The anesthetic solution is delivered to cancellous bone through the 27-gauge short needle placed into the hole made by the perforator. The X-Tip® (Dentsply) anesthesia delivery system consists of an X-Tip that separates into two parts: a drill and a guide sleeve (Fig. 21.17b). The drill (a special hollow needle) leads the guide sleeve through the cortical plate until it is separated and is then withdrawn. The remaining guide sleeve is designed to accept a 27-gauge needle to inject anesthetic solution. The guide sleeve is removed after the intraosseous injection is complete. Bone is perforated 2 mm apical to the intersection of lines drawn horizontally along the gingival margins of the teeth and a vertical line through the interdental papilla. The site should be distal to the tooth to be treated, and care should be taken to avoid the area of the mental foramen. The volume of anesthetic injected ranges from one-third to two-thirds of a dental cartridge (0.6–1.2 mL). The onset of anesthesia is immediate, and pulpal anesthesia will last for 15–45 min.

Local Complications of Local Anesthetic Administration

The administration of local anesthetics is associated with complications that may occur locally in the region of the injection. These include (1) needle breakage, (2) paresthesia, (3) facial nerve paralysis, and (4) self-inflicted soft tissue injury.

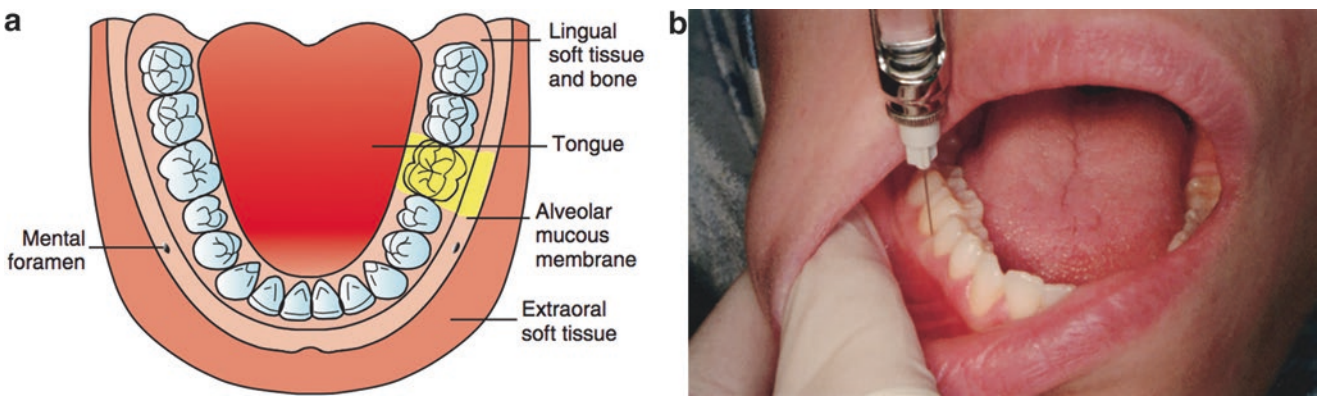

Fig. 21.15 Periodontal ligament injection (PDL) ((**a**) area anesthetized; (**b**) technique)

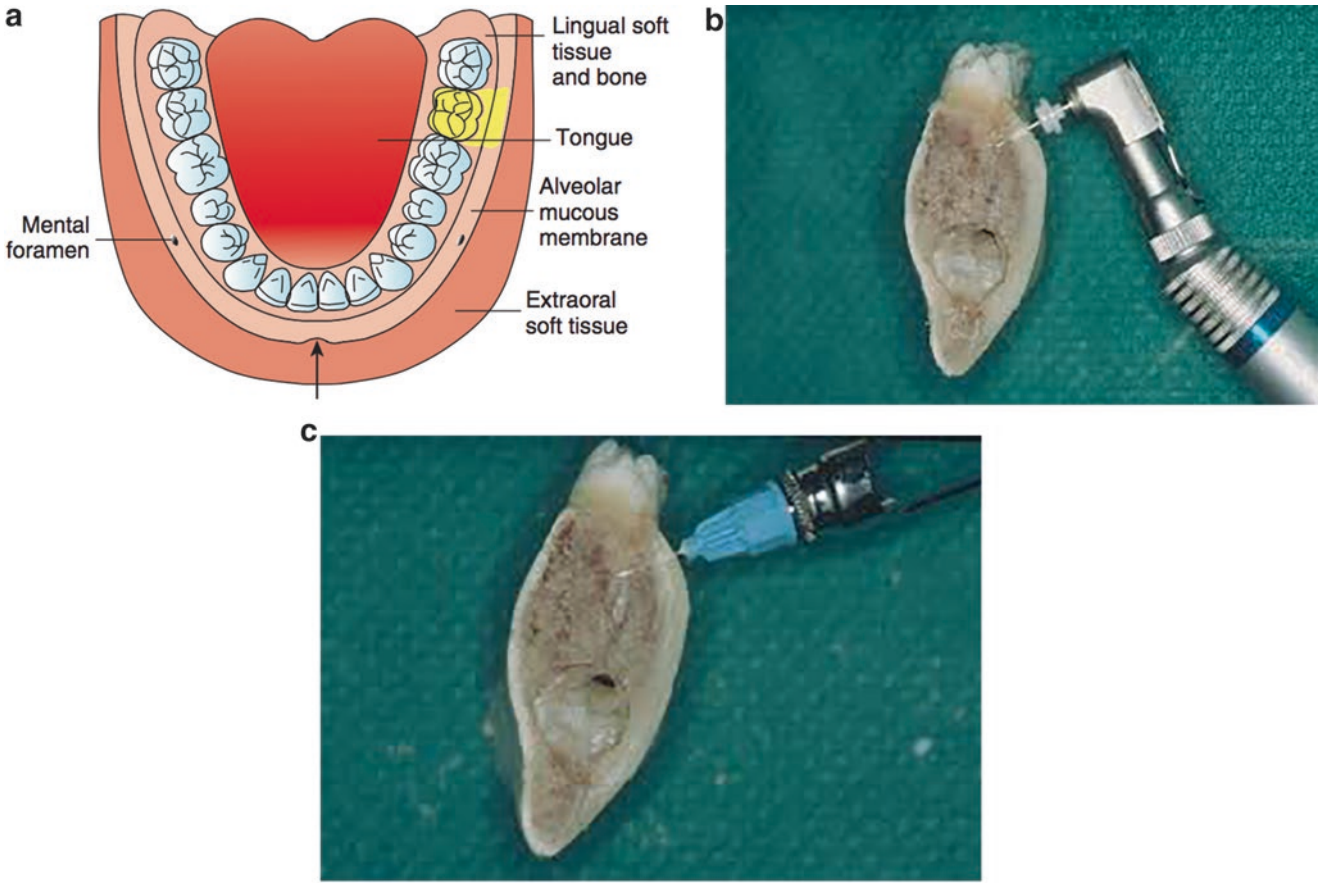

Fig. 21.16 Intraosseous injection ((**a**) area anesthetized; (**b**) technique-1; (**c**) technique-2)

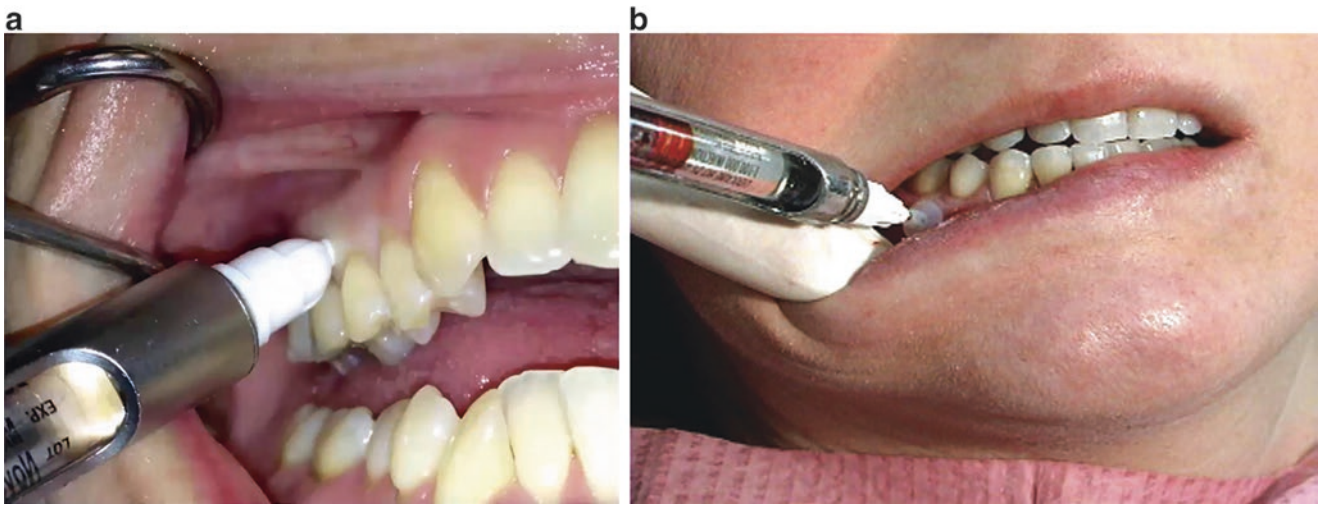

Fig. 21.17 (**a**) Stabident Intraosseous Injection System (courtesy Fairfax Dental). (**b**) X-Tip Intraosseous Injection System (courtesy Dentsply)

Needle Breakage

Since the introduction of nonreusable, stainless steel dental local anesthetic needles, needle breakage has become an extremely rare complication of dental local anesthetic injections (Fig. 21.18). Pogrel has (roughly) estimated the risk of needle breakage among Northern California dentists at 1 in 14 million inferior alveolar nerve blocks [32]. In the United States, 1.43 million boxes of dental needles (100 needles per

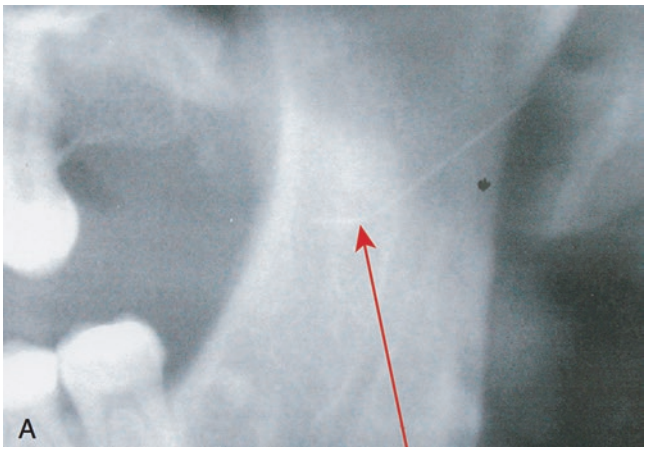

Fig. 21.18 Broken dental needle (*arrow*) Retained in pterygomandibular space

Table 21.2 Analysis of broken dental needle reports

	IANB	PSA	30-gauge	27-gauge
Individual citations	15	5	10	1
Pogrel	15	1	13	3
Malamed	32	1	33	1
Reed	17	0	17	0
Manufacturer	N/A	N/A	27	0
Total	79	7	100	5

IANB inferior alveolar nerve block, *PSA* posterior superior alveolar nerve block, *N/A* not applicable

box; 143,000,000 needles) were sold by one needle manufacturer in 2004, 1.56 million boxes in 2005, and 1.43 million boxes in 2006 [33].

Table 21.2 summarizes a review of the dental literature of reports of broken dental needles from 1950 through 2010 [34]. Reports of 105 cases were found. In all but five reports, the needle involved was a 30-gauge short (20-mm length) or 30-gauge ultrashort (10-mm length). In five cases, a 27-gauge short needle was involved. Inferior alveolar nerve block the technique administered in 79 of the 86 reports in which the injection technique was identified; the posterior superior alveolar nerve block was identified in the remaining seven. The factual information clearly identifies commonalities in most cases: use of 30-gauge short or ultrashort needles in injection techniques in which the needle is inserted to its hub ("hubbing of the needle").

Long dental needles most likely have broken during injection. However, because the long needle is unlikely to have been inserted to its full length (approximately 32 mm) into soft tissue, some portion of the needle would remain visible in the patient's mouth. Retrieval of the fragment with a hemostat is easily accomplished. Litigation does not occur in such incidents (Fig. 21.19). Additional factors with needle fracture include (1) intentional bending of the needle by the doctor before injection, (2) sudden unexpected movement by the patient while the needle is still embedded in tissue, and (3) forceful contact with bone.

Where the needle has been inserted to its hub and the soft tissue has dimpled under pressure from the syringe, the broken fragment will not be visible when the syringe is withdrawn from the patient's mouth. The needle fragment remaining in the tissue poses a risk of serious damage being inflicted on the soft tissues for as long as the fragment remains. Although it does not often occur, needle fragments can migrate.

Though rare, dental needle breakage can, and does, occur. There are several commonalities which, when avoided, can minimize the risk of needle breakage with the fragment being retained [34]. These include the following: (1) Do not use short needles for inferior alveolar nerve block in adults or larger children. (2) Do not use 30-gauge needles for inferior alveolar nerve block in adults or children. (3) Do not bend needles when inserting them into soft tissue. (4) Do not insert a needle into soft tissue to its hub, unless it is absolutely essential for the success of the injection. (5) Observe extra caution when inserting needles in younger children or in extremely phobic adult or child patients.

Paresthesia

Paresthesia is defined as persistent anesthesia (anesthesia well beyond the expected duration), or altered sensation well beyond the expected duration of anesthesia. In addition, the definition of paresthesia should include hyperesthesia and dysesthesia, in which the patient experiences both pain and numbness [35].

Trauma to any nerve may lead to paresthesia. Paresthesia is a not uncommon complication of oral surgical procedures and mandibular dental implants [36–38]. The incidence of paresthesia associated with local anesthetic administration is quite low. Haas estimated the overall risk of paresthesia (either transient or permanent from all local anesthetic formulations) in Ontario, Canada, at 1:785,000 injections [39].

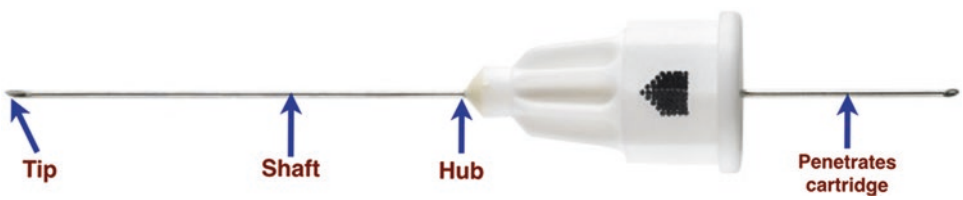

Fig. 21.19 Anatomy of the dental local anesthetic needle. Fracture occurs at the hub of the needle—the least flexible portion of the needle

Garristo et al. estimated the overall risk in the United States at 1:13,800,970 injections [40]. In dentistry, most reports of paresthesia occur in the mandible (>95 %) most commonly following inferior alveolar nerve block (>90 %). The lingual nerve is most often involved (>90 %) [41].

A patient's clinical response can be profuse and varied, including sensations of numbness, swelling, tingling, and itching. Associated oral dysfunction, including tongue biting, drooling, loss of taste, and speech impediment, may be noted. Direct trauma to the lingual nerve occurring during inferior alveolar nerve block is thought to be the most common etiology of paresthesia. An 'electric shock' or 'zap' is experienced by the patient during injection.

Neurotoxicity of all local anesthetic drugs may be responsible for some cases of paresthesia. Reports in the dental literature asserted that 4 % anesthetic formulations (articaine, prilocaine) had greater risks of producing paresthesia than 2 and 3 % local anesthetic formulations (lidocaine, mepivacaine, bupivacaine) [39, 40, 42]. All reports are anecdotal case reports. There is no scientific evidence that articaine possesses a greater risk of paresthesia than any other dental local anesthetic formulation [43, 44].

Direct needle contact with a nerve during local anesthetic administration cannot always be avoided. The doctor is attempting to deposit a volume of local anesthetic in very close proximity to 'the nerve' without physically contacting it. Given that once a needle penetrates mucous membrane (or skin, if extraoral), all injections are blind, and paresthesia can, and does, happen—fortunately on extremely rare occasion. Garristo et al. reported on the duration and resolution of paresthesia in 108 cases (of 248 reported) [40]. Resolution ranged from 1 to 736 days, with confirmed resolution in 34 of the 108. Of the 34, 25 resolved completely within 2 months, the remaining 9 within 240 days. 'Tincture of time' is the recommended treatment for paresthesia.

Transient Facial Nerve Paralysis

Transient facial nerve paralysis is commonly caused by the introduction of local anesthetic into the capsule of the parotid gland, which is located at the posterior border of the mandibular ramus. Directing the needle too far posteriorly during an inferior alveolar nerve block may place the tip of the needle within the body of the parotid gland. If local anesthetic is deposited, transient paralysis of the muscles of facial expression can result. The duration of the motor paralysis is equal to that of the soft tissue anesthesia usually noted for that drug (see discussion of drugs, earlier, usually 3–5 h). The primary problem associated with transient facial nerve paralysis is cosmetic: the person's face appears lopsided (Fig. 21.20). No treatment is known, other than waiting until the action of the drug resolves.

A secondary problem is that the patient is unable to voluntarily close one eye. The protective lid reflex of the eye is abolished. Winking and blinking become impossible. The cornea, however, does retain its innervation; thus if it is irritated, the corneal reflex is intact, and tears lubricate the eye. Transient facial nerve paralysis is almost always preventable by adhering to protocol with the inferior alveolar and

Fig. 21.20 Facial nerve paralysis secondary to local anesthetic deposition in parotid gland (patients left side)

Vazirani–Akinosi nerve blocks. A needle tip that comes in contact with bone (medial aspect of the ramus) before depositing local anesthetic essentially precludes the possibility that anesthetic will be deposited into the parotid gland during an IANB. Management includes the following: (1) Reassure the patient. Explain that the situation is transient, will last for a few hours, and will resolve without residual effect. (2) Contact lenses should be removed until muscular movement returns. (3) An eye patch should be applied to the affected eye until muscle tone returns. (4) Record the incident on the patient's chart.

Self-Inflicted Soft Tissue Injury

Self-inflicted trauma to the lips and tongue is frequently caused by the patient inadvertently biting or chewing these tissues while still anesthetized (Fig. 21.6). Trauma occurs most frequently in younger children, in mentally or physically disabled children or adults, and in oldest-old (>85 years) patients; however, it can and does occur in patients of all ages [45] (Table 21.3). Prevention includes (1) advising the parent or guardian to watch the child to prevent them from chewing their soft tissues; (2) select a short-duration local anesthetic (e.g., mepivacaine 3 %) if appropriate for the planned procedure; (3) select the appropriate technique which minimizes residual soft tissue anesthesia, such as infiltration, periodontal ligament injection (PDL), or intraosseous (IO); and (4) consider administration of a local anesthesia reversal agent—phentolamine mesylate (OraVerse™ [see discussion later]) [46].

Systemic Complications

Toxicity (Overdose)

Most adverse drug reactions develop either during the injection or within 5–10 min [12]. Overdose of local anesthetic can result from high blood levels caused by a single inadvertent intravascular injection or repeated injections [47]. Local anesthetic overdose manifests initially as an excitation followed by depression of the central nervous system (CNS). Signs of toxicity involve the CNS and include circumoral numbness, facial tingling, restlessness, dizziness, anxiety, confusion, slurred speech, shivering, and potentially tonic–clonic seizures. Unconsciousness and possible respiratory arrest may occur [47].

The cardiovascular system (CVS) response to local anesthetic toxicity mimics the excitation followed by depression of the central nervous system (CNS). The CVS is more resistant to the effects of local anesthetic overdose than the CNS [48]. Initially, during CVS stimulation, heart rate and blood pressure may increase, but as plasma levels of the anesthetic increase, hypotension due to relaxation of the arteriole vascular smooth muscles, followed by depression of the myocardium with subsequent fall in blood pressure, occurs. Bradycardia and cardiac arrest may follow. The cardiodepressant effects of local anesthetics are not seen until there is a significantly elevated local anesthetic blood level, roughly twice that required for CNS changes [47, 49] (Fig. 21.21).

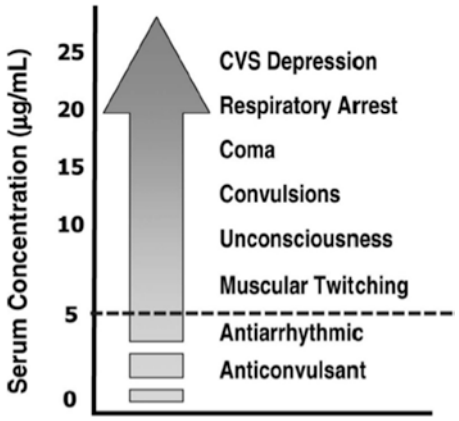

Fig. 21.21 Approximate serum concentrations and systemic actions of lidocaine

Local anesthetic toxicity can be prevented by careful injection technique, diligence in observing the patient, and knowledge of the maximum dosage based on weight (mg/kg) as well as absolute maximum recommended dosages. Practitioners should aspirate before every injection and inject slowly [12]. Following injection, the doctor or an assistant should remain with the patient while the anesthetic begins to take effect. Early recognition of an adverse response is critical to effective management. When signs or symptoms of toxicity are noted, administration of the local anesthetic should be discontinued. Additional emergency management is based on the severity of the reaction [12, 47].

Allergy to Local Anesthesia

Allergic reactions to local anesthetics are extremely rare, despite the frequent use of these drugs. Most adverse reactions are caused by manifestations of systemic toxicity or are psychogenic reactions in response to the act of receiving an injection (e.g., syncope, hyperventilation). Allergic reactions are not dose dependent, but are due to the patient's heightened capacity to react to even a small dose. Hypotension associated with syncope may be psychogenic or vagally mediated, whereas tachycardia and palpitations may occur from systemic absorption of epinephrine. Allergies can manifest in a variety of ways, some of which include urticaria, dermatitis, angioedema, fever, photosensitivity, or anaphylaxis [12]. Emergency management is dependent on the rate and severity of the reaction. There are no preservatives in local anesthetic cartridges unlike multidose vials used in medicine, there are however antioxidants (bisulfites) that protect the vasoconstrictor from oxidation.

Fig. 21.22 Computer-Controlled Local Anesthetic Delivery System—The Wand

Future Considerations

Although local anesthesia remains the backbone of pain control in dentistry, research continues, in both medicine and dentistry, with the goal of improving all areas of the local anesthetic experience, from that of the administrator to that of the patient.

Computer-Controlled Local Anesthetic Delivery (C-CLAD)

In 1997, an innovative dental local anesthetic delivery system was introduced [50]. Originally called The Wand (later renamed The CompuDent/Wand; Milestone Scientific, Inc., Livingston, NJ) it represented the first computer-controlled local anesthetic delivery (C-CLAD) system. C-CLAD devices provide clinicians with the ability to precisely control the rate of delivery of the local anesthetic solution, an important factor determining patient comfort during injection [51]. The most recent iteration of C-CLAD, The STA-Wand (Fig. 21.22) incorporates dynamic pressure-sensing (DPS) technology that provides visual and audible in-tissue pressure feedback that helps to (1) identify tissue types for the health care provider, (2) show when certain types of tissue have been penetrated, and (3) ensure that injection of drugs occurs at the precise targeted location. Ghelber and coworkers were the first to publish clinical data related to a medical application for this innovative technology [52]. C-CLAD enables the dentist to administer more comfortable injections to patients with a greater rate of success.

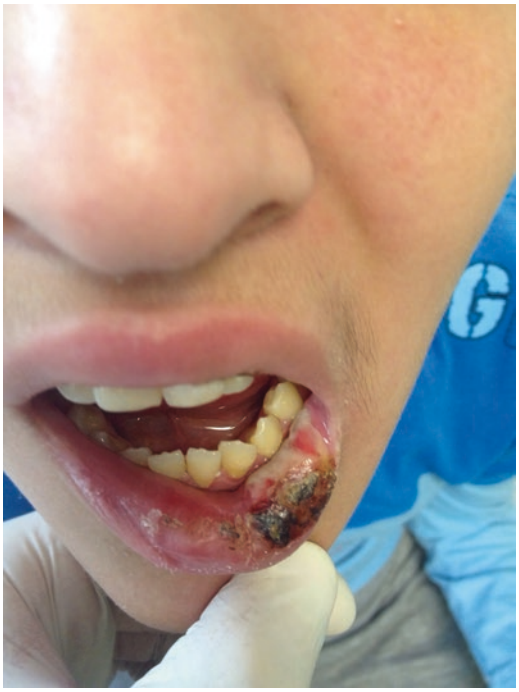

Fig. 21.23 Self-inflicted soft tissue injury

Table 21.3 Incidence of self-inflicted soft tissue injury following dental injection, by age

Age	% with soft trauma
<4 years	18 %
<4–7 years	16 %
<8–11 years	13 %
12+	7 %

College C, Feigal R, Wandera A, Strange M. Bilateral versus unilateral mandibular block anesthesia in a pediatric population. *Pediatr Dent.* 22(6):453–457, 2000.

Phentolamine Mesylate: Reversal of Local Anesthesia

Epinephrine is commonly added to local anesthetic solutions to increase both the depth and duration of anesthesia as well as decreasing the blood level of the anesthetic drug, enhancing safety. Treatment time is increased, allowing most dental procedures to be completed comfortably. As anesthesia of the soft tissues (e.g., lips tongue) persists considerably longer than pulpal anesthesia, patients are discharged from the dental office with these tissues still anesthetized. Self-inflicted soft tissue injury can result when the patient bites or chews this insensitive tissue (see earlier—Local Complications) (Fig. 21.23). Self-inflicted injury to soft tissues, most commonly the lip or tongue, is more apt to be noted in younger children and in mentally disabled adult and pediatric patients [45, 53] (Table 21.3). Phentolamine is an

Table 21.4 Phentolamine mesylate-Indications

OraVerse
• Conservative dental treatment
• Nonsurgical periodontics (SRP)
• Pediatric dentistry
• Medically compromised patients:
e.g.: Diabetics
• Geriatric patients
• Special needs patients
• Postmandibular implants

α-adrenergic receptor antagonist approved for use by the U.S. Food and Drug Administration (FDA) in 1952. Approved uses of phentolamine currently include (1) diagnosis of pheochromocytoma, (2) treatment of hypertension in pheochromocytoma [54, 55], and (3) prevention of tissue necrosis after norepinephrine extravasation [56]. An early use of injectable phentolamine involved the management of impotence (erectile dysfunction) [57].

Phentolamine is a short-acting, competitive antagonist at peripheral α-adrenergic receptors. It antagonizes both α_1 and α_2 receptors, thus blocking the actions of the circulating catecholamine's epinephrine and norepinephrine. Phentolamine also stimulates β-adrenergic receptors in the heart and lungs. Clinical effects of phentolamine include peripheral vasodilatation and tachycardia. Vasodilatation results from both direct relaxation of vascular smooth muscle and α blockade [54].

Phentolamine was marketed in dental cartridges (1.8 mL) in the United States in February 2009 [58]. The dental formulation of phentolamine is approximately 1/30 the concentration used in medicine (0.17 mg/mL versus 5.0 mg/mL). The drug is injected at the conclusion of the traumatic dental procedure into the same site at which the local anesthetic was administered previously. Vasodilatation produced by phentolamine increases the rate at which the local anesthetic is removed from the nerve, entering into the cardiovascular system. Duration of residual soft tissue anesthesia is significantly reduced with minimal (nonsignificant) increase in the local anesthetic blood level [59]. Administration of phentolamine is indicated when there is no requirement for postoperative pain management (most dental treatment) and there is an increased likelihood of self-inflicted soft tissue injury (Table 21.4).

Buffered Local Anesthetics

Increasing the pH of a local anesthetic solution, from 3.5 (epinephrine-containing local anesthetic) to approximately 7.4 (1) increases the comfort of injection, (2) increases the speed of onset of anesthesia, and (3) increases the depth of anesthesia. Buffering has long been an integral part of local anesthetic administration in medicine [60, 61], but has only recently been introduced into dentistry [62]. In a clinical trial, the onset of pulpal anesthesia following inferior alveolar nerve block (with lidocaine with epinephrine 1:100,000, pH 3.5) was 6-min, 31-s versus 1-min, 51-s with a buffered solution (pH 7.4) [63].

Intranasal Local Anesthetic Mist

Trypanophobia, fear of needles, is quite common among dental patients. Indeed, syncope is the most common medical emergency encountered in dental offices (50.3 %), most often occurring during the administration of local anesthesia (54.9 %) [64]. FDA approved in June 2016, an intranasal local anesthetic mist Kovanaze) has been developed that, sprayed into both nares, provides pulpal anesthesia to ten maxillary teeth (incisors, canine, and two premolars on either side) [6]. Using 3 % tetracaine with oxymetazoline, a 96 % success rate was obtained on these ten teeth compared with a 93 % success rate with injectable local anesthetic (lidocaine 2 % with 1:100,000 epinephrine).

Summary

Local anesthetics are the most used drugs in dentistry worldwide. In 2015 1.96 billion dental local anesthetic cartridges were manufactured world wide. Their discovery made available painless dental care to almost all patients (infected mandibular molars are often times extremely difficult to adequately anesthetize). Five highly effective drugs, in nine formulations, are available to dentists in North America. Research continues to develop more effective techniques and drugs.

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Local and Regional Anesthesia in the Emergency Room

22

Andrew A. Herring

Key Points

- Regional anesthesia is being increasingly adapted into emergency department practice as training and technological improvements (e.g., ultrasound) become more prevalent. The same precautions and considerations for patients receiving nerve blocks in the perioperative setting should be followed for patients in the emergency department.
- Occasionally, specialized regional procedures, such as "hematoma blocks," are used in emergency practice and are associated with rare but significant complications, for example, local anesthetic toxicity.
- Accurate documentation relating to the block, good communication among the health care team, and a readily available and appropriately stocked block cart are essential for safe regional anesthesia in the emergency department. Administration of the block should be done as close to the time of injury as possible.
- Choosing the appropriate local anesthetic can help avoid complications of prolonged block, premature block resolution, and systemic toxicity.
- Intoxicated patients present various challenges to performance of regional anesthesia in an emergency setting; alternative or modified measures (e.g., sedation or delaying the block) may have to be undertaken if the patient is not deemed competent to tolerate a nerve block.

A.A. Herring, MD (✉)
Emergency Department, Highland Hospital–Alameda Health System, Oakland, CA, USA

Department of Emergency Medicine, University of California, San Francisco, San Francisco, CA, USA
e-mail: andrew.a.herring@gmail.com

Introduction

Emergency physicians are expanding access to the benefits of regional anesthesia for acute trauma and minor surgical procedures beyond the preoperative setting with innovative application of peripheral nerve blocks to the myriad injuries and procedures in modern emergency practice [1–7]. As emergency department clinicians adopt the use of regional anesthesia, required safety can be maintained to the highest standards with proper training and equipment. Ultrasound guidance has become the standard of care in emergency medicine for most procedures including peripheral nerve blocks. This chapter will discuss the special considerations for safety while practicing regional anesthesia in the emergency department.

In regards to the major potential complications of regional anesthesia, namely, nerve injury, local anesthetic toxicity, and delayed diagnosis of compartment syndrome, there are no existing reports of serious complication from emergency department regional anesthesia [8]. That no reports exist should not be taken to suggest they have definitively not occurred or that due vigilance is not warranted. The discussion that follows should be understood as complementary to the fundamentals of safe regional anesthesia practice discussed in detail elsewhere in this text.

Scope of Regional Anesthesia Practice in the Emergency Department

In day-to-day practice, regional anesthesia in the emergency department is typically used for procedural anesthesia, such as setting fractures, reducing dislocations, abscess incision and drainage, and injury analgesia, such as for hip fractures or severe burns [6, 9, 10]. While peripheral nerve blocks have long been integral to emergency practice, emergency medicine's early adoption of point-of-care ultrasound led to a rapid application of ultrasound-guided regional anesthesia to emergency department clinical scenarios [11]. The range of regional anes-

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_22

Fig. 22.1 Organization of Emergency Department Regional anesthesia Panel A. (1) *Acute pain service/anesthesiologist*. This is an obvious partner with emergency clinicians. There are few scenarios where the anesthesiology service has the capacity to cover the ED in a timely manner for unforeseen acute injuries at all hours. To realize the goal of a seamless continuum of optimal care, collaboration and partnership is essential. (2) *Nursing, pharmacy, and logistical support*. Collaborative training and protocol development facilitates efficiency and safety. Important areas for nursing education and training include indications for regional anesthesia, recognition and treatment of local anesthetic toxicity, compartment syndrome evaluation, and postblock care. Crucial pharmacy issues include maintaining availability of various local anesthetic agents, establishment of guidelines for multimodal analgesia, and maintaining lipid rescue capacity [25]. A well-stocked area with appropriate blocks needles and equipment helps promote safety and efficiency. Nursing can be a valuable partner to develop a system quality assurance and follow up. (3) *Trauma/general surgeon*. Blocks are best used as part of multimodal analgesic bundle. The concept of early use of blocks in the trauma may be new to some surgeons. Development of ED trauma pain protocols that integrate regional anesthesia is helpful [35]. (4) *Ultrasound machine*. A modern, well-maintained, appropriately cleaned machine with linear and curved array transducers should be readily available for rapid use at the bedside. (5) *Patient selection*. Blocks should be matched to injury, contraindications excluded, and a collaborative plan for integration of the block into the longitudinal plan of care made before any block is placed. Patient, provider, and machine should be ergonomically positioned with an unobstructed line of site. (6) *Documentation*. The undifferentiated emergency patient may have numerous consultant exams. Delaying blocks for consultant exams should be avoided by establishing a consensus for preblock extremity and neurologic exam that is sufficient, comprehensive, and clear so that all involved consultants can trust in it. The time of block should be marked on the extremity with marker pen to avoid later confusion in regards to neurologic deficits. Thorough documentation of block details should be available to all participating providers

thetic techniques performed by emergency physicians includes very simple, low-risk techniques such as digital blocks to advanced techniques such as paravertebral blocks and placement of perineural catheters [5, 12]. However, like anesthesiologists in the preoperative setting, there is currently significant variation in the degree to which individual emergency department physicians apply regional anesthetic techniques to their practice. Neuraxial anesthesia such as epidural and spinal blocks is not typically part of emergency practice. Figures 22.1 and 22.2 provide an illustration of optimal organization and layout of a dedicated emergency department regional anesthesia area.

Fracture Hematoma Blocks

Direct infiltration of the periosteum at the site of an acute bone fracture is referred to as a "hematoma block." Currently, hematoma blocks are likely the most common form of regional anesthesia for long bone fractures in the emergency department. This technique is most commonly used by orthopedists and emergency clinicians for distal radius fracture analgesia [13, 14]. The hematoma block can be placed by palpation of the fracture site or ultrasound can be used to directly visualize the fracture. Less commonly, hematoma blocks can be applied to a variety of acute fractures including, humerus, clavicle, and femur fractures [15–18].

Overall, several investigations of distal radius fracture hematoma blocks have found good analgesic outcomes without any significant complications, suggesting this is a safe technique [14, 15, 19, 20]. However, the only reported cases of local anesthetic toxicity in the emergency department setting have occurred with hematoma blocks [21–23]. Of note, in both cases, a seizure occurred after injection of subtoxic doses of lidocaine into a distal radius fracture hematoma. The first case involved a 40 kg, 94-year-old

Fig. 22.2 Organization of Emergency Department Regional anesthesia Panel B. (7) *Orthopedist*. Close partner in evaluating for compartment syndrome and neurologic injury. Collaborative research, training, journal clubs, and protocols promote effective integration of emergency and orthopedic pain management. (8) *Monitoring*. Local anesthetic toxicity risk can be lessened with meticulous ultrasound-guided technique, use of the smallest possible quantity, and use of less cardiotoxic agents such as 2-chloroprocaine and lidocaine. Bupivacaine holds the greatest risk of toxicity and should be used only in settings adequately prepared to identify and treat LAST. Continuous cardiopulmonary monitoring is recommended for all bocks. (9) *Informed consent*. ED nerve blocks are only performed on awake patients able to comprehend the risks and benefits. (10) *Preparation for complications*. Any ED performing regional blocks should be prepared to rapidly initiate lipid rescue without delay in cases of LAST. Standard resuscitation equipment should be at hand. (11) *Emergency physician*. Blocks should only be performed by physicians adequately trained to execute the blocks safely. Training pathways begin with simulator and cadaver models and progress to supervised clinical practice, culminating with independent practice and skill maintenance

woman who received an injection of 10 mL of 2 % lidocaine (200 mg or 5 mg/kg) into the fracture site. She experienced a tonic clonic seizure immediately after injection that lasted for 2 min, resolving spontaneously with no intervention or further complication. The second case, reported by Dezfuli et al. involved a 65 kg 88-year-old woman also with a distal radius fracture who received a hematoma block with a 20 mL mixture of 1 % lidocaine (100 mg) and 0.25 % bupivacaine (25 mg) both without epinephrine [21]. Immediately after injection the patient became unresponsive and was observed to have tonic clonic jerks. The episode lasted for 5 min and resolved spontaneously without intervention or further complication.

There is only limited data on the uptake of local anesthetic after hematoma block into the systemic circulation. Quinton et al. evaluated arterial lidocaine concentrations among nine patients undergoing hematoma blocks for distal radius fracture analgesia with 1 % and 2 % lidocaine [23]. Among the patients blocked with 2 % lidocaine, the mean peak level of arterial lidocaine was 2.6 μg/mL which is similar to serum lidocaine levels after brachial plexus blockade. Patients blocked with 1 % lidocaine had significantly lower mean peak concentration of 0.85 μg/mL. Peak levels occurred 10–15 min after injection. Use of relatively dilute lidocaine (1 %) and avoidance of more potent local anesthetics, such as bupivacaine, may be a practical safety measure for routine practice.

Finally, hematoma blocks do involve entry into a sterile anatomic space and can rarely introduce infection. Bassu et al. reported a case of osteomyelitis following a hematoma block for distal radius fracture reduction despite the use of sterile precautions [24]. Contaminated skin, open fractures, immune compromise may pose additional risks for infection and may not be appropriate for a hematoma block.

Promoting Regional Anesthesia Safety and Efficiency with an Emergency Department Block Cart

A dedicated block cart is a convenient and effective way to create space to organize practical materials related to emergency regional anesthesia, such organization promotes an organized, consistent practice to accepted standards of safety [25] (Fig. 22.3). Block cart contents may include:

- Reference materials and textbooks on regional anesthesia.
- Phantoms for practicing ultrasound guidance.

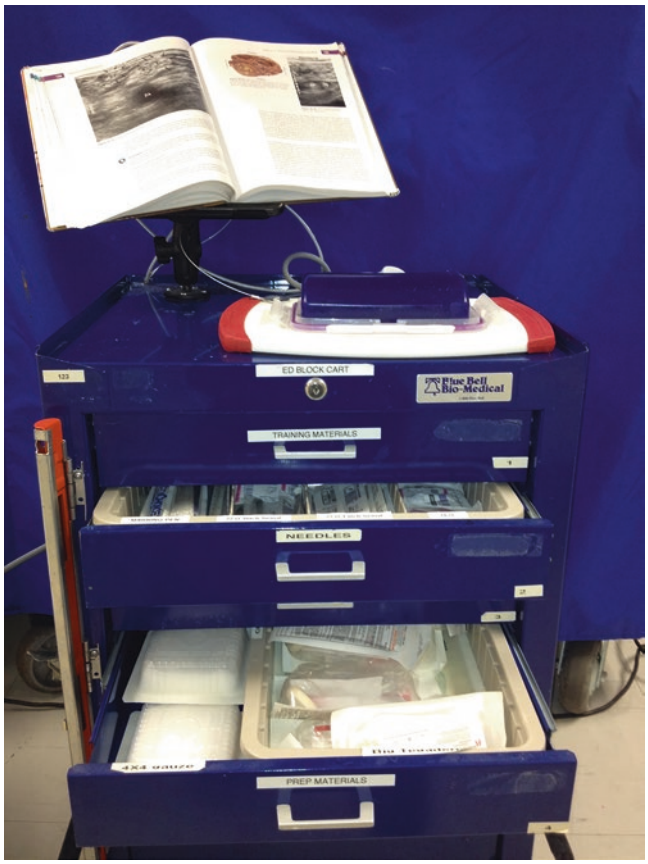

Fig. 22.3 Emergency department block cart. The emergency department block cart can serve multiple functions to promote safety and reduce potential complications. Educational and simulation materials for practice and continuous learning support staff to maintain and advance skills. Convenient location of all the necessary supplies and documentation sheets promotes efficiency and enhances provider adoption of best practices

- Specific, procedure related, protocols, checklist, and guidelines.
- Block-specific equipment including:
- Materials to ensure sterility such as drapes, gloves, probe covers, sterile gel, skin cleansers.
- Block needles of varying lengths.
- Extension tubing.
- Syringes.
- Local anesthetics and intralipid.
- Resuscitation equipment.

Emergency Department Regional Anesthesia Documentation

Clear and comprehensive documentation assures that all providers caring for a patient understand what block was done, when it was done, and what type of local anesthetic was used. This understanding will guide appropriate safety precautions to prevent adverse block-related events such as falls from attempting to ambulate with a block or compression necrosis to an insensate arm pressed against the railing of the hospital bed.

Without effective communication and documentation emergency nerve blocks can cause potentially dangerous confusion around possible neurologic injuries. If a clinician renders a limb insensate, but a clinical team member is not aware the block was placed, it can trigger distracting, and potentially harmful confusion. Effective communication and documentation is particularly important for the emergency trauma patient who may have multiple consulting services and an evolving set of injuries. Without proper communication and documentation, the loss of sensory and motor function could be mistakenly considered a new focal neurological deficit triggering evaluation for cord injury or stroke.

Strategies for Emergency Department Communication and Documentation

Verbally communicate with relevant consultants and the admitting clinical team prior to and after block placement so that they are aware of:

- The time the block was placed.
- The expected sensory and motor deficit.
- The medication used and the expected range of block duration.
- Block care precautions such as maintaining nonambulatory status or protection of blocked arm with a sling.
- Any monitoring concerns for potential compartment syndrome.
- Any procedural complications.

Appropriate Local Anesthetic Selection

Appropriate choice of a local anesthetic (Table 22.1) can improve safety and help prevent several complications [26, 27] including

- Prolonged block after clinical need for anesthesia has passed.
- Premature resolution of the block.
- Local anesthetic toxicity.

Notably, concern for ischemic complications in distal extremities due to epinephrine-containing local anesthetics has been debunked (Textbox 1).

Textbox 1: Myth Debunked: Lidocaine with Epinephrine is Safe for Anesthesia of Fingers, Nose, Penis, and Toes.

It was once a common teaching that avoiding the use of lidocaine with epinephrine for anesthetizing the distal appendages—fingers, nose, penis, and toes—should be avoided due to risk of ischemic necrosis. This concern

Table 22.1 Selection of local anesthetics for emergency regional anesthesia

The Ultra-short & ultra-safe procedural block: 3 % 2-Chloroprocaine *Maximum dose = 800–1000 mg (20-30 mL of the 3 % solution)*
Comments 3 % 2-Chloroprocaine is used for ultra-short blocks in the 60–90 min range. This is perfect for reductions or procedures where you would like a brief block. As an ester rapidly metabolized in the blood (<60 s half-life), the risk of toxicity is very low. This low toxicity allows safe use of a high concentration (3 %) that likely contributes to the fast onset of the block Use this med when you as the ED provider are in control of your time and the procedure. It really does wash out quickly, which is great if you completed the procedure, not so great if it wears off before you even get started!!! ***Example**: 20 ml 3 % 2-Chloroprocaine interscalene brachial plexus block for shoulder reduction*
Procedural block where 2–3 h of surgical anesthesia is needed: 1.5 % Mepivacaine *Maximum dose = 5-6 mg/kg (20 mL 1.5 % solution)*
Comments Intermediate potency amide perfect for when a several hour window of surgical level anesthesia is needed. Fast onset with 2–3 h of dense surgical anesthesia. Consultants can be unexpectedly delayed and it is very, very disappointing to have a block wear off just as the procedure is starting. Mepivacaine gives dense block and a nice window for this scenario. Mepivacaine does not have a strong vasodilatory affect and is typically used without epinephrine ***Example**: 20 mL 1.5 % Mepivacaine infraclavicular brachial plexus block for distal radius fracture reduction and splinting*
The long block, e.g., hip fracture: 0.5 % Ropivacaine *Maximum dose = 3 mg/kg (no more than 30 mL 1.0 % solution or 300 mg total)*
Ropivacaine is lipophilic amide structurally similar to bupivacaine. Based on animal studies that suggest that ropivacaine is less arrhythmogenic and resuscitation in case of overdose more successful, ropivacaine is generally considered a safer alternative to bupivacaine. It remains a powerful local anesthetic that should be used with caution. Clinicians using ropivacaine should know how to recognize and treat LAST and intralipid should be at hand ***Example**: 40 ml of 0.5 % ropivacaine for hip fracture analgesia*

dates back to reported cases of gangrene following the use of anesthetic with epinephrine from the late 1900s. Subsequently, several large studies have established the safety of local anesthesia with epinephrine for distal extremities and the penis.

Avoiding a Prolonged Block

Many emergency procedures require a brief period of surgical anesthesia. Using a long-acting local anesthetic such as bupivacaine, will needlessly expose the patient to the risks associated with an insensate extremity, as well as delay identification of any procedure-related nerve injury. For brief painful procedures without need for prolonged analgesia such as a shoulder dislocation reduction, a short-acting local anesthetic such as 2-chloroprocaine is ideal [11].

Avoiding a Premature Resolution of the Block

In the emergency department, procedures may be performed by consultants who may arrive at the bedside to perform the needed procedure according to an unpredictable timeline as they juggle various clinical duties. Placement of a block that then wears off too early is obviously not desired as it exposes the patient to the risks of the nerve block without benefit. In this scenario, such as a large abscess in need of surgical drainage, an intermediate-acting local anesthetic with a 2–3 h window of anesthesia, like 2 % lidocaine or 1.5 % mepivacaine, is ideal [27].

For fractures, such as a hip fracture, where prolonged analgesia is desired, use of relatively dilute, long-acting local anesthetic such as 0.5 % ropivacaine or 0.25 % bupivacaine is an acceptable option. Perineural catheters offer more flexibility to adjust local anesthetic concentration, flow rate, and bolus volume to achieve optimal analgesia [5, 28].

Avoiding Local Anesthetic Toxicity

Emergency clinicians are at times asked to perform under crisis conditions, where neither ideal procedural equipment nor preparation time is practically available. In this situation, harm may be reduced by avoiding the more potent local anesthetics such as bupivacaine and ropivacaine. Short-acting local anesthetics, such as lidocaine or chloroprocaine, are far less toxic and almost never associated with serious cardiac complications [27, 29].

Reducing Risk of Nerve Injury with Appropriate Needle Selection

Most emergency departments are stocked with long bevel, cutting tip needles for vascular access and medium bevel Quincke tip needles for lumbar puncture (Fig. 22.4). Stocking dedicated, blunt tip regional block needles involves added

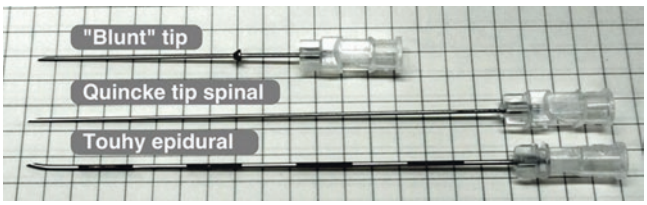

Fig. 22.4 Emergency department block needle options. Most emergency departments are stocked with Quincke-tipped spinal needles. Stocking short-bevel block needles and Tuohy needles is a first step for developing a safer practice environment for emergency regional anesthesia

cost and logistical effort. As ultrasound guidance has become standard practice, nerve stimulation is not commonly utilized by emergency clinicians.

Consensus expert opinion and limited animal data suggest a reduced risk of intraneural or intrafascicular injection with blunt-tipped needles. Additionally, the risk of intravascular injection and resulting systemic local anesthetic toxicity may be reduced by enhanced transmission of tissue resistance with a blunt-tipped needle. However, skillful and cautious technique involving clear visualization of the needle tip with ultrasound guidance and avoidance of needle-to-nerve contact is likely more important than needle tip angle [30–34].

Common emergency department peripheral nerve blocks performed on distal peripheral nerves such as the radial, median, and ulnar in the forearm or the posterior tibial nerve in the lower extremity, are likely safe with any needle type if used with caution and care. While definitive evidence is lacking, proximal blocks, in particular, brachial plexus blocks above the clavicle, are likely higher risk for complications that may be reduced by use of blunt-tipped needles.

Preexisting Neurologic Injury

Evaluation for any preexisting neurologic injury must be well documented. Aside from the concerns of causing neurologic harm via a "double crush" event, any new neurologic deficit is a relative contraindication to an emergency nerve block [30]. If a patient is found to have a neurologic deficit after injury, the course of that nerve injury is unpredictable and sorting out if an emergency physician placed a nerve block, had any contributory role to worsening outcome, will be very difficult to determine. In unusual circumstances, a block can be potentially placed in a patient with neurologic deficit, only with consensus of the entire care team and written patient consent.

Reducing Unnecessary Delay

For many conditions such as acute fractures and dislocations amenable to regional anesthesia, the placement of a block should occur as close to the time and place of injury as possible. In the complex process of initiating care for a traumatically injured patient, analgesia can be inadvertently deprioritized. Establishing a clinical consensus among all of the relevant clinicians that a given block is both indicated and safe to perform, can require multiple conversations and duplicated physical exams. The result is that, to the detriment of patient care, placement of emergency nerve blocks for traumatic injury can frequently be delayed for hours.

Strategies to Promote the Timely Utilization of Regional Anesthesia in the Emergency Department

- Develop a well-stocked regional anesthesia cart with needed supplies.
- Develop standing, multidisciplinary agreements that explain what common injuries (such as a hip fracture), can be blocked without delay (Fig. 22.5).
- Set goals for "Door-to-block time" for common injuries amenable to block, such as hip fractures and shoulder dislocations (Table 22.2).
- Develop an emergency department clinical culture that prioritizes analgesia.
- Develop collaborative nurse education and training programs that promote nurse physician partnership around emergency regional anesthesia.

Unique Patient Considerations in the Emergency Setting

Emergency Departments are potentially an ideal setting for regional anesthesia. Emergency providers are well trained and equipped to manage potential complications and facile with a variety of procedures from central venous catheter placement to emergent thoracotomy. However, certain realities of emergency practice deserve special attention to prevent error.

The Intoxicated Patient

Acute injuries or procedural needs commonly occur in emergency patients who are intoxicated. Intoxication often occurs in patients with comorbid psychiatric disease presenting as a complex clinical state that can range from an odd affect and slight disinhibition to agitated delirium and psychosis. The necessity of urgent intervention for such injuries as a fracture, dislocation, or abscess requires emergency clinicians to work with actively intoxicated patients and patients with decompensated psychiatric disease. This is an inherently unpredictable and potentially high-risk aspect of emergency care that is unavoidable.

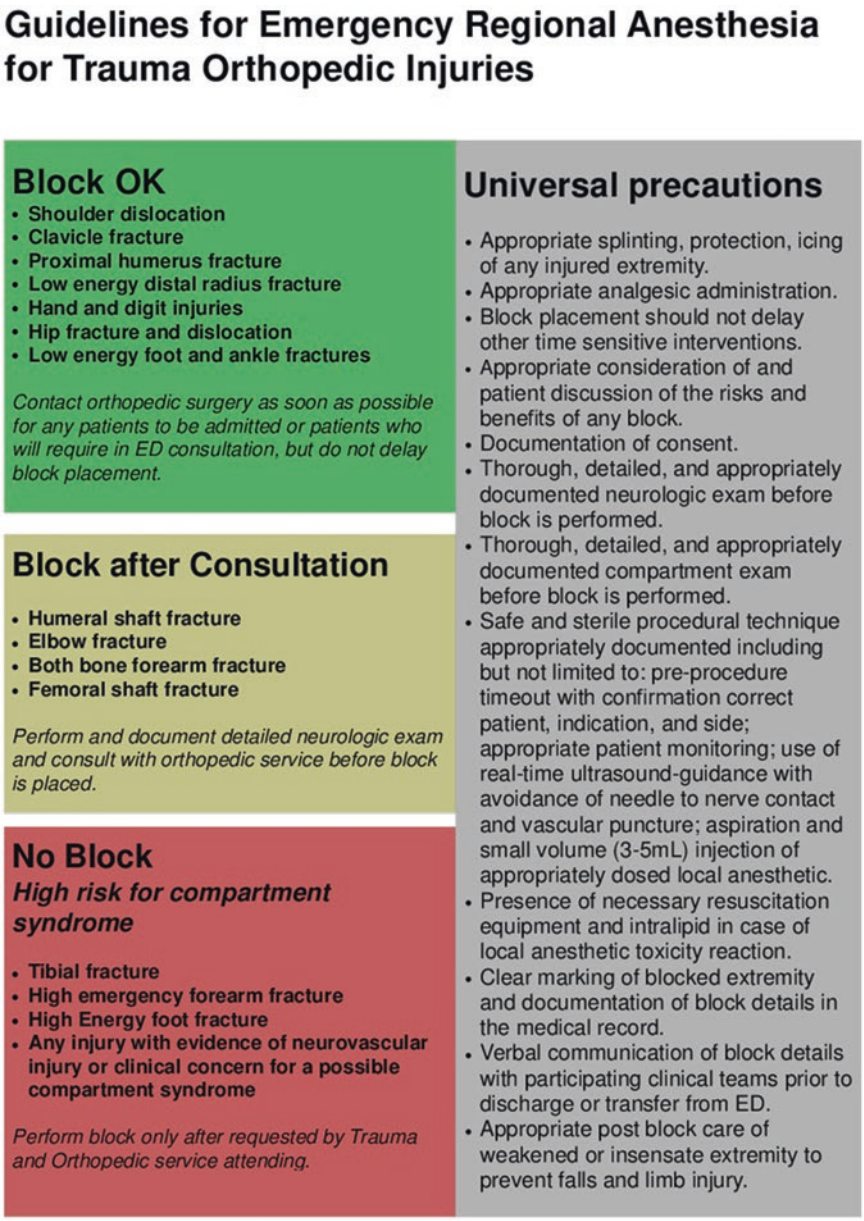

Fig. 22.5 Example collaborative guide between the emergency department and orthopedic surgery. Confusion in regards to what injuries are best cared for with an emergency department peripheral nerve block can lead to both delays in placing blocks for patients who would benefit from a block and overuse of regional anesthesia in other patients. Establishing a consensus guide helps clarify this confusion and promotes appropriate and collaborative use of emergency peripheral nerve blocks

Potential Risks Associated with Performing Regional Anesthesia in an Intoxicated Patient

- Lack of competence to provide informed consent.
- Inability to follow directions.
- Inability to be still during the procedure.
- Reduced level of consciousness and inability to perceive and communicate needle-to-nerve contact or intraneural injection.
- Inability to appropriately care for and protect a blocked extremity.
- Emotional distress resulting from experience of an insensate limb.

Reducing the Risks Associated with Intoxicated Patients

Consider Moderate or Deep Sedation as Alternative to Regional Anesthesia

Careful consideration of necessity balancing the risks and benefits of alternatives. Procedural sedation may be a superior option in some cases.

Table 22.2 Prioritizing door-to-block time

Goal
Promote optimal emergent pain management for hip and femoral fractures presenting to the ED
Inclusion criteria
Patients presenting to the ED with obvious deformity of the upper leg consistent with hip or femoral fracture confirmed either by bedside ultrasound or x-ray
Exclusion criteria[a]
1. Clinical features suggestive of acute compartment syndrome of the thigh. This includes tense or firm compartment on palpation, expanding hematoma of the thigh, or neurologic deficit in femoral distribution 2. Neurological deficit in the femoral distribution; specifically, loss of touch sensation on the anterior thigh 3. Any sign of vascular injury, coagulopathy, or hemodynamic instability
ED care
1. Immediate consultation with on-call orthopedist to discuss activation of femoral block protocol with goal of ultrasound-guided femoral block placed within 15 min of arrival to ED 2. Implementation of balanced analgesia including acetaminophen, Cox-2 NSAID, and titrated IV opioids in addition to nerve blockade 3. Appropriate positioning, splinting, ice, elevation of injured leg 4. Documented transfer of block-related care to inpatient service

[a]In addition to standard regional anesthesia contraindications, such as, inability to provide consent, allergy to local anesthetic, coagulopathy, pre-existing neurologic injury, or neuromuscular disease

Consider Judicious Use of Light Sedation

Light sedation in the acutely intoxicated patient is a clinical challenge that may require a titrated empiric approach to achieve an optimal state of calm and cooperation without excessive sedation. The most common option is a low dose of midazolam. This is effective in most cases. Alternatively, low-dose neuroleptic sedation with an agent such as haloperidol may be considered.

Consider Delaying Regional Anesthesia

Procedural interventions may be safely delayed in some patients. The patient can be allowed to metabolize any intoxicant and the procedure reconsidered at a later time.

The Patient in Acute Withdrawal

Acute withdrawal from alcohol, opioids, and sympathomimetics, is commonly encountered in emergency department patients who may benefit from regional anesthesia. In these patients achieving a calm, cooperative mental state will require treatment of the withdrawal state.

Alcohol Withdrawal Treatment Options

Benzodiazepines.

Barbiturates such as phenobarbital.

Adjunctive medications that may be considered.

Centrally acting alpha 2-adrenergic agonists such as clonidine or dexmedetomidine.

Anticonvulsants such as carbamazepine or gabapentin.

Opioid Withdrawal Treatment Options

Opioids.

Centrally acting alpha 2-adrenergic agonists such as clonidine.

Gabapentin.

Gentle use of antipsychotics such as haloperidol.

Sympathomimetic Treatment Options

Benzodiazepines.

Gentle use of antipsychotics such as haloperidol.

Summary

The potential complications of emergency department regional anesthesia include the universal concerns for risk of block-related infection, nerve injury, and local anesthetic toxicity, or delay to diagnosis of compartment syndrome. Additionally, the emergency department presents distinct challenges to maintain safety including, communication and care handoffs, working with intoxicated patients, and organization of appropriate peripheral nerve block supplies.

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Recognizing and Mitigating Risk of Ophthalmic Regional Anesthesia

23

Brad Wakeman, Robert William Andrew Machuk, Rizwan Somani, Dean Y. Mah, and Ian M. MacDonald

Key Points

- With appropriate training and experience, regional anesthesia can be delivered safely and effectively to patients undergoing ophthalmologic procedures.
- Major complications of ophthalmologic regional anesthesia can be circumvented by avoiding deep penetration of the orbit, not inserting the needle tip 31 mm beyond the orbital rim during retrobulbar injection, and having the patient direct their eyes in primary gaze position during needle insertion and injection.
- Specific complications that may arise in conjunction with ophthalmologic regional anesthesia include hematoma, brainstem anesthesia, damage to the globe or optic nerve, strabismus, and unintended intra-arterial injection of local anesthetics.
- Topical anesthetics (local anesthetic drops) have become increasingly popular for cataract surgery; drawbacks include risk of corneal toxicity, short block duration, and inability to immobilize the globe and eyelid.
- Sub-Tenon's anesthesia is an alternative to blocks using peri- and retrobulbar injections. Although popular and considered overwhelmingly safe, the sub-Tenon's approach does carry risk of complications, including pain, chemosis, and subconjunctival hemorrhage.

B. Wakeman, BSc, OC(C) • R.W.A. Machuk, BSc, MHA, MD
R. Somani, MSc, MD, FRCSC, ABO • D.Y. Mah, MD, MSc, FRCSC • I.M. MacDonald, MD, CM, FCCMG, FRCSC, FCAHS (✉)
Department of Ophthalmology and Visual Sciences, University of Alberta, Edmonton, AB, Canada
e-mail: Brad.Wakeman@albertahealthservices.ca; rwa.machuk@gmail.com; rizsomani@me.com; dymah@ualberta.ca; macdonal@ualberta.ca

Introduction

For the anesthesiologist or the ophthalmic surgeon, a sound knowledge of orbital anatomy, ophthalmic physiology, and the pharmacology of anesthetic and ophthalmic drugs are prerequisites before creating regional ophthalmic anesthesia. Training in techniques obtained in clinical settings from either anesthesiologists or ophthalmologists with significant experience and knowledge in ophthalmic anesthesia will benefit those beginning this practice [1, 2]. Whereas regional anesthesia with a block is far less common now in ophthalmic surgery, the concepts and understanding of potential risks are still important to consider.

Optimal Management of Patients Undergoing Ophthalmic Regional Anesthesia

There are relative advantages to regional anesthesia versus general anesthesia, in terms of safety, efficacy, and patient comfort. The choice of regional anesthesia for ophthalmic surgery should consider the surgeon's and the patient's preference, the patient's age, and also anatomical considerations and comorbidities.

All patients require a thorough preoperative assessment, including a review of their medical history and a physical examination with open communication about risks and potential complications of the procedure. Each patient should provide a list of all current medications to ensure that essential therapy is continued through the perioperative period and to minimize the risk of drug interactions. Laboratory and radiologic investigations are ordered when indicated and appropriate to the management of the patient [3]. Many patients having ophthalmic surgery are elderly and many of them have significant comorbidities including common diseases such as hypertension, coronary artery disease, chronic

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_23

obstructive pulmonary disease, diabetes, and obesity. Every effort must be made to have patients in the best possible medical condition before surgery. Most ophthalmic surgery is performed electively; therefore, there is ample opportunity to optimize the management of the patient's medical condition in advance of surgery.

In the modern operating suite, a culture promoting quality of care and patient safety has emerged to mitigate the risk of surgery and anesthesia. Wrong-sided surgery unfortunately continues to occur, and surgery under regional ophthalmic anesthesia is not exempt [4]. A safe surgery checklist actively engaging the patient has become an important norm in most centers and can be tailored to high-volume ophthalmic surgery. The use of two patient identifiers, asking the patient directly what is your name and date of birth is an important step, as the anesthesiologist commonly sees the patient for the first time at surgery.

The monitoring requirements for ophthalmic anesthesia/surgery, in the awake patient, are no different than those required for procedures being performed under general anesthesia [5]. If sedation is required, it should be prescribed judiciously and in small increments so that the patient will be comfortable yet remain alert, calm, and cooperative. The advantages of regional anesthesia can be quickly negated with excessive use of sedation [6]. A multicenter study confirmed that intravenous anesthetic agents administered to reduce pain and anxiety were associated with an increased incidence of side effects and adverse medical events [7]. Regional anesthesia for intraocular surgery aims to provide analgesia and motor blockade to minimize ocular movement; incomplete regional anesthesia is best managed with block supplementation before proceeding with surgery.

The following case is an example of how the dynamic use of various approaches in ophthalmic anesthesia can gain patient cooperation and achieve an excellent surgical outcome for a medically high-risk patient.

Case 1: A 50-year-old diabetic suffered a calamitous event with a vascular stroke and a third nerve palsy. His cognitive function was poor. He suffered from severe sleep apnea and was overweight. After careful preoperative assessment in a preadmission clinic, surgical repair of his horizontal strabismus was corrected under general anesthesia. He was admitted to hospital after surgery and monitored overnight. A residual vertical deviation from the third nerve palsy necessitated a second surgery months later. This was accomplished with topical anesthesia and intravenous sedation. Postoperative adjustment using topical anesthesia was performed while the patient was awake and alert. The patient could then perceive if double vision was present and that could be resolved with the careful placement of the vertically acting inferior rectus tendon.

Complications of Ophthalmic Regional Anesthesia

Needle advancement within the confines of the orbit is essentially a blind procedure and has the potential for serious complications. The Atkinson "up and in" globe positioning has been discredited [8]. Unsold and colleagues in 1981 revealed the danger of the elevated and adducted globe [9]. This position places the optic nerve closer to the advancing needle. They demonstrated using computed tomography studies in the fresh cadaver that with the globe in primary gaze, looking straight ahead, the optic nerve is less vulnerable. Similarly, as demonstrated by magnetic resonance imaging in a normal subject, with the globe elevated and adducted, the optic nerve would be brought closer to the needle track with the risk of optic nerve injury [10].

For the purposes of this chapter, we will define retrobulbar as behind the globe and peribulbar as around the globe but by inference, not behind the globe. Some authors refer to intraconal injection, a retrobulbar block that is within the muscle cone made up of the extraocular muscles, within which are the optic nerve, the nerves to the extraocular muscles, and the vascular supply to the nerve. Extraconal would lie outside the cone. Avoidance of deep penetration of the orbit with any technique is advisable to prevent serious block complications. The needle length introduced beyond the orbital rim for retrobulbar injection should not exceed 31 mm to assuredly avoid damage to the optic nerve in all patients [11]. Many serious complications are avoided by having patients direct their eyes in primary gaze position during needle placement and subsequent injection.

Hemorrhage

In a Cochrane Review, retrobulbar hemorrhage was noted only once among 1438 subjects in six trials comparing peribulbar with retrobulbar anesthesia for cataract surgery [12]. One could conclude that neither technique is less likely to result in a retrobulbar hemorrhage. The patient should be monitored immediately after the needle is withdrawn for any indication of hemorrhage. Signs of severe hemorrhage are rapid and taut orbital swelling, marked proptosis with limitation of ocular movement, and ecchymosis of the lids and conjunctivae. Serious impairment of the vascular supply to the eye may result from retinal vascular occlusion. The ophthalmic surgeon will be able to determine by fundus examination if there is occlusion of the central retina vessels at the optic nerve, warranting immediate intervention with lateral canthotomy to relieve orbital pressure [13].

Brainstem Anesthesia

Brainstem anesthesia is a form of central nervous system (CNS) toxicity and was reported to occur in 1 in 350–500 intraconal injections [14]. Brainstem anesthesia is not caused by increasing levels of local anesthetics in the systemic circulation (including CNS) but by direct spread of local anesthetic to the brainstem from the orbit, along submeningeal pathways. In the absence of direct vascular injection, the usual doses of local anesthetics used for eye surgery do not result in plasma levels of local anesthetic that could result in systemic toxicity [15].

Typically, the patient first describes symptoms within 2 min of retrobulbar injection. The zenith is reached at 10–20 min and resolves over 2–3 h. As this potential complication could occur on any occasion that an orbital block is performed, the patient should not be draped for surgery until 15 min have elapsed after completion of the block, otherwise identification and corrective action may be dangerously delayed. Ophthalmic regional anesthesia should not be performed in any location unless all the necessary monitoring and resuscitation equipment is immediately available [13].

Brainstem anesthesia may produce initial signs that vary from agitation and mild confusion to unconsciousness with apnea and marked cardiovascular instability [14]. Other signs may include marked shivering [16], or convulsions [17], and multiple cranial nerve palsies (3,4,6,9,10,12, including the optic nerve with contralateral amaurosis) [18–20] and dysarthria [21]. Treatment is primarily supportive: ventilation with oxygen, intravenous fluid therapy, and pharmacologic circulatory support as appropriate, dictated by close monitoring of the vital signs [1].

Globe Penetration and Perforation

Penetration of the globe refers to an object entering the globe while perforation refers to an entry and exit of the globe. Ocular penetration or perforation by a retrobulbar needle may result, particularly in a myopic patient with a longer than average axial length of the globe. Extra care must then be taken to reduce the risk of globe injury in those patients with significant myopia: patients presenting for repair of a retinal detachment or with a history of refractive surgery such as laser in situ keratomileusis (LASIK). Precise axial length measurement of the eye is required for intraocular lens selection prior to cataract surgery. It is good practice to check this measurement before injection, if it is available. In a series of 20 eyes in which perforation had occurred during retrobulbar or peribulbar anesthesia, 45 % had axial lengths greater than 26 mm [22]. In patients with high myopia (axial length greater than 29 mm), Vohra and Good noted a higher incidence of staphyloma usually located inferior to the posterior pole of the globe and advocated a medial canthal blockade in these patients rather than an inferior temporal approach [23].

The use of blunt-tipped needles does not protect against penetration and perforation; 5 of 12 cases of ocular perforation reported by Grizzard and colleagues [24], and 7 of 23 cases of ocular penetration reported by Hay and colleagues were caused by blunt needles [25]. Blunt-tipped needles are painful for the patient and require sedation during insertion, whereas fine disposable needles cause much less discomfort and sedatives are less often required.

Although there are proponents of retrobulbar or peribulbar techniques, safe anesthesia can be accomplished using either method; likewise, serious complications can arise with either technique if performed incorrectly. One study by Loots and colleagues remarked on the poor level of akinesia (less than 50 %) in peribulbar blocks [26]. With this in mind, one might consider attempting blocks with small-volume injection at the apex of the orbit, but the risks of optic nerve damage and hemorrhage are too great, and this must be avoided. Needles should never be advanced beyond 31 mm as measured from the orbital rim [11], nor should a needle advancing from an inferior temporal entry be allowed to cross the midsagittal plane of the eye (Fig. 23.1). All needles used for intraconal and periconal insertion should be orientated tangentially to the globe with the bevel opening faced toward the globe [26, 27]. If a tangentially aligned needle contacts the sclera, globe penetration is less likely to occur than a needle approaching at a greater angle. Some practitioners favor a percutaneous approach from a more lateral inferior temporal entry point than frequently practiced, after preliminary local anesthesia of the skin (Fig. 23.2) [28]. By using a percutaneous entry, patients with narrow palpebral fissures, and those with excessive blinking, present less of a problem. All needles in the orbit are potentially hazardous in the wrong hands; careful supervision and training in technique have great relevance in the avoidance of serious complications [2]. Techniques requiring multiple needle placements are associated with an increased incidence of complications when compared with a single or reduced number of injections.

The diagnosis of perforation may be suspected with hypotony, a poor red reflex, a patient complaint of poor vision, or flashes of light; however, more than 50 % of iatrogenic needle penetrations of the globe go unrecognized at the time of their occurrence [22]. The patient may report marked pain and the intraocular pressure will be high if the anesthetic is inadvertently injected intraocularly [29]. Ocular rupture may occur rarely with regional anesthesia as a result of intraocular injection with catastrophic consequences [30].

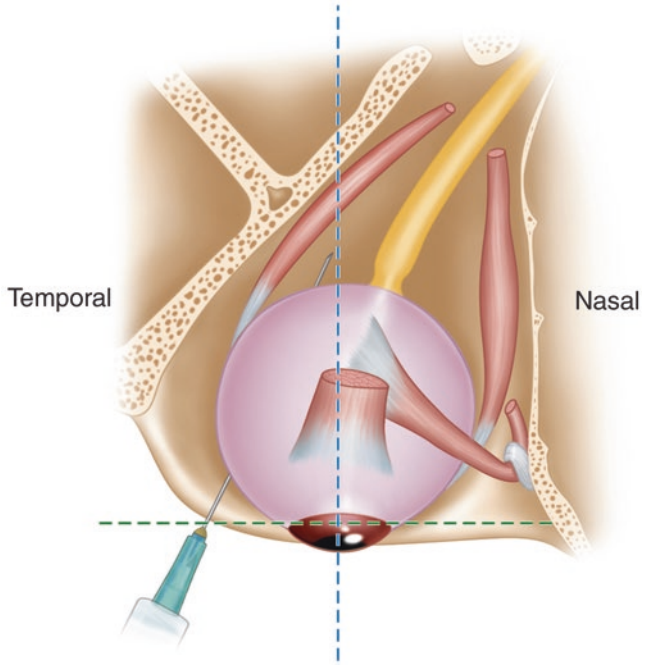

Fig. 23.1 Right globe in primary gaze, top view. Green dashed line indicates the plane of the iris; blue dashed line indicates the mid-sagittal plane of the eye and the visual axis through the center of the pupil. The optic nerve lies on the nasal side of the mid-sagittal plane of the eye. Note how the temporal orbit rim is set back from the rest of the orbit rim at or about the globe equator, making for easy needle access to the retrobulbar compartment. A 31-mm needle is advanced beyond the equator of the globe and then directed toward an imaginary point behind the macula, being careful not to cross the mid-sagittal plane of the eye. In a globe with normal axial length as illustrated here, when the needle/hub junction has reached the plane of the iris, the tip of the needle lies 5–7 mm beyond the posterior surface of the globe

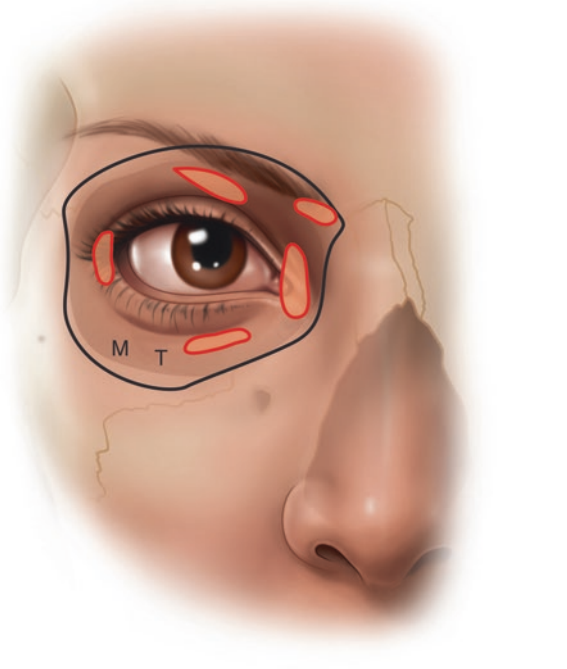

Fig. 23.2 Photo of a patient with a superimposed template of the orbital walls and extraocular muscles at the level of the junction of the optic nerve and the posterior pole of the eye. The traditional inferior block injection site ("T") is just inside the orbit rim at the junction of the medial two-thirds and lateral third of the inferior orbital rim. A modified injection site ("M") is just inside the orbit rim at the junction of the inferior and lateral orbital rims. Injection at the modified site is best with a percutaneous approach, the entry point on the skin being 4–5 mm inferior to the lateral canthus

The initial management of potential/suspected globe perforation requires indirect ophthalmoscopy (fundus examination) by the ophthalmologist [31]. If perforation is identified, immediate referral to a retinal specialist is appropriate. Cases with minimal vitreous hemorrhage enabling a view of the retinal perforation site can be managed with laser photocoagulation or cryotherapy at the time of surgery if the site is outside the macula. If visualization of the fundus is not possible as a result of vitreous hemorrhage, the patient should be referred to a specialist for urgent examination and B-scan ultrasonography to rule out a retinal detachment [29, 31, 32].

Strabismus

Transient diplopia and ptosis is not uncommon for 24–48 h postoperatively when long-acting local anesthetics have been used in large volume for regional anesthesia. However, when this persists for days or weeks, or fails to recover, it may be evidence of toxic reaction within muscle, or damage to the support structures of the ocular motor apparatus. Despite a perfect surgical outcome, the patient will be bitterly disappointed by diplopia if the eyes become permanently misaligned.

Local anesthetics have been used to induce muscle necrosis in skeletal muscle regeneration studies [33–35]. Higher concentrations of local anesthetic agents are more likely to result in myotoxicity [34]. A common cause of prolonged muscle malfunction, whatever concentration has been used, is intramuscular injection [36]. Muscle necrosis, degeneration, and regeneration follow a typical sequence and time course (Table 23.1).

Case 2: A 76-year-old female underwent uncomplicated cataract surgery after a painful infero-temporal retrobulbar block. From the first day after surgery, she complained of vertical diplopia. At day six, her examination was consistent with left inferior rectus under action (inability of the left eye to look down) due to direct intramuscular anesthetic injection. With time there was resolution of the apparent left inferior rectus palsy but then reversal of the vertical diplopia secondary to progressive late fibrosis/contracture of the damaged left inferior rectus muscle (inability of left eye to look up) (Fig. 23.3).

Table 23.1 Time course of muscle degeneration and regeneration induced by aminoacyl local anesthetics

Minutes to hours	Muscle fiber swelling and increased eosinophilia
Day 1–3	Phagocytic degeneration of muscle fibers
Day 4	Myoblasts appear in remaining basal lamina of degenerated muscle fibers
Day 5	Myoblasts fuse to form myotubules (the beginning of sarcomeres) macrophages still present
Day 7	Myotubule maturation well underway, organized myofibrillar bundles, macrophage numbers decreasing

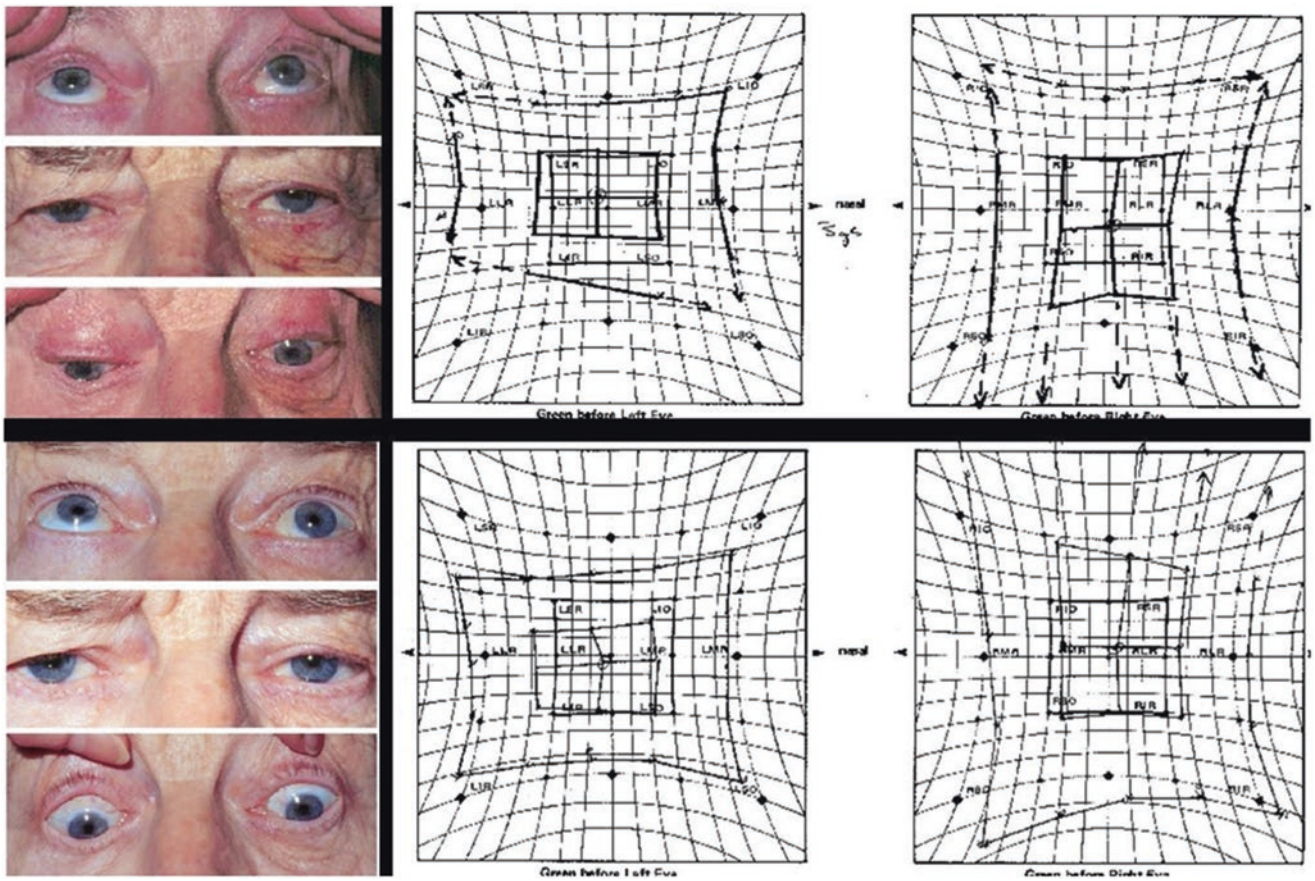

Fig. 23.3 *Top*: 6 days after surgery, photos and Hess chart show a left hypertropia with limitation of depression of the left eye. *Bottom*: 2 weeks after surgery, photos and Hess chart show reversal of strabismus to hypotropia of the left eye with restricted elevation

Once the angle of deviation of the eye was stable, she underwent strabismus surgery under general anesthesia with muscle adjustment under topical anesthesia immediately post op and regained a good functional area of single vision.

Etiologies of these muscle malfunctions include direct trauma with anesthetic myotoxicity [36–42], disruption of the LR/SR band which holds the lateral rectus in its anatomical position [43], surgical trauma, inappropriately placed antibiotic injection, and ischemic contracture of the Volkmann's type after trauma or hemorrhage [39]. It is imperative to have a good three-dimensional knowledge of the anatomy of the orbit and its contents to accurately place injections. A number of articles report damage to the inferior rectus muscle [36, 39, 41, 42], likely associated with the infero-lateral approach of the retrobulbar block and proximity of the muscle. Less frequently affected are the superior oblique [40], the inferior oblique [37], and the superior rectus muscles [38]; however, it should be recognized that any muscle is susceptible depending on needle placement. Extraocular muscles are more easily avoided by using an infero-temporal orbital entry point for the retrobulbar injection.

Effects on Ocular Circulation

After completion of regional anesthetic blocks, mechanical orbital decompression devices [44–47] are frequently used to promote ocular hypotony and reduce the vitreous volume [48], especially when larger volumes of orbital injectate have been used (as in periconal or peribulbar blocks). Because blood flow to the retina and optic nerve depends on the balance between the intraocular pressure and the mean local arterial blood pressure, it is possible for these devices to induce ischemia [49, 50].

In the presence of significant local arterial disease, orbital hemorrhage, or in patients with glaucoma, vascular occlusion may result [51]. Preexisting small vessel disease, as seen in diabetes mellitus, may increase the likelihood of this complication. The omission of epinephrine from the retrobulbar injectate may be prudent in these cases [25, 52]. The retrobulbar block may also tamponade the vessels within the optic nerve and/or the small vessels supplying the nerve itself either by the volume of drug injected or by causing intrasheath hemorrhage [53–55].

Optic Nerve Damage

The incidence of this complication, while rare, is unknown, as is the exact etiology. Most cases associated with cataract surgery are thought to be due to direct nerve injury or vascular occlusion (central retinal artery or vein) resulting in optic neuropathy. Management would include ocular examination and neuroimaging for confirmation. The administration of systemic steroid has been suggested but its effectiveness remains unknown [56].

Pupillary Anomalies

A permanently dilated pupil may be seen occasionally after intraocular surgery. The pupil fails to constrict with pilocarpine. The mechanism is thought to be related to trauma to the pupillary sphincter from the intraocular surgery itself [57, 58]; however, a case of damage to the ciliary ganglion within the muscle cone has been reported with regional anesthesia for strabismus surgery [59]. In cases of denervation due to ciliary ganglion damage, pupillary constriction in response to topical pilocarpine should be preserved.

Therapeutic Misadventures (Including Systemic Toxicity)

The incidence of systemic toxicity with local anesthetics is related to the total dose given, vascularity of the site of injection, drug used, speed of injection, and whether epinephrine has been used as an additive to delay systemic release. The amount of local anesthetic agent required to be effective in ophthalmic anesthesia is relatively small in comparison with regional anesthesia for most other types of surgery, and so, systemic toxicity is unlikely [15]. That being said, if given rapidly, unintentional intravenous injection of the total volume of local anesthetic required for an eye block may result in systemic toxicity to the CNS and myocardium. Aspirating before injection and injecting slowly reduces the likelihood of this complication. Inadvertent intra-arterial injection of local anesthetics with retrograde flow to the cerebral circulation may result in an acute grand mal seizure [60, 61].

Seventh Nerve Block Complications

An isolated facial nerve block is rarely necessary in modern ophthalmic practice. Complications associated with blocking the main trunk of the facial nerve at the base of the skull have been reported [62, 63]. In these cases, patients experienced difficulty swallowing and respiratory obstruction related to unilateral vagus, glossopharyngeal, and spinal accessory nerve blockade. For facial blockade at this site, experts suggest injecting no deeper than 12 mm and avoiding hyaluronidase in the injectate [63, 64]. Bilateral facial nerve block is not recommended [65].

Allergy

True allergy to local anesthetics is extremely rare [66]. Allergic reactions are almost exclusively confined to the ester-linked drugs (e.g., tetracaine or proparacaine as used in topical anesthesia). The breakdown product of the esters, para-aminobenzoic acid, is thought to trigger an allergic reaction in certain individuals. Reaction with preservatives, such as methylparabens, in multidose vials is possible; hence, it may be better to use preservative-free vials where a history of the problem exists. Hyaluronidase, an enzyme that enhances the spread of a local anesthetic agent, is sometimes added to the injection and can cause an allergic reaction, as in angioedema [67]. A myasthenia-like response to various agents including local anesthetics has been reported [68]. Well-documented cases of true allergy to amide agents (procaine, mepivacaine, and lidocaine) have been reported [69, 70].

Anticoagulants and Antiplatelet Therapy

A reduction or discontinuation of anticoagulant therapy for some days is common before nonophthalmic elective sur-

gery. Whereas this action may be appropriate for more major ophthalmic surgical procedures, such as orbital surgery, its advisability in cataract surgery has been questioned. No serious complications were observed in 26 eyes of patients on coumadin who underwent cataract surgery with an extracapsular technique requiring an anterior scleral incision and greater risk of bleeding [71]. Discontinuation of anticoagulant medication may result in thrombotic complications such as cerebral vascular accident, pulmonary embolism, and death. Hemorrhagic complications associated with continuance of anticoagulants, including retrobulbar hemorrhage, had no long-term effects on visual acuity [72]. This implies that the risk of stopping anticoagulants for this type of surgery is probably greater than any risk imposed by their continuance.

As most cataract surgery is performed with a clear corneal incision, the risk in this case is not related as much to surgery as to the choice of anesthesia, where retrobulbar hemorrhage might be possible if regional anesthesia was chosen over topical anesthesia. In a review of almost 20,000 cataract surgeries in nine centers in the USA and Canada, there was no evidence to suggest that patients who continued regular anticoagulation were at more risk of retrobulbar hemorrhage, nor was there evidence that patients who stopped anticoagulation were at increased risk of medical events [73]. At present the medical risks of altering or stopping the regimen of antiplatelet or anticoagulation medication outweigh the risks of regional anesthesia for cataract surgery. Further, there is no strong evidence to support the use of a blunt cannula in a sub-Tenon's approach over a sharp needle with a peribulbar block [74]. A consensus statement on the perioperative management of patients on antiplatelet therapy for coronary artery disease identified the potential risk of these agents in patients undergoing vitreo-retinal surgery (bleeding within a closed space) [75]. The management of these cases should be individualized and deferred to their medical team. Formal guidelines concur with the last statement as this applies to cases in which the ophthalmic surgery is more complex and the risk of bleeding is higher [76].

Alternative Methods of Ophthalmic Anesthesia

Ongoing reports of rare but serious complications of intraconal anesthesia stimulated editorials and reintroduced the concept of alternative nonakinetic methods of regional anesthesia for ophthalmic surgery [77, 78]. These fall into three groups: subconjunctival (perilimbal) [78–82], injection of local anesthetic by needle or cannula beneath Tenon's capsule [83–86], and solely topical corneo-conjunctival anesthesia [87–89]. With these methods, the surgeon encounters a varying limitation of ocular movement and lid closure, and sensitivity of intraocular contents, particularly the iris and ciliary muscle with solely topical anesthesia [78, 90]. A systematic search of the literature concluded that retrobulbar block provided better pain control than topical anesthesia [90]. Topical anesthesia is increasingly used for cataract surgeries and intravitreal injection of anti-VEGF agents for the treatment of age-related macular degeneration. Pain control did not appear to be superior with subconjunctival lidocaine injection or a lidocaine-soaked pledget [91].

Intravitreal and subconjunctival injections and sub-Tenon's infusions are best performed by an ophthalmologist due to the skill and familiarity required for safe ocular manipulation. The patient's ocular history is important to consider. Previous retinal surgery with scleral buckle may make sub-Tenon's injection impossible. Similarly, patients with cicatrizing conjunctival diseases (such as Stevens–Johnson syndrome) may not be good candidates for sub-Tenon's or subconjunctival injections. Extreme caution must be exercised if a patient has had a filtering procedure for glaucoma with a subconjunctival bleb to avoid bleb failure and preserve the conjunctiva for future procedures.

Summary and Current Practice of Anesthesia for Cataract Surgery

Topical anesthesia alone for standard cataract surgery has now been widely accepted as safe, efficacious, and cost effective. The advantages of topical anesthetic over injectable forms of anesthesia include the relative ease of application, elimination of patient pain and anxiety related to injection, avoidance of injection-related complications, and quicker postoperative visual recovery without diplopia or ptosis [92, 93].

Anesthetics which are commonly used include 2 % lidocaine gel, 0.5 % proparacaine, or 0.5 % tetracaine drops. Topical anesthesia is performed by placing local anesthetic directly on the patient's cornea and conjunctiva. Usually, lidocaine gel is placed within the inferior fornix, and the eyelid is taped closed by the anesthetist 10–15 min prior to draping. An additional sterile anesthetic drop can be given just prior to the actual start of surgery.

Topical anesthesia should not be considered in those with communication problems (deafness, language, comprehension), in younger patients more susceptible to pain, or those with more difficult or complicated cases anticipated to last more than 20–30 min. Drawbacks to topical anesthesia include the risk of corneal toxicity, the short-acting nature of the anesthesia and possible need for intraoperative supplementation, and the lack of globe and lid akinesia which can make even short routine surgery challenging [92].

Topical anesthesia may not provide the same level of pain control compared to retro- or peribulbar anesthesia, as anterior segment structures are not directly anesthetized [94, 95].

Patients may sense pressure changes or discomfort when the iris is touched. As such, intracameral injection of nonpreserved 1 % lidocaine is an effective and safe adjunct to reduce patient pain intraoperatively [96, 97].

Intravenous or oral sedation can be helpful in those patients who exhibit higher than normal levels of anxiety or unease. Although it may not be routinely beneficial [98, 99], in select patients, adjuvant sedation during topical anesthesia can decrease patient pain and anxiety, while improving patient operative satisfaction. It is imperative that blood pressure, heart and respiration rate, and pulse oximetry be properly monitored by trained personnel during sedation. A minimal dose of intravenous midazolam (0.5–1.0 mg) or oral diazepam (2.5–5.0 mg) is often adequate to avoid oversedation, allowing for both full patient cooperation during surgery and a smooth, uneventful postoperative recovery [100].

Sub-Tenon's Anesthesia

Sub-Tenon's anesthesia was introduced in the late 1990s as a safer alternative to the rare but sight-threatening complications of peribulbar and retrobulbar blocks [101]. An incision is made in the inferonasal conjunctiva, 7–10 mm from the limbus. This location is preferred as it avoids the typical sites of retina and anterior segment surgery. Using scissors, Tenon's capsule is carefully dissected posteriorly toward the inferonasal quadrant. A blunt curved cannula is then inserted through the opening in the conjunctiva and directed posteriorly. The local anesthetic mixture is directed toward the posterior globe.

This block has been rapidly adopted because of its simplicity and presumed safety. In the United Kingdom, a recent survey of anesthesiologists indicated that 87.8 % of respondents used this technique regularly in their practice [102]. Previously, sub-Tenon's block was either used to augment peribulbar and retrobulbar blocks or used primarily in patients at risk of bleeding. However, recent studies have proven sub-Tenon's blocks to provide excellent akinesia and anesthesia during surgery. In a recent case series of 6000 consecutive sub-Tenon's injections reported by Guise [103], 96 % of all blocks were rated by the surgeon as suitable for surgery.

Studies documenting patient pain with sub-Tenon's anesthesia rated this symptom as mild in 25 % of cases with moderate and severe pain only occurring in 5.4 % and 1.5 %, respectively [103]. This was subjectively described as a "stinging or burning" sensation or a "pressure" sensation when the sub-Tenon's space was being expanded [104]. Some guidelines have suggested that the most effective way to reduce pain is adequate local anesthetic and careful insertion of the cannula with slow infiltration of anesthetic solution [105].

Ophthalmologists and anesthesiologists consider sub-Tenon's blocks to be safe. Complications occur frequently, but are of limited clinical significance including pain, chemosis, and subconjunctival hemorrhage. Subconjunctival hemorrhage occurs through the dissection of the conjunctiva or through disruption of the small blood vessels when the cannula is introduced and the anesthetic infiltrated. Typically, the hemorrhage involves only one quadrant, but can potentially spread more circumferentially [106]. Previous studies have reported hemorrhage in 7.4 % to 100 % of cases [103, 105].

Chemosis typically indicates anterior spread of the anesthetic during injection or incorrect injection into the subconjunctival space [105]. This can be confined to the injection site or can move to other quadrants. The incidence of chemosis can be reduced with the use of a longer cannula and gentle side-to-side movement along with infiltration of lower volumes of anesthetic [107]. Typically, this is not an issue with retina and cataract surgery but may adversely affect glaucoma filtering surgery.

Although rare, major life- and sight-threatening complications include: brainstem anesthesia, globe perforation, retrobulbar hemorrhage, retinal ischemia, optic nerve damage, rectus muscle dysfunction, and orbital cellulitis. Signs of brainstem anesthesia are quite variable from drowsiness, confusion, loss of verbal ability, to more serious complications of cranial nerve palsy, convulsions, respiratory depression, and cardiac arrest. Two cases of brainstem anesthesia have been reported in the literature following sub-Tenon's anesthesia. The first case, reported by Ruschen, resulted in prolonged unresponsiveness to verbal commands and a reduced Glasgow Coma Scale for 3 h following uneventful sub-Tenon's block [108]. Cardiorespiratory depression did not occur and there were no focal neurological signs. Eventually, the patient made a full recovery without any persistent neurological sequelae. Quantock and Goswami reported another case in an 82-year-old woman who was blocked for cataract surgery [109]. One minute after performing the block the woman had a generalized tonic–clonic seizure and went into ventricular fibrillation. Cardiopulmonary resuscitation was not successful and the patient died; autopsy showed severe coronary artery disease.

Globe perforation has been reported in 3 cases; one was identified 5 weeks after surgery and the remaining two were known at the time of surgery. Of these two, the first case reported by Frieman and Friedberg occurred in a 40-year-old male with a previous scleral buckle who was undergoing a second rhegmatogenous retinal detachment repair [110]. Upon opening the conjunctiva, resistance was present, so sharp scissors were used to cut the tissue and release adhesions [110]. Upon advancing the scissors, the resistance dramatically decreased and the globe suddenly became soft. Indirect ophthalmoscopy identified a vitreous hemorrhage

with a small perforation. The second case, reported by Faure and colleagues, occurred in a patient with previous scleritis who was undergoing cataract surgery [111]. During surgery, a vitreous air bubble was noted after the placement of the intraocular lens. Vitrectomy confirmed the location of two retinal breaks with a localized retinal detachment in the infra-nasal quadrant.

Retrobulbar hemorrhage has been described in three cases between the initiation of the block and the start of the procedure [105, 112]. In each case, the cause was difficult to ascertain, although one patient was taking aspirin and clopidogrel [105]. Anatomical variation in the location of the temporal vortex vein in these patients may have been present or possibly the metal sub-Tenon's cannula was inserted too far posteriorly [105, 112]. Due to the limited number of published events, it is difficult to determine common characteristics that may prevent complications.

Optic neuropathy was reported in a single case after sub-Tenon's block [113]. The patient's initial visual acuity was 20/200 secondary to a significant nuclear sclerotic cataract and macular fibrosis. The eye had an axial length of 23.97 mm; a 23 mm Masket cannula was used with infiltration of 2 ml of 4 % lidocaine for cataract surgery. After cataract surgery, vision worsened to no light perception with an afferent pupillary defect. Postoperative fundus examination showed peripapillary hemorrhage. The damage was further confirmed with magnetic resonance imaging that showed increased T2 signal in the affected optic nerve. Kim and coauthors concluded that the 23 mm Masket, 22 mm Eagle, and 26 mm Visitec cannulas all have the potential to easily reach the optic nerve in a 24 mm globe if blunt dissection of the conjunctiva occurs 3–5 mm posterior to the limbus [113]. This indicates the need for proper selection of shorter cannulae that are unable to reach this aspect of the globe but still are capable of getting the anesthetic agent close to the optic nerve.

Diplopia is a known complication seen in patients after sub-Tenon's injection. In one series of 1080 patients receiving sub-Tenon's blocks for cataract surgery, three cases of rectus muscle restriction occurred [114]. In all cases of this series, there was immediate periorbital bruising and muscle paresis leading to muscle restriction over time. Direct trauma was thought to be the likely cause, although myotoxicity from the local agent could not be ruled out. Previous authors have shown that myotoxicty is more likely to occur if large volumes of anesthetic are injected [115]; this has been confirmed in animal models [33]. One other case series by Merino and coworkers described eight patients who had incomitant diplopia immediately after sub-Tenon's injection [116]. The inferior rectus was the most commonly affected muscle; overall strabismus surgery was required in four cases while the remainder was treated with botulinum toxin or prisms.

Orbital swelling can develop immediately or within the first few days after sub-Tenon's injection. Swelling is more commonly associated with sterile inflammation, but potentially vision-threatening episodes of infection have been reported. Kumar and colleagues reported three cases of sub-Tenon's anesthesia with a combination of 2 % lidocaine, 1:200000 epinephrine, and up to 300 IU/ml hyaluronidase [117]. These patients developed severe orbital swelling without pyrexia and had no evidence of systemic infection based on blood tests. They were treated with a combination of intravenous antibiotics and in certain cases with oral prednisone; all cases resolved without visual sequelae. The inflammatory reaction was thought to be due to the hyaluronidase. As a result, the authors reduced the concentration of hyaluronidase to 15 IU/ml for sub-Tenon's anesthesia. A case of endophthalmitis after sub-Tenon's anesthesia was reported by Lip and colleagues [118]. The patient, a 77-year-old female underwent uncomplicated cataract extraction. Two days later she developed proptosis, ocular pain with hand motion vision; orbital cellulitis with endophthalmitis was diagnosed due to *Streptococcus pneumoniae*. Despite maximal therapy, the patient developed phthisis bulbi with no light perception vision. In this case, the infection was thought to be related to the sub-Tenon's block, as all other infectious foci were ruled out.

Techniques to create ophthalmic anesthesia and akinesia continue to be refined. There is a place for all these techniques to enable the surgeon to perform surgery safely and provide the best outcome for the patient. Careful preoperative evaluation of the patient with a consideration of comorbidities, selecting the method of anesthesia, and counseling the patient as to what to expect are all necessary steps in the preparation of the patient for surgery. Finally, some flexibility needs to be considered on the day of surgery as the patient's condition and level of cooperation may change.

Acknowledgements This chapter is based largely on the previously published and valuable expert opinion of Robert C. (Roy) Hamilton, Gimbel Eye Centre, Alberta, now retired. The original Chapter has been extensively revised to account for changes in practice.

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Local Infiltration Analgesia for Orthopedic Joint Surgery

24

Sugantha Ganapathy, James L. Howard, and Rakesh V. Sondekoppam

Key Points

- Local infiltration analgesia with ropivacaine, ketorolac, and epinephrine provides excellent analgesia following total knee joint arthroplasty.
- Local infiltration analgesia following THA provides analgesic benefit in the early part of postoperative period but may not offer any additional benefits after the first 6 h, over and above what is provided by oral multimodal analgesia
- The motor sparing effect of LIA translates into better range of motion and early physiotherapy but does not correlate with hospital length of stay or decreased patient falls.
- Continuous catheter techniques for periarticular and intra-articular infusion offer analgesic benefits over placebo and single injections but at the same time increase the risk of infections.
- LIA techniques for arthroscopic surgeries may increase the risk of glenohumeral chondrolysis, and hence continuous intra-articular infusions into joints with intact articular cartilage are discouraged.

S. Ganapathy, MBBS, FRCA, FRCPC
Department of Anesthesiology and Perioperative Medicine, Western University, London, ON, Canada
e-mail: sganapat@uwo.ca

J.L. Howard, MD, MSc, FRCSC
Department of Orthopedic Surgery, Western University, London, ON, Canada
e-mail: James.Howard@lhsc.on.ca

R.V. Sondekoppam, MBBS, MD (✉)
Department of Anesthesia and Pain Medicine, University of Alberta, Edmonton, AB, Canada
e-mail: vijayash@ualberta.ca

Introduction

Total joint arthroplasty has been one of the most important developments in the field of orthopedic surgery. Recently, total hip arthroplasty was called "the surgery of the century" due to its impact on patient's quality of life. It is estimated that by the year 2030 in the U.S, about half a million patients will receive hip replacements and about 3.5 million patients will receive knee replacements every year [1]. The economic constraints due to such increasing volume of cases require patients to be discharged from the hospital within a couple of days to improve hospital resource utilization. In the era of such "fast-track" arthroplasty regimen, more and more minimally invasive techniques and less disruptive approaches are being employed and the analgesic techniques have to be modified commensurate with such surgical advances.

Although the pain and quality of life substantially improve following joint replacement surgery in the long run, postoperative pain is a significant burden. A variety of techniques are available to manage acute postoperative pain which include continuous peripheral nerve blocks (PNB) [2–5], local infiltration analgesia (LIA) [6–22], oral multimodal analgesia [23], and neuraxial analgesia [24]. Each of these interventions has advantages and disadvantages (Table 24.1). Modern management of perioperative pain involves a multimodal approach including elements of preemptive analgesia, neuraxial anesthesia, peripheral nerve blockade, periarticular injections, and multimodal opioid and non-opioid medications.

Wound infiltration with local anesthetics has been practiced for several decades due to its simplicity, ease of administration, and effectiveness [25]. Since a single injection has a limited analgesic duration, a multitude of techniques have been used in the last decade to prolong analgesia which includes local infiltration analgesia (LIA), continuous or intermittent injections through the wound catheters and liposomal local anesthetic formulations. Local infiltration analgesia (LIA) also known as High Volume Local Infiltration

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_24

Table 24.1 Advantages and disadvantages of different modalities used for knee analgesia

Modality	Advantages	Disadvantages
Spinal anesthesia	• Better analgesia in the early postoperative period • Prolonged analgesia with the addition of morphine (150–300 mcg; 4–10 mcg/kg) • Attenuates neuroendocrine response and prevents DVT • Cost effective • Reliable and rapid onset	• Unable to control the rate of spread • Limited duration • Difficult to perform in uncooperative patients • Spine abnormalities (kyphosis and scoliosis) and previous spine instrumentation may prevent placement • *Contraindications*: patient refusal; clotting abnormalities; hypovolemia and systemic infections • *Potential adverse events*: severe hypotension, neuraxial hematoma, abscess formation, total spinal anesthesia, postdural puncture headache, nerve dysfunction, and damage. • Neuraxial opioids can cause respiratory depression, nausea, pruritus, and urinary retention.
Epidural analgesia	• Benefits similar to spinal anesthesia • May slowly dose epidurals • Prolonged the duration of analgesia	• Similar disadvantages as spinal anesthesia • Early ambulation may be delayed • Additional costs to perform and maintain epidural • Risk of muscle weakness and falls
Peripheral nerve block	• Limited cardiovascular or pulmonary side effects • Proximal blocks (lumbar plexus + sciatic nerve blocks) can surgical anesthesia or analgesia depending on the dosing • Superficial blocks (femoral nerve blocks and adductor canal blocks)	• Potential for local anesthetic systemic toxicity • Requires technical skill and additional costs to perform and maintain continuous PNB • Proximal blocks (lumbar plexus) carry the same risks of a neuraxial block (hematoma, spinal, or epidural drug spread) • Risk of falls (minimized with adductor canal blocks)
Local infiltration analgesia	• Easy to administer • Cost effective • Analgesia equivalent to neuraxial techniques and peripheral nerve blocks • No motor weakness as a result of the technique	• Cannot be performed in intact joint • Risk of infection if sterile precautions are not ensured • Single injection blocks have limited duration of action

Analgesia (HV-LIA) is a form of wound infiltration which commonly refers to the administration into the surgical field of large volumes of local anesthetics with or without added adjuvants perioperatively.

In this chapter, we will first present the techniques and the evidence regarding local infiltration analgesia for total knee replacement from an orthopedic surgeon's perspective, and then we will discuss and summarize the efficacy and implications of LIA, for total knee replacement other orthopedic procedures.

Historical Perspective

In the ensuing years following the discovery of local anesthetic properties by Carl Koller in 1884, [26] cocaine was primarily utilized for topical anesthesia and regional nerve blockade [27]. Carl Ludwig Schleich is credited with introducing and standardizing the technique of "infiltration anesthesia" in 1892 [28, 29]. His technique involved infiltrating the different layers of the surgical wound with a series of overlapping injections as the surgery proceeded. The earliest cases of infiltration analgesia also revealed the first cases of complications associated with the technique. Schleich noted local anesthetic toxicity after using higher concentration of cocaine (2 and 5 %) and hence recommended the use of dilute solutions (0.001, 0.1, and 0.2 %) and larger volumes (to a total dose of 50 mg). He also noted improved analgesia when cocaine was combined with morphine. Although frowned upon at the time, we have come to realize that all of these ideas apply to LIA even today. Infiltration techniques were found to be efficacious for a wide variety of surgeries subsequently and have been accepted as a part of practice [30–36]. The initial description of local anesthetic infiltration and infusion following lower limb arthroplasty was performed by Bianconi et al. in 2003 (see below). They infiltrated 40 ml of 0.5 % ropivacaine for wound infiltration intraoperatively followed by an infusion of 0.2 % ropivacaine at 5 ml/hr. [37] Local infiltration analgesia was the term coined by Dr. Dennis Kerr and Dr. Lawrence Kohan for high volume local anesthetic infiltration, performed in a systematic way during total knee arthroplasty [16]. The infiltrate is usually a cocktail of a long-acting local anesthetic (ropivacaine), an NSAID (ketorolac), and a vasoconstrictor (epinephrine), with or without a corticosteroid.

Surgeon's Perspective: Local Infiltration Anesthesia in Total Knee Arthroplasty

Total knee arthroplasty (TKA) can be associated with substantial pain in the perioperative period. Pain that is inadequately controlled may impair mobility, reduce the ability to participate in rehabilitation, and reduce patient satisfaction. In addition, in some patients, inadequately controlled pain may result in the development of chronic pain. Traditional general anesthesia combined with patient-controlled opioid analgesia may be associated with undesirable side effects, including postoperative nausea and vomiting, hypotension, urinary retention, respiratory depression, delirium, and postoperative infections. For many surgeons, local infiltration anesthesia (LIA) in recent years has become a key element of the pain management paradigm for total knee arthroplasty patients.

Interest in local infiltration anesthesia among orthopaedic surgeons has increased since the first trials were published, demonstrating its efficacy as a technique. Subsequently, multiple trials comparing LIA to placebo, peripheral nerve blocks and central neuraxial blocks, were performed which has established the role of LIA in arthroplasty surgery. Busch et al. [38] completed one of the first randomized clinical trials evaluating the use of local infiltration analgesia. Sixty-four TKA patients were randomized to receive either; a periarticular intraoperative injection containing ropivacaine, ketorolac, epimorphine, and epinephrine or to receive no injection. Other aspects of perioperative pain management were standardized between the two groups. The patients who had received the injection used significantly less patient-controlled analgesia at 6 h, 12 h, and over the first 24 h following surgery. In addition, they had higher visual analog scores for patient satisfaction and lower visual analog scores for pain during activity, immediately following surgery and four hours after the operation. No cardiac or central nervous system toxicity was observed in patients who received the injection. Similarly, Vendittoli et al. [39] evaluated patients who received perioperative LIA combined with self-administered morphine, compared to a group of patients who received self-administered morphine alone. Both groups demonstrated high satisfaction rates and good pain control. However, morphine consumption was significantly lower in the local analgesia group than it was in the control group at 24 and 48 h following surgery. Jiang et al. [40] has completed a review of 21 randomized controlled trials evaluating LIA compared to placebo in total hip and total knee arthroplasty patients. Pooled results showed that the LIA group had better pain relief, less opioid consumption, a larger range of motion, and lower rates of nausea and vomiting, than the placebo group.

The contents and dosing of medications in local infiltration analgesia cocktails has varied significantly in the published literature. The mixture used by Busch et al. [38]1 contained 400 mg ropivacaine (80 mL of 0.5 % ropivacaine at 5 mg/mL), 30 mg ketorolac (1 mL at 30 mg/mL), 0.6 mg of 1:1000 epinephrine (0.6 mL at 1 mg/mL), and 5 mg morphine (0.5 mL at 10 mg/mL) diluted to a volume of 100 mL. Kelly et al. [41] reported on a mixture containing ropivacaine, epinephrine, and ketorolac combined with clonidine, an alpha-2 adrenergic receptor agonist intended to produce synergistic effects, with local anesthetics and opioids. Others have described infiltration cocktails with the addition including steroids (methylprednisolone) and antibiotics (cefuroxime) [42].

In order to understand the essential components of a local infiltration anesthetic cocktail, Kelley et al. [41] evaluated 150 patients who received one of four different periarticular injection mixtures when undergoing TKA. The patients were divided into four groups based on the mixture received. Group A received ropivacaine, epinephrine, ketorolac, and clonidine; Group B received ropivacaine, epinephrine, and ketorolac; Group C received ropivacaine, epinephrine, and clonidine and Group D was the control. They found that patients who had received periarticular injections containing ropivacaine, ketorolac, and epinephrine with or without clonidine had substantially less pain in the immediate postoperative period than did those patients who received injections containing ropivacaine and epinephrine alone. This suggested that ketorolac was a key component that should be considered for inclusion in all local infiltration cocktail mixtures.

The technique of administration of local infiltration analgesia in the operating room has also varied in the published literature. In the description by Busch et al. [38], the injection of the cocktail was divided into distinct phases. The first portion of the injection occurred just prior to component implantation. At that point in the procedure, 20 mL mixture of the 100 mL cocktail is injected into the posterior capsule and medial and lateral collateral ligaments (Fig. 24.1). This is completed prior to component implantation to give better access to the posterior aspect of the knee to allow for effective posterior capsular injection. Care is taken to avoid excessive infiltration in the posterolateral corner in the area of the common peroneal nerve. Once the components have been implanted and the cement is curing, 20 mL is injected into the quadriceps and retinacular tissues (Fig. 24.2). Finally, after component implantation is complete and prior to closure, the remaining 60 mL is infiltrated into the fat and subcutaneous tissues. Subsequent authors have included the addition of infiltration into the medial and lateral periosteum, meniscal remnants, PCL, pesanserinus, and illiotibial band [41, 42].

Local infiltration anesthesia has been prospectively compared to peripheral nerve blocks (PNB) in a number of studies. In one of the first such trials, parvataneni et al. [42] evaluated 60 patients in a prospective study comparing local infiltration anesthesia to femoral nerve block (FNB) combined with patient-controlled analgesia (PCA). The LIA group had an improved ability to perform a straight leg raise

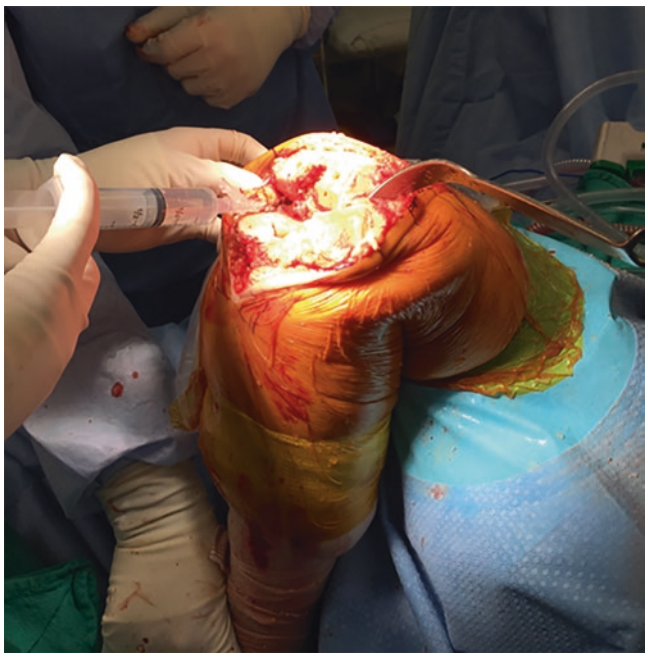

Fig. 24.1 Injection of local anesthesia infiltration into the posterior capsule of a total knee replacement. Injection is completed prior to placement of the definitive implants to allow easy access to the posterior aspect of the knee

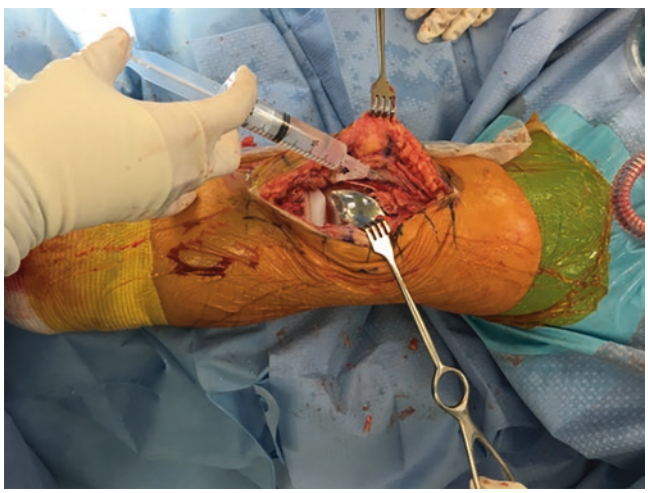

Fig. 24.2 Following definitive component placement infiltration of the quadriceps and retinacular tissues as well as the fat and subcutaneous tissues superficially

on postoperative day 1 (63 % vs. 21 %). Similar pain scores were demonstrated between both groups during their postoperative hospital course. The results suggested that LIA provides pain control equivalent to that of FNB with the added advantage of maintaining quadriceps motor strength. Similarly, Spangehl et al. [43] compared patients receiving LIA to a group of patients who received a continuous femoral nerve block and single shot sciatic nerve block. Although pain scores were lower on the day of surgery in the PNB group, they were similar for the remainder of the hospital stay. The patients in the PNB group experienced more acute postoperative falls and lower quadriceps function measured by the ability to perform a straight leg raise on postoperative day 1 (24 % vs. 79 %). In addition, the patients receiving PNBs had more peripheral nerve dysesthesias at 6 weeks postoperatively.

Approved for use in the United States EXPAREL (Pacira Pharmaceuticals, Inc., San Diego, CA, USA) is a slow releasing bupivacaine medication designed to reduce the risk of bupivacaine toxicity and provide an extended duration of postoperative pain relief following surgery. Bramlett et al. [44] examined four varying doses of liposomal bupivacaine (133, 266, 300, and 532 mg) compared with a control of non-liposomal bupivacaine (150 mg). Treatment with liposomal bupivacaine was associated with greater analgesia while patients were at rest after surgery compared with bupivacaine although this was seen only in the cohort receiving a dose twice the recommended value (532 mg). Subsequent studies have failed to demonstrate significant benefits in morphine consumption, pain scores, knee range of motion, length of stay with the use of liposomal bupivacaine compared to LIA [45–47]. Furthermore, it is important to consider the cost of liposomal bupivacaine compared to traditional techniques. Wholesale costs for a vial of EXPAREL266 mg/20 mL is $14.25 compared to a 10 mL vial of 0.25 % bupivacaine HCl costing $0.29 [48]. Therefore, current available evidence shows no benefit to the use of liposomal bupivacaine compared to a traditional LIA cocktail for the management of pain following total knee arthroplasty.

In conclusion, from a surgeon's perspective, local infiltration analgesia is an effective strategy for management of pain following lower limb total joint arthroplasty and can be easily employed by all surgeons without the need for specialized training or equipment. LIA can be easily combined as a part of multimodal postoperative pain management protocols. It should continue to be a component of pain control paradigms for the majority of patients undergoing total joint arthroplasty.

Why Is LIA Popular for Arthroplasties and Can It Be Used for All Joint Surgeries?

Proximal joints of the limbs such as shoulder, hip, and knee have multiple nerves supplying the joints. Upper limb surgeries are effectively covered by brachial plexus blocks since the ensuing motor blockade is not much of a concern for postoperative physiotherapy and rehabilitation.

Proximal lower limb surgeries on the one hand require the patients to actively mobilize after surgery. Ankle and foot surgeries on the other hand does not have the same concerns as that of hip or knee surgeries since they are typically advised not to weight bear for the first couple of days and hence analgesia in these cases can be effectively accomplished with popliteal sciatic nerve block with or without saphenous nerve block. Traditional approaches for hip and knee analgesia have employed neuraxial techniques (intrathecal opioids, epidural analgesia) or peripheral nerve blocks (lumbar plexus or femoral nerve blocks with or without sciatic component) to ensure effective analgesia. The accompanying motor blockade is a cause for concern in lower limb surgeries since they not only interfere with physiotherapy but also may pose a risk for patient falls [49, 50]. Hence, a site-specific modality such as LIA may be suitable for such proximal lower limb surgeries. The popularity of local infiltration analgesia is due to its low cost and ease of administration by the surgeons intraoperatively without the need for regional anesthesia experts to initiate the intervention. LIA being site specific in its action is supposed to lack the motor weakness seen with PNB and thereby may permit early ambulation and physiotherapy.

The following safety concerns need to be considered before LIA:

- What concentration and total volume of LA is appropriate for the patient?
- Can the joint clear local anesthetic in a reasonable period of time in order to avoid toxicity?
- Do we need single injection or continuous catheter?
- Is the articular cartilage intact after surgery?
- Are there factors influencing the risk of local and systemic toxicity?

All local anesthetics are chondrotoxic and hence should not be injected into an intact joint (see section "Chondrotoxicity"). Fortunately, the articular surfaces are removed in total joint arthroplasties and hence the chondrotoxic effect is not of much concern in these situations. The LIA is avoided in situations when there is a chance of an intact synovial or joint cartilage remaining, such as arthroscopic surgery, unicompartmental knee replacement, hip resurfacing arthroplasty, hand and foot surgery among others [25, 26].

Anatomical Consideration

It is essential to know the neuro-anatomy of the joint for the success of the LIA technique since not all areas within a joint have the same amount of mechanoreceptors or free nerve endings. Hence, the technique of LIA should target the areas of higher innervation compared to others.

Most of the joints in body follow Hilton's law with some exceptions [51]. Hilton's law states that "The same trunks of nerves whose branches supply the groups of muscles moving a joint furnish also a distribution of nerves to the skin over the insertions of the same muscles; and what at this moment more especially merits our attention the interior of the joint receives its nerves from the same source." The adaptation of this law is that not all the muscles crossing a joint give articular branches but the source of articular innervation and the overlying skin is derived from the same source supplying the agonist and antagonist muscles acting across a joint.

Innervation of the Hip Joint

The main innervators of the hip joint are the femoral nerve via the nerve to rectus femoris, the sciatic nerve via the nerve to the quadratus femoris and branches from the anterior and posterior divisions of the obturator nerve. The skin over the hip joint is supplied by the lateral femoral cutaneous nerve with contributions from the dorso-lumbar nerve (T12-L1). A majority of the innervation is to the joint capsule compared to the intra-articular structures. The femoral nerve covers the antero-lateral aspect of the hip capsule while the obturator covers the medial aspect of the hip. The sciatic nerve and the superior gluteal nerve together cover the posterior aspect of the hip capsule.

Inside the joint, the acetabulum has the highest amount of sensory innervation followed by the periosteum surrounding the proximal femur. A few studies have recently looked at the distribution of the sensory nerve endings and mechanoreceptors within the hip joint and have consistently found the antero-superior and postero-superior aspect of the acetabular labrum [52] to contain the highest amount of receptors. This is followed by the postero-inferior and the antero-inferior part of the labrum. The rest of the intra-articular components including ligamentum teres have very little contribution to nociception.

Innervation of the Knee Joint

The knee receives innervation from the femoral, sciatic, and obturator nerves through its various branches. Inside the knee joint, several regions have higher neuro-sensory perception compared to others areas [53]. These include (1) The suprapatellar pouch and quadriceps tendon; (2) The medial and lateral retinaculum; (3) The patellar tendon; (4) The medial and lateral collateral ligaments along with the menisci; (5) The tibial attachment of PCL and the femoral attachment of ACL. It is important to cover these areas of increased nociceptive and proprioceptive inputs for the success of LIA.

Equipment and Technique of Injection

The success of LIA like that of any other technique depends on the operator's performance and variability with infiltration technique is a problem especially with newcomers. Traditionally, a "moving needle" technique has been recommended using a non-cutting small gauge needle (22 Ga) attached to a syringe containing the LIA cocktail and injected in small aliquots of 2–3 ml in different tissue planes. The goal of the technique is to deliver a majority of the drugs into those tissues with increased neuro-sensory perception. A staged fashion of infiltration where the LIA is begun with incision and continued until the closure of the wound is widely adapted. Use of smaller syringes with control for aspiration before injection should be used in areas of potential complications such as in the posterior knee area.

Composition of LIA

Different mixtures have been utilized for infiltration in the studies and include a long-acting local anesthetic such as ropivacaine or bupivacaine; morphine, ketorolac, and epinephrine are added variably. Currently, we do not know definitively as to which component provides the maximum analgesia benefit in the cocktail. The adjuvants added to the local anesthetic can show either an additive or synergestic effect with the local anesthetic. Epinephrine is added to the mixture to delay and minimize the systemic LA absorption but it additionally benefits patients due to its hemostatic effects thereby minimizing wound hematoma and the need for drains. The epinephrine is also known to possess alpha-2 adrenergic agonistic effects which may have a synergistic analgesia effect on local anesthetic. The addition of opioids to the mixture is based on animal and limited human evidence of increased expression of peripheral opioid receptor population at the surgical site [54]. The NSAID's are added for their local anti-inflammatory properties and analgesia effects. Whether the adjuvant effect is true in humans and whether the same can be achieved using systemic route of administration was studied by Spreng et al. [55]. The patients in their study were randomized to receive either epidural analgesia, LIA with ropivacaine, epinephrine, morphine 5 mg, and ketorolac 30 mg (LIA) or LIA with ropivacaine, epinephrine, and IV morphine and ketorolac (LIA-IV). LIA showed considerably better analgesia and lower opioid consumption compared to epidural or LIA-IV. Although further evidence is needed, like any other multimodal drug strategy, the combination of the drugs in the cocktail seems to work best compared to individual components given by different routes. The optimal dose of each of the components also need to be determined for LIA.

Practical Consideration

LIA in Total Hip Arthroplasty [56]

For both direct anterior and posterior approaches, the LIA begins before the placement of the acetabular cup and the femoral liners are placed. Preferably, the capsular attachment to acetabular labrum is infiltrated with 15–20 ml of LIA cocktail from antero-superior to postero-superior aspect. The femoral periosteum, the posterior capsule and the origin of quadriceps muscles are infiltrated with about 30 ml of cocktail before the placement of the implants. Following the insertion of prosthesis, the anterior capsule and adjacent structures are injected with another 30 ml of LAI cocktail. The remaining 20–30 mL of LAI cocktail is infiltrated into the different layers of closure including rectus femoris, fascia lata, and the wound incision.

LIA in Total Knee Arthroplasty [53, 57]

The exact technique of injection varies from one institution to another but the general principles of injection remain the same. The knee arthroplasty at our institute is performed using the posterior stabilized prosthesis with the para-patellar or vastus sparing incision. The menisci are stripped prior to proximal tibial resection after application of knee retractors. The distal femur and proximal tibia are resected using box cuts which also remove the ACL, MCL, and the PCL. With the retractors in situ, certain surgical areas are infiltrated with LIA cocktail which includes the femoral attachment of ACL, tibial attachment of PCL, remnants of menisci, the medial and lateral collateral ligaments. Several milliliters of the cocktail is also injected into the posterior capsule using a smaller syringe and negative aspiration before injection (Fig. 24.1). After cementing the prosthesis, the LIA cocktail is injected into the quadriceps tendon and while the cement is curing, several milliliters of the PAI cocktail are injected into the anterior capsule, the quadriceps tendon, and the suprapatellar pouch. The knee fat pad in the superior and medial aspect of the knee joint is injected by some surgeons before the closure (Fig. 24.2). The surgical wound and the skin flaps are closed in the usual fashion, and the residual LIA cocktail is injected into the wound at the end. A total of 80–110 mL of the cocktail is used depending on the age, comorbidities, and patient weight.

Other orthopedic surgeries: The evidence of LIA in other orthopedic surgeries is sparse. LIA is currently not popular for shoulder surgeries due to concerns of glenohumeral chondrolysis (see section "Chondrotoxicity"). A single trial has so far evaluated LIA following spine surgery where continuous infiltration with ropivacaine showed no benefit compared to systemic analgesia alone; [58] Arthroscopic

surgeries such as ACL reconstruction [59–63] and hip arthroscopy [64] have utilized periarticular and intra-articular local anesthetic injections with analgesic benefits similar to peripheral nerve blocks but it is our practice to avoid LIA in such situations. LIA for unicompartmental knee joint resurfacing has been a point of debate. While there are studies which have shown analgesic benefit of HV-LIA in unicompartmental knee joint surgeries [65, 66], the presence of an intact synovium and articular cartilage in the majority of the joints after surgery is a cause for concern. Since the surgery is being performed due to the degenerative joint disease, steps to avoid any iatrogenic damage to joint are important for both patient safety and medicolegal reasons. Hence, it is our practice to avoid LIA in any of the above situations when the joint cartilage is intact post surgery.

LIA in Arthroscopy Surgeries

A number of benefits have been reported for LIA including lower pain scores at rest and on movement, lower impact on motor power, reduced incidence of falls, early mobilization, improved early functional scores, and reduced length of hospital stay. The literature looking at the benefits of LIA in comparison to other modalities has been ever increasing in the last decade with some reporting the above benefits while others refuting them. A summary of these findings have been reported in 10 systematic reviews in the last few years which are summarized in Table 24.2. Most of the reviews are consistent regarding the analgesic benefits of LIA since this has been consistently looked into in all the trials evaluating it. When the secondary outcomes such as functional scores, length of stay, range of motion, motor power are looked into, the evidence is inconclusive due to the fewer number of studies reporting these outcomes exclusively.

Clinical Evidence

Hip Arthroplasty

There have been four systematic reviews evaluating the benefits of LIA in comparison to placebo, epidurals, intrathecal morphine, and peripheral nerve blocks. Compared to placebo [40], LIA has been shown to result in better resting pain scores at 6 and 24 h and better dynamic pain scores at 6 h while it was no better than a placebo beyond 24 h for rest pain and beyond 6 h for dynamic pain. A review by Andersen et al. [67] furthered this evidence by showing that LIA in itself was comparable or superior to epidural, intrathecal, morphine (ITM) or peripheral nerve blocks but was no better than a placebo in the context of background systemic multimodal analgesia treatment regimen. The comparability of LIA with PNB and epidural has been supported by other reviews on the topic [68, 69].

Total Knee Arthroplasty (TKA)

In the last 3 years, nine reviews have looked into the benefit of LIA in TKA. LIA provided longer duration of analgesia following TKA in both rest pain and movement in comparison to the analgesic benefit seen in THA [40, 67, 70]. The LIA provided better analgesia compared to placebo in four reviews [40, 67, 70, 71]. In comparison to epidurals, LIA provided comparable analgesia in the first 24 h and superior analgesia in the 24–48 h period [67, 69, 72]. When LIA was compared to peripheral nerve blocks, the evidence varies regarding the superiority of one technique over the other depending on the review and their included studies. Among the five reviews, Andersen et al. [67] (5 studies) and Albrecht et al. [73](14 studies) noted comparable analgesia both at rest and movement but on the other hand, while noting comparable resting pain scores between the two, Mei et al. [74] (6 studies) and Huet al [72] (16 studies) noted better analgesia with PNB on movement. In contrast, another review by Fan et al. [75] (8 studies) noted better resting pain scores with LIA and comparable pain scores on movement in the first 24 postoperative hours.

Non-analgesia Benefits of LIA in Lower Limb Arthroplasty Surgeries

- *Impact on motor power/falls*: Although the technique of LIA does not impact the motor power of the leg muscles unlike that from peripheral nerve blocks, it is to be remembered that the majority of the muscle weakness is as a result of the surgery itself. Hence, the motor sparing effect of LIA does not translate to a decrease in patient falls as seen in a recent systematic review [73]. It is to be noted though that the preservation of motor power did translate to better range of motion in the first few days postoperatively [40, 70, 72, 73, 75].

- Functional outcomes: Apart from the range of motion, the 3 month and 1 year knee society scores were analyzed in two recent systematic reviews which noted the long-term outcomes were comparable between LIA and regional anesthetic techniques.

- *Hospital stay*: Eight of the ten systematic reviews looked at the impact of LIA on the length of stay. Fast track arthroplasty protocols are amenable to discharge the patients earlier but are still dependent on other system

Table 24.2 Summary of systematic reviews of LIA in hip and knee arthroplasty

Author name (year)	Number of trials included/number of patients	Comparison	Key outcomes
Jiang et al. [40]	21 studies/1769 16 studies on TKA (1447 patients) 5 studies on THA (322 patients)	HV-LIA versus placebo for TKA and THA	• LIA compared to the placebo had less opioid consumption, better function recovery, lower rates of nausea and vomiting for patients with TKA or THA. • THA: Lower VAS scores with rest at 6 and 24 h and lower VAS scores with movement at 6 h compared to placebo. • TKA: lower VAS scores with rest at 6, 24, 48 h, and lower VAS scores with movement at 6 and 24 h compared to placebo. • Length of hospital stay did not show a significant difference between the LIA and placebo groups for patients undergoing TKA and THA. • Range of motion was significantly greater with LIA during the first 72 h postoperatively in comparison to the placebo group.
Andersen et al. [67]	27 studies/888 TKA and 756 THA 14 (LIA vs. Placebo) 5 (LIA vs. PNB) 4 (LIA vs. Epidural) 3 (LIA vs ITM) 1 (LIA vs. systemic analgesia)	LIA versus other modalities in both THA and TKA	• THA: No additional analgesic effect of LIA compared with placebo in THA when a multimodal analgesic regimen was administered perioperatively. • THA: Compared with intrathecal morphine and epidural analgesia, LIA was reported to have similar or improved analgesic efficacy. • TKA: most trials reported reduced pain and reduced opioid requirements with LIA compared with a control group treated with placebo/no injection. • TKA: Compared with femoral nerve block, epidural or intrathecal morphine LIA provided similar or improved analgesia in the early postoperative period. • The use of wound catheters for postoperative administration of local anesthetic was not supported in the included trials, and LOS was not related to analgesic efficacy.
Xu et al. [70]	18 studies/1858	Single injection LIA vs Placebo for TKA	• The VAS values at postoperative 2, 4, 6, 12, 24, and 48 h per patient were significantly lower in the LIA group than in the placebo. • LIA also had less morphine consumption and better early functional recovery including range of motion, time to straight leg raise and 90° knee flexion than the latter group. • No significant difference in length of hospital stay or side effects was detected between the two groups. • This review included a wide variety of LIA volumes and concentration. Heterogeneity in reported outcomes and method of LIA.
Jime'nez-Almonte et al. [68]	15 (pairwise LIA vs placebo)/1128 patients; 12 (pairwise PNB vs. Placebo)/732 patients 35 RCT's for network meta-analysis (comparing LIA or PNB with intrathecal opioids or epidural)	Pairwise and network meta-analysis (LIA vs. PNB for THA)	• No differences between peripheral nerve blocks and local infiltration analgesia in terms of postoperative pain scores and cumulative opioid consumption at 24 h after THA • Use of local infiltration analgesia had a greater probability of being ranked most effective for both outcomes.
Fan et al. [75]	8 studies/752	HV-2LIA vs. PNB for TKA (both single injection and continuous catheter studies included)	• On POD 1: The NRS values for pain on rest were lower in LIA than those in PNB. • No significant difference between the two regarding the NRS score with activity. • On postoperative day 1, the morphine consumption on POD 1 was lower in LAI than that in PNB. • Both subgroups showed no significant difference in knee ROM at 3 months postoperatively. • Opioid-related side effects (nausea/vomiting and dizziness) less, while infection and urinary retention were more in LIA. • LOS was less in LIA compared to PNB.

Sun et al. [71]	10 studies/735 patients	Continuous HV-LIA versus placebo in TKA	• Continuous infusion analgesia provided better pain control with rest at 24 h only and with mobilization at 24 and 48 h. • Pain scores at rest were comparable at rest at 48 and 72 h and pain scores on movement were comparable at 72 h. • Continuous infusions increased the rate of infection and the rate of nausea or vomiting. • There were no significant differences in the length of hospital stay, deep venous thrombosis, or duration of surgery.
Mei et al. [74]	6 studies/306	HV-LIA vs. FNB for TKA	• Pain scores at rest and narcotic consumption were comparable between LIA and FNB in the first 24 postoperative hours. • Pain scores on movement were better with FNB in the first 24 postoperative hours.
Albrecht et al. [73]	14/1122	LIA vs. PNB for TKA (five trials compared single shot and nine trials compared continuous catheters)	• The primary outcomes of i.v. morphine consumption, pain scores at rest and on movement on postoperative day one (analog scale, 0–10) showed no difference. • No clinical differences in functional outcomes or rates of complications (cardiovascular, neurological, falls, and knee infection). • Range of motion on postoperative day 2, knee society score at 6 weeks and length of stay were statistically different but without direct clinical relevance.
Yan et al. [69]	9 Studies/537	HV-LIA vs. Epidural for THA and TKA	• THA: In the first 24 postoperative hours, resting pain scores were comparable but epidural provided better dynamic pain scores. • THA: At 48–72 postoperative hours, both LIA and epidural provided comparable analgesia both at rest and movement. • TKA: Comparable resting and dynamic pain scores in the first 24 postoperative hours. • TKA: at 48–72 h, LIA provided better analgesia than epidural both at rest and movement. • The range of knee flexion was better with LIA at 24, 48, and 72 postoperative hours (3 studies). • LIA failed to reduce the hospital length of stay (4 studies).
Hu et al. [72]	16 studies/1206	HV-LIA vs. RA (Epidural and FNB) for TKA	• LIA showed significantly lower pain score in the first 24 h at rest. There was a tendency for lower pain scores on movement with PNB but not with EA in comparison to LIA. • No difference in morphine consumption or complication rate between the two groups. • Early functional recovery (Range of motion and Straight leg raise) on POD 1 and 3 weeks was better with LIA group but not at 3 months. • Long-term functional recovery scores were comparable (knee society score). • Length of hospital stay of the LIA group was marginally shorter than that of the RB group.

factors which are not influenced by the patient's scores for discharge. Such factors include the availability of physiotherapy staff at the hospital and in the community, home care, and nursing support available after discharge, medical, or surgical comorbidities. Hence, it is not surprising to see a majority of these reviews not finding any difference in length of stay in comparison to either placebo or regional anesthetic techniques [40, 67, 69–74] except for one review [75].

An Institutional Experience of Implementing LIA to Analgesic Paradigm

We started using this technique having visited Kohen and Kerr but the technique did not work predictably in a teaching hospital set up with multiple individuals responsible for pain management after hours. Around the same time, the importance of opioid receptor expression in injured surgical tissue gave us an opportunity to add morphine to the cocktail for its peripheral analgesic effects. Unlike the observation by Essving et al., in spite of the effective periarticular infiltration, the immediate analgesia was short lasting (less than 24 h). The wound complications noted by earlier groups, generated concern about the high dose of epinephrine in the mixture. Thus at our site, we use only 2.5 mcg/mL of epinephrine but add 10 mg of morphine to the mixture, usually added freshly prior to infiltration as we have no data on the stability of the mixture. Some of the studies have reported reinjecting the catheters on the night of surgery and the morning after surgery. We were concerned with reinjection through the implanted catheters. Hence, we utilize a closed periarticular infusion system initiated by the surgeon intraoperatively. The concentration of ropivacaine that we selected also was a lower volume higher concentration (0.35 %) for infiltration and infusion. We did not add ketorolac to the infusion but all patients had oral multimodal analgesia with gabapentin, acetaminophen, naproxen/celecoxib and rescue oxycodone and a short course of oxycontin (9 doses as needed). Spinal anesthesia with opioid-free local anesthetic was our method of choice. This facilitated early ambulation as early as 4 h after surgery and we could discharge 85 % of the patients home between 24 and 36 h after surgery with good functional outcome (unpublished data). There has been one episode of cardiovascular collapse and arrhythmia with reinjection. Other complications encountered with this technique include wound dehiscence requiring a gastrocnemius flap.

Continuous Catheter Techniques

Wound infusion system was described by Kohen et al. where they placed the epidural catheter tip adjacent to the implanted prosthesis. They placed the catheter tip between the prosthesis and the posterior capsule and subsequently passed the catheter along the medial femoral condyle in knee joint. For hip arthroplasty, the catheter tip was placed at the anterosuperior aspect of the capsule within the joint and the catheter taken out from the posterior aspect of the surgical wound in retrograde fashion through a Tuohy needle.

The use of this technique worked very well for total hip arthroplasty and hip resurfacing arthroplasty by Kerr and Kohan but this single catheter technique did not provide satisfactory analgesia to the back of the knee when implemented at our institution. Thus, we developed a system of three catheters implanted by the surgeon, one in the posterior knee fat pad, second in the suprapatellar pouch, and the third in the subcutaneous tissue anteriorly along the incision. Note that one of the catheters was placed in the joint space and therefore could pose a risk of joint infection. A study by Dobrydnjov et al. [76] showed that an extra-articularly placed catheter in the soft tissue around the joint provided comparable analgesia to intra-articularly placed catheters. Hence, it may be adequate to place the catheter tip extra-articularly if the team is concerned about the risk of infections but more evidence is needed for this practice. Irrespective of intra- or extra-articular placement of the catheter tip, we recommend the routine use of closed infusion systems initiated in a sterile fashion by the surgical team intraoperatively and also to routinely use a 0.2 μm filter for both single injections and continuous infusions. Currently, the numbers are so small that we cannot recommend the routine use of this three catheter technique until more robust data are available. Most surgeons at our institution are not happy with an intra-articular catheter remaining for 48 h and liposomal bupivacaine may be a good alternative.

Incidence and Management of Complications and Adverse Events from LIA

Chondrotoxicity [77–83]

Local anesthetics injections into a joint following office-based orthopedic joint procedures and arthroscopic surgery have been performed for a long time. Local anesthetic induced chondrolysis garnered attention after reports of articular damage in association with the use of intra-articular infusions of local anesthetic used for 24–48 h. This was particularly noted when continuous intra-articular local anesthetic infusion pumps were used for analgesia following shoulder arthroscopies. Chondrolysis after surgery is a potential problem in intact joints and is multifactorial in nature (Fig. 24.3). Apart from exacerbation of the primary joint disease following surgery, other factors such as surgical trauma, local anesthetic infusions, thermal injury, irrigation solutions, intra-articular pres-

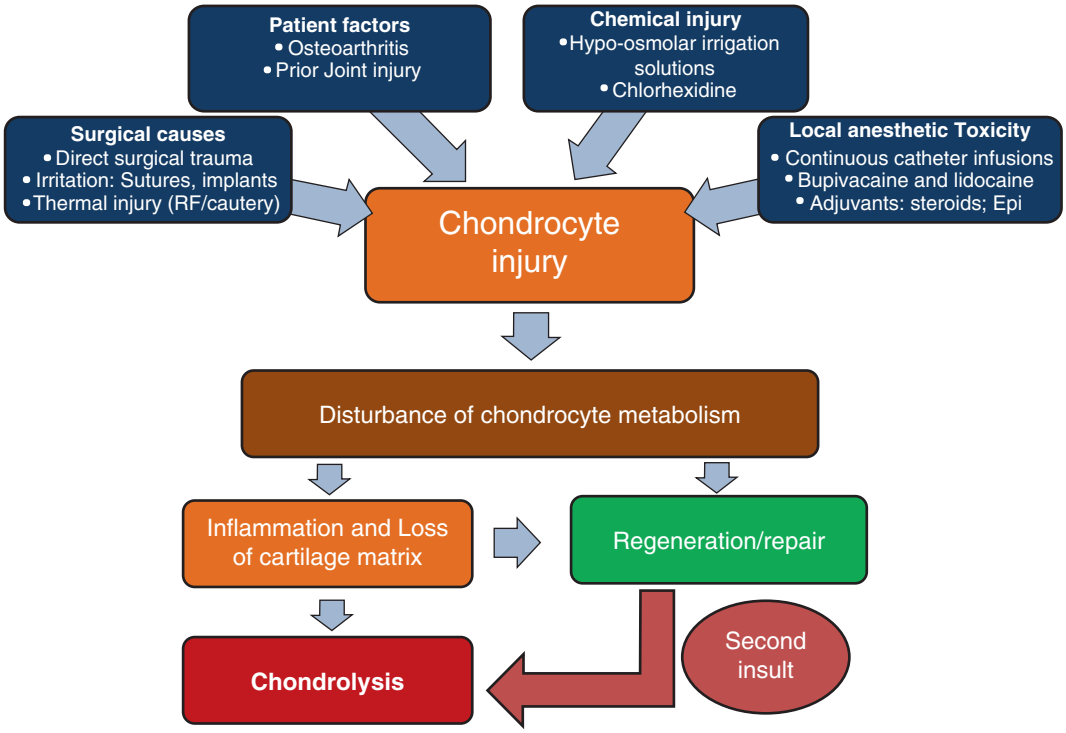

Fig. 24.3 Patho-mechanism of chondrolysis following surgery. Initial chondrocyte injury can be due to a variety of insults and often leads to chondrocyte dysfunction. This may proceed to sterile inflammation, loss of extracellular matrix. The chondrocytes can regenerate and repair until this stage but if the initial insult is prolonged or if there is a second injury, the deeper layers of the cartilage get exposed and result in chondrolysis.

sure changes, and irritation from implants have all been implicated [82, 84].

The effect of LA on cartilages has been well studied using both in vitro and animal models [85–88]. From in vitro studies, it is evident that all local anesthetics are toxic to the chondrocytes but not all have the same chondrotoxic potential [82]. The amount of LA induced chondrotoxicity is further exacerbated with the combination of epinephrine or corticosteroids [89]. The chondrotoxicity is both concentration and time dependent [84, 87]. The effect of concentration was demonstrated in an animal model where higher concentration (0.5 % bupivacaine or 2 % lidocaine) resulted in chondrocyte death even after brief exposure [85]. When low concentrations of local anesthesia are used (0.125 % bupivacaine), the effect was minimal.

The most likely mechanism is that the local anesthetics inhibit chondrocyte metabolism and induce apoptosis. This may lead to a decreased synthesis of extracellular matrix necessary for chondrocyte survival. Chondrocytes usually recover from minor insults but when they are subjected to multiple insults or continually exposed to injurious agents, the damage is irreversible. This is especially true for joints at risk of injury due to pathological processes such as trauma or osteoarthritis. Single injections result in lesser chondrocyte injury compared to a continuous intra-articular infusion [87]. Chondrotoxicity may not be clinically apparent especially when single injections are used but, lack of clinically apparent injury does not necessarily mean a lack of cartilage injury. The local anesthetic chondrotoxicity may be one of the many insults to an already "at-risk joint" and subsequent insults to the cartilage may lead to exacerbation of such cartilage loss. Clinical proof is still limited to case reports/series and studies to definitively establish this concept may be difficult due to ethical constraints and the variability in patient population. Apart from the local anesthetic mass, other factors affecting local anesthetic clearance inside the joint include the volume of the joint, compliance of the capsule, presence of drains, and dilution due to a joint effusion or hemarthrosis.

If one chooses to use intra-articular local anesthetics into an intact joint, it is advisable to use dilute local anesthetics single injections (10–20 mL of 0.125 % bupivacaine or 0.2 % ropivacaine) and avoid higher concentrations or longer duration of exposure of the joint cartilage to the local anesthetic. A recent meta-analysis of randomized controlled trials looking at the safety and efficacy of intra-articular bupivacaine with morphine also found that single injection following knee arthroscopy did have analgesic benefits without increased risk of adverse event compared to placebo [90]. Fortunately, the concerns following any total joint arthroplasty are fewer since there is no cartilage left in the joint. Although LIA has

not been used following shoulder arthroplasty, one recent study comparing LIA to interscalene block for total shoulder arthroplasty however noted inferior analgesia with LIA at all time intervals within the first 24 h [91].

Shoulder Surgery and Glenohumeral Chondrolysis

Shoulder joint is a typical example of chondrolysis following prolonged local anesthetic exposure. It is a smaller joint in comparison to knee and hip and hence has minimal clearance of local anesthetics from the joint. When infiltration and continuous infusions with bupivacaine and lidocaine was used in the shoulder following arthroscopic surgeries, glenohumeral chondrolysis was noted in many cases [82]. It may have a variety of presentations and can be subtle with increased shoulder pain or may also have decreased range of motion, joint stiffness, joint crepitus, and radiological evidence of joint space narrowing. Although mechanical and thermal factors for post-arthroscopic glenohumeral chondrolysis may play a role, chondrotoxicity of bupivacaine following its delivery into a tight shoulder space cannot be ignored. In a systematic review of glenohumeral chondrolysis, the use of continuous intra-articular pain pumps was observed in 67 % of the 88 reported cases, which could reflect the time dependent chondrotoxicity of LA [82]. Hence, the use of continuous LA infusions into an intact joint is highly discouraged.

Risk of Infection

Placement of catheters close to the prosthesis and performing repeated injections through them has the potential to spread infections into the surgical wound and the joint. Earlier and recent clinical trials have acknowledged this complication with a recent systematic review of periarticular infusions concluding that the use of periarticular and intra-articular catheters increased the risk of joint infections and revision surgery [20, 71, 92]. Recent reports have also indicated that even single injection LIA may have led to an increased risk of revision hip surgeries as a result of deep infections [93].

It is well known that bacterial colonization of CPBNs occurs easily and the incidence varies between 27 and 57 % [94]. The most frequently identified organisms are skin commensals such as *Staphylococcus epidermidis* (71 %), enterococcus (10 %), and klebsiella (4 %) [95]. We currently are not aware of a similar incidence for intra-articular catheters. Whether such colonization may impact the incidence of catheter-related joint infections and the impact of perioperative antibiotic cover is currently unknown. It is always prudent to look for signs of infection such as erythema, tenderness at the catheter insertion site, fever, rising CRP levels or leucocyte count [96]. The result of such infection can be self-limiting but can proceed to cellulitis or even septic arthritis, and hence it is our practice to discontinue the catheters if any of the warning signs are present at the earliest and send the catheter tips for bacterial cultures. Further management of suspected infections depends on the severity of the infection and may range from simple observation for small infections to antibiotic cover for milder forms and more severe infections requiring surgical options. The risk of infection following continuous nerve block is known to be higher in patients with uncontrolled diabetes or malignant diseases due to weaker host defenses and the same may be true for periarticular catheters. For further discussion of the topic, please refer to Chaps. 9 and 10.

Practice Points to Minimize the Risk of Infections

- Strict adherence to aseptic precautions is the cornerstone for preventing infections in both single injections and continuous catheter techniques.
- The catheters are to be considered preferably in the background of antibiotic cover and only after ruling out signs of active infection.
- We recommend using a small bore, non-cutting needle with a 0.2 μm filter attached between the syringe and the needle be used, for LIA injections and infusions.
- Closed system infusions initiated under aseptic precautions by the surgeon intraoperatively is preferred over reinjection techniques.
- Minimize the duration of infusions to less than 3 days.

Nerve Injury

Pre- and postoperative examination by physicians and trained nurses should be a part of routine care to help in the early recognition of these cases. The sciatic nerve is particularly prone to injuries following lower limb arthroplasty. Peripheral nerve injuries, particularly peroneal injury can occur due to tourniquet, cement, and varus correction following TKA [97] and caused by cement or bone impaction following THA.

Multiple factors can influence the occurrence of neurologic injury which can be specific to patient, procedure, or guidance.

- Patient-specific factors include presence of preoperative neuropathy, proximity of nerve to the joint or anatomical variations of the nerve.
- Procedural factors include patient positioning, needle trauma, tourniquet-related pressure injury, local anesthetic neurotoxicity, pressure injury from injection, hematoma or cement impaction.
- The guidance factors mainly include the technique of performing injections, incorporation of a safety culture into the practice and the use of guidance techniques such as ultrasonography.

A thorough understanding of regional anatomy and avoiding deeper injections (beyond 2–3 cm than the tissue plane) may minimize neurologic complications. Large bore needles and cutting needle design can result in greater degree of nerve injury compared to a smaller bore needle and those with a Tuohy needle tip [98–101]. Although negative aspiration is considered a safe practice when performing injections in dangerous areas, it may not be useful in preventing nerve injuries. Higher concentrations of local anesthetics are seldom used for LIA; hence, concerns about local anesthetic neurotoxicity are minimal. Performing LIA should be safe in the presence of preexisting nerve injury or neuropathy and such decisions should be made on a case-to-case basis. Upon suspicion or discovery of a neurologic injury following a nerve block, development and course of the injury should be investigated. Injuries with motor weakness or progressive neurologic deficit require urgent remedy to prevent long-term morbidity while minor and stable symptoms of nerve dysfunction may require observation and follow-up. For further discussion on the topic, please refer to Chaps. 4 and 7.

Vascular Puncture

The incidence of vascular puncture following the insertion of wound catheters are known to be around 5 % [86]. It is important not to inject more than 2–3 cm deeper than the tissue plane for LIA. Use of control syringes to aspirate before injections into dangerous areas may minimize the problem. Although this may be useful in total hip arthroplasty, the use of a tourniquet may make it unreliable in knee surgery. The incidence of bleeding and hematoma is increased in situations where any preexisting coagulopathy or use of anticoagulants or other agents, which may exacerbate bleeding, are used concomitantly. The concerns of bleeding complications for LIA are similar to those delineated for superficial nerve blocks in Chap. 8.

Local Anesthetic Systemic Toxicity (LAST)

Local infiltration analgesia utilizes a large volume of local anesthetics and hence has a potential for LAST. It is well known in peripheral nerve blocks that the systemic absorption of local anesthetic differs depending on the site of the block due to differences in regional blood flow and tissue binding [102]. The same principles apply to LIA and given the large amount of local anesthetics used, plasma levels of local anesthetics do rise following single injection or continuous infusions but below toxic levels required to precipitate LAST. The addition of epinephrine to the LIA cocktail and the vasoconstrictive properties of ropivacaine may contribute to a delayed systemic absorption and reduce peak concentrations of local anesthetics in blood. Two studies have looked at plasma local anesthetic levels following LIA in hip and knee arthroplasty. Following a single injection of 200 mL of 0.2 % ropivacaine (400 mg) without adjuvants, Brydone et al. [103] continued 0.2 % ropivacaine infusion at 10 mL/Hr in patients undergoing TKA. The total and unbound plasma ropivacaine levels in the 24 h period were between 0.147–3.093 μg/ml and 0.001–0.104 μg/ml, respectively. Although total levels were above the higher level of clinically accepted range (2.2 μg/ml) [104], none of the patients had symptoms of LAST and probably because the unbound plasma ropivacaine levels were within normal range (0.15 ± 0.08 μg/ml. A similar study of single injection of LIA following THA (180 mL of 0.2 % ropivacaine) showed the total and free plasma ropivacaine concentrations were in the range of 0.081–1.707 μg/ml and 0.000–0.053 μg/ml [105]. The addition of epinephrine to the cocktail may further impede the systemic absorption of LA. A second line of protection is provided by an increase in α1-acid glycoprotein, an acute phase reactant known to increase post surgery. α1-acid glycoprotein is the main binding protein of local anesthetics in the blood, and its increase in the immediate postoperative period may act as a buffer for the systemically absorbed local anesthetics [106, 107]. The maximum allowable doses of local anesthetics commonly used for LIA are given in Table 24.3 but it must be remembered that the final clinical picture is the result of a balance between systemic absorption (impeded by epinephrine, ropivacaine, tourniquet) and elimination (α1-acid glycoprotein binding and liver function) and the doses have to be reduced when elimination pathways are impaired.

Some institutions practice combining adductor canal blocks with LIA for TKA where LA overdose may occur if communication is not made adequately. Combining multiple peripheral nerve blocks with LIA may result in toxic doses of local anesthetic being administered particularly in some of the smaller patients. In addition, risks of LAST re-bolus via catheter also had been reported by Tofdahl et al. [20] where two patients had symptoms of LAST during reinjection through the catheter.

Practice Points to Minimize LAST in the Context of LIA

- Normal doses of local anesthetic range from 200–400 mg of ropivacaine in healthy individuals. Use epinephrine if doses more than 200 mg are to be used and preferably never go beyond 300 mg for single injections.
- Rather than calculating the maximum allowable doses, minimum effective doses need to be utilized for each patient after due consideration of age, weight, and comorbidities.
- Restrict the volume of local anesthetic mixture to 60–80 ml in patients who are asthenic, weight less than 60 kg or in the presence of liver, kidney, or heart disease.
- If multiple peripheral nerve blocks are done, do not combine it with LIA.

Table 24.3 Local anesthetic doses commonly employed for infiltration analgesia

Local anesthetic	Maximum allowable dose for single injection	24 h allowable dose	Volumes of commonly used LA solutions
Lidocaine	300 mg (5 mg/kg) q 2 h	20–50 mcg/kg/min	Not used for LIA
Levobupivacaine/ Bupivacaine	150 mg (2 mg/kg) q 4 h	400 mg (5.5 mg/kg) Infusion rates of 4–10 ml/h. of 0.1 % or 0.125 % solution	0.1 %—150 ml 0.125 %—120 ml 0.25 %—60 ml (rare) 0.5 %—30 ml (rare)
Ropivacaine	225 mg (3 mg/kg) q 4 hours	800 mg (11 mg/kg) Infusion rates of 4–10 ml/hr. of 0.2 %	0.2 %—150–200 ml 0.3 %—100 ml 0.35 %—80 ml 0.5 %—50 ml (rare) 0.75 %—30 ml (rare)

Impact on Wound Healing/Revision Surgery

Earlier studies documented 2/80 patients developing wound complications requiring plastic surgery [20]. Since the ingredients in the LIA cocktail contain multiple drugs, all drugs are to be tested for their impact on wound healing. Local anesthetics have been tested in vitro for their impact on wound healing and were found to be safe and did not impact wound healing [108]. The original cocktail recommended a high concentration of epinephrine (10 mcg/ml). We have reduced the dose of epinephrine to 2.5–5.0 mcg/ml in our institution. Ketorolac is a common ingredient of the LIA cocktail which has shown analgesia benefits when combined with ropivacaine and epinephrine [109]. Ketorolac and other NSAIDs may have an adverse impact on bone metabolism and fibroblast activity thereby potentially impacting new bone formation and wound healing [110, 111]. A long-term follow-up study of THA patients (mean follow-up period of 7.3 years) has put this fear to rest showing no increased risk of prosthesis loosening when ketorolac was used for LIA [112].

Future Directions

LIA can provide superior analgesia with a lower incidence of side effects in Total Knee Arthroplasties. In future, LIA may play an even more important role with the introduction of liposomal bupivacaine. Liposomal bupivacaine (Exparel) is a long-acting depot formulation of bupivacaine which is particularly suited for LIA. This might obviate the need for catheters in the wound and thus avoid catheter-related problems with LIA. The results from ten different phase 2 and 3 trials indicate EXPAREL having a similar analgesia profile and impact on wound healing as that of conventional bupivacaine [113, 114]. This drug has the potential to make LIA really attractive for these painful orthopedic procedures and needs to be evaluated further.

Conclusion

Presently, the efficacy of LIA may not be superior to oral multimodal analgesia but LIA seems to perform better compared to PNB in THA. Lack of motor block with LIA compared to peripheral nerve blocks may impact early recovery scores but its impact on discharge from the hospital needs further evidence. LIA is cheap and easy to administer but should be avoided in situations where an intact synovium is to be encountered. Continuous intra-articular infusions may improve analgesia but increase the risk of surgical infections. Further studies are required with the use of long-acting bupivacaine for LIA. Studies are also required to evaluate its role in preventing chronic postsurgical pain. In addition, there are still many questions needed to further address. Which component of LIA is the contributing factor for analgesia beyond the duration of action of ropivacaine? Does LIA alter wound healing? What is the role of adjuvants such as morphine and corticosteroids in the mixture? Is there a role of long-acting ropivacaine or liposome bupivacaine for LIA? Does the use of LIA improve global outcomes in patients undergoing arthroplasty? Currently, most of the patients that have received LIA for early discharge are all relatively healthy. More studies are needed to evaluate its efficacy in the elderly. For one to benefit from LIA, a paradigm shift with patient processing and rehabilitation is essential. Currently, most of the patients that have received LIA for early discharge are all relatively healthy. More studies are needed to evaluate its efficacy in the elderly.

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Local and Regional Anesthesia in Plastic Surgery: Safety Considerations and Management of Adverse Events

25

John Mesa, Don Lalonde, and Luis O. Vasconez

Key Points

- Plastic surgery procedures rely on different approaches to local and regional anesthesia. Tumescent anesthesia (injection of large volumes of dilute local anesthetic, most commonly lidocaine) is used for liposuction and face-lift surgeries, while digital blocks are commonly used for hand surgeries. Traditional regional approaches (e.g., paravertebral or epidural blocks) have been used for breast augmentation.
- Local anesthetic systemic toxicity—and its associated symptoms—is the primary complication associated with plastic surgery regional anesthesia. Injection of rapidly absorbed local anesthetics into vascular areas heightens the risk. Topical anesthetics have also been implicated in local anesthetic toxicity.
- Other complications described following regional anesthesia for plastic surgery procedures include Horner syndrome, pneumothorax, direct injury to the nerve, block failure, and problems associated with infusion pumps.
- General considerations for avoiding local anesthetic toxicity for plastic surgery include use of epinephrine and appropriate local anesthetic doses, avoiding intravascular injection, and allowing sufficient time before reinjecting an area. Proper monitoring and an intervention plan in case of toxicity are also mandatory.

J. Mesa, MD (✉)
Private Practice Plastic Surgeon, 200 South Orange Ave, Suite 255, Livingston, NJ 07039, USA
e-mail: jmesa@doctormesa.com

D. Lalonde
Division of Plastic and Reconstructive Surgery, Saint John Regional Hospital and St Joseph's Hospital, Saint John, NB, Canada
e-mail: dlalonde@drlalonde.ca

L.O. Vasconez
Birmingham Veterans Affairs Medical Center, Birmingham, AL, USA

Children's Hospital of Alabama, Birmingham, AL, USA
e-mail: luis.vasconez@ccc.uab.edu

Introduction

The use and toxicity of local and regional anesthesia in the modern plastic surgery practice is arguably the most important topic for any anesthesiologist and/or surgeon working in this field of medicine. Lidocaine toxicity, primarily in the context of suction assisted lipectomy, lipoplasty, or liposuction, has historically accounted for a significant proportion of patient morbidity and mortality [1–4].

Local anesthetics vary considerably in their potential for causing systemic toxic reactions. In clinical practice, the systemic toxic responses to local anesthetic drugs may result from unintentional intravascular injection of an appropriate dose or from excessive dosing in the appropriate location. Toxicity secondary to extravascular administration is related to the pharmacokinetic properties of the drug and absorption of injected solutions from peripheral sites [5].

Lidocaine, the most common local anesthetic used in plastic surgery, has inherent vasodilating properties. At the capillary bed level, vasodilatation acts to accelerate the absorption of lidocaine from injected tissues. The addition of epinephrine to a solution of lidocaine nearly doubles the duration of lidocaine activity because the vasoconstriction produced offsets the vasodilatation from the lidocaine. When using local or regional anesthesia in plastic surgery, preoperative evaluation should be performed in all patients, preferably in advance of the scheduled surgery in elective cases. Patients should be fasting whenever possible according to the institutional policy for the type or procedure.

The surgeon and surgical team must be always prepared to induce general anesthesia when the local or regional anesthesia fails and the surgery should be completed as per situation

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_25

evaluation. Therefore, all necessary equipment (intubation equipment), personnel (anesthesiologist, CRNA), and medications should be immediately available at hand depending on the case.

This chapter will focus on the use of local anesthesia and regional anesthesia as it pertains to the practice of plastic surgery. This chapter will not discuss issues related to pediatric local or regional anesthesia.

Local and Regional Anesthesia in Liposuction (Tumescent Anesthesia)

The 2014 census by the American Society for Aesthetic Plastic Surgery (ASAPS) records the number of lipoplasty procedures for that year to be 342,494. Liposuction ranks as the number one most popular cosmetic surgical procedure performed on an annual basis in the United States. Liposuction has seen a 94 % increase in the number of procedures performed since ASAPS initiated its first survey in 1997.

Tumescent liposuction involves infusion of a solution of diluted local anesthetic into the subcutaneous fat layer. This serves to hydrate the fat layer in preparation for aspiration. Then fat is removed from the targeted areas by the aspiration through microcannulas [2, 6]. The tumescence solution typically consists of 1 l of normal saline containing 500–1000 mg of lidocaine, 0.25–1.0 mg of epinephrine, and 12.5 mmol of sodium bicarbonate [2, 7]. Its components provide prolonged local anesthesia and minimize blood loss. Large-volume liposuction, defined as the removal of more than 5000 ml of fat, may require the infusion of several liters of this solution [6, 8].

Historically, the maximum "safe" dose of subcutaneous lidocaine injection has been limited to 4.5 mg/kg without epinephrine and 7.0 mg/kg with epinephrine [9]. This topic has been the source of considerable confusion for clinicians and between plastic surgeons and anesthesiologist not familiar with local anesthesia in cosmetic plastic surgery. Multiple factors, such as the concentration of the local anesthetic, dilution of the local anesthetic, site(s) of injection, etc., affect the maximum safe dose of local anesthetics.

Lidocaine has a long-term, excellent safety record in dentistry and several surgical procedures [8, 10]. Tooth extraction and oral surgery, skin excisions, hand surgery, and liposuction can be performed under local anesthesia without the need of either general anesthesia or IV sedation [8, 10–12]. The maximum safe dose of lidocaine in liposuction by the tumescent technique is considerably higher than what is recommended with dry techniques (7 mg/kg). Studies by Klein have shown that even high doses of lidocaine tumescence anesthesia of 35 mg/kg [13] and 55 mg/kg [8] for large volume liposuction are safe since the peak lidocaine serum levels (average 2.37 μg/ml) remained below the threshold for subjective toxic levels (3 μg/ml). According to the author, large doses of lidocaine can be administered safely during tumescent liposuction because of dilution by the wetting solution, slow infiltration into a poorly vascularized space, and the vasoconstrictive effect of epinephrine, which delays and diminishes systemic absorption of the drug. The slow absorption curve of lidocaine in this situation keeps its peak blood level low and prolongs its effect in peripheral tissue. Several authors have replicated these findings [14–16].

Tumescence Liposuction Combined with Local and Regional Anesthesia in Plastic Surgery

Studies by Burt and Vasconez et al. have shown the safety of combining tumescence liposuction surgery with esthetic plastic surgery of the face and breast that requires infiltration of additional lidocaine with epinephrine [17]. In their study, when patients were infiltrated tumescence anesthesia consisting of lidocaine with epinephrine in normal saline with a mean dose of 22.9 mg/kg (range of 11.2–38.3 mg/kg) and additional 0.5 % lidocaine with epinephrine was infiltrated in the face, breast, or abdomen (additional average dose 5.38 mg/kg, range 0.4–12.1 mg/kg), the peak levels of lidocaine were safely below 3 μg/ml [17]. No patient presented subjective clinical signs of lidocaine toxicity.

Swanson also has reported the safety of lidocaine and bupivacaine used as tumescence solution containing epinephrine in patients undergoing liposuction and abdominoplasty [18]. In his prospective cohort, patients received infusions containing 0.05 % lidocaine (liposuction) and/or 0.025 % bupivacaine (abdominoplasty) with 1:500,000 epinephrine. Plasma levels of lidocaine, bupivacaine, and epinephrine were studied in 76 consecutive patients. The maximum lidocaine dose was 3243 mg and the maximum level was 2.10 μg/ml. The maximum bupivacaine dose was 550 mg and the maximum level was 0.81 μg/ml. No clinical toxicity was encountered.

Caution must be exercised when injecting local anesthetics in patients with liver disease because their ability to metabolize local anesthetics is impaired. The t1/2 for lidocaine following IV administration in healthy patients is 1.4 h and increases to 7.3 h in patients with active hepatitis [19]. The clearance of ropivacaine is decreased by 60 % in patients with end-stage liver disease compared with healthy volunteers [20]. Single-injection techniques using the recommended doses of local anesthetics are safe in patients with hepatic dysfunction. However, repeated injections may increase the risk of toxicity, thus the subsequent doses should be decreased. Renal function also affects the local anesthesia toxicity. The half-life of the lidocaine metabolites can increase and therefore cause central nervous system toxicity.

The dose of local anesthetic should be reduced by 20–30 % in uremic patients even with single-injection techniques, and especially when large doses of drugs are usually required.

Local and Regional Anesthesia in Abdominoplasty

Abdominoplasty, traditionally performed in the inpatient setting, is becoming an outpatient procedure with advancements in anesthetic and surgical techniques. Early discharge to home, decreased costs, and proven safety in performing such procedures in the outpatient setting are the proposed reasons for this trend. Using local or regional anesthesia techniques in abdominoplasties, multiple authors have described the avoidance of traditional inhalational general anesthesia [21–23]. Michaels and Eko described the use of use of rib blocks with conscious sedation to facilitate abdominoplasty in the outpatient setting with excellent results [21]. Mustoe et al. detailed the use of conscious sedation and local anesthesia for abdominoplasties, with extremely good outcomes and almost no unplanned hospitalizations, and with high patient satisfaction rates [22]. Rosenberg et al. described 106 abdominoplasties performed with procedural sedation and local anesthesia [23].

Local Anesthesia in Hand Surgery

Hand surgery has been traditionally performed under either general anesthesia or IV sedation or local anesthesia. Lalonde et al. have shown that it is possible to perform successful wide-awake hand surgery under local anesthesia without the need of IV sedation or general anesthesia [11, 24, 25]. The author has shown that is it possible to perform hand tendon repair under pure local anesthesia without the use of tourniquet or any type of sedation or other anesthesia modality [11]. Chan et al. have also shown that carpal tunnel release can be successfully performed under local anesthesia using either lidocaine or ropivacaine [26].

Traditional medical texts have perpetuated the belief that local anesthesia containing epinephrine should not be injected in fingers, toes, ears, and nose [27, 28]. All of the evidence for the antiadrenaline dogma comes from 21 mostly pre-1950 case reports of finger ischemia associated with procaine and cocaine injection with epinephrine. Thompson et al. performed an in-depth review of the literature surrounding this topic [29]. They carefully examined each of the 48 cases of digital necrosis cases associated with local anesthesia. Of those 48 patients, 21 had epinephrine injected with the local anesthetic. The fact that there were actually more cases of local anesthetic-related digital infarction in which epinephrine was not involved leads to the logical conclusion that epinephrine was not the only factor inducing digital necrosis in the time period before 1950 when 42 of these cases occurred. Almost all of the 48 cases of finger death associated with local anesthetics involved procaine. Procaine or cocaine is known to potentially cause digital infarction. However, the fact that finger infarction was linked to the use of adrenaline established the dogma, based on invalid evidence, of "avoiding the use of epinephrine in fingers."

Lalonde et al. performed a prospective multicenter study to examine the incidence of digital infarction in a large series of patients in whom local anesthesia with adrenaline was injected electively into the hand and fingers from 2002 to 2004. A total of 3110 consecutive cases of elective injection of low-dose epinephrine (1:100,000 or less) in the hand and fingers and none produced any instance of digital tissue loss. Phentolamine was not required to reverse the vasoconstriction in any patients. The authors concluded that incidence of finger infarction in elective low-dose epinephrine injection into the hand and finger was likely to be remote, and that therefore hand (finger) surgery could be performed with local anesthesia containing epinephrine [30].

Long-acting local anesthetics have been also found to be safe in hand surgery. Keramidas et al. studied the efficacy and safety of ropivacaine vs. lidocaine in digital nerve block in a prospective study of 70 adult patients. Patients that underwent immediate reconstruction for traumatic injuries of the digits with either ropivacaine or lidocaine had effective pain control during the procedure and no local anesthetic-associated side effects [31].

Local Anesthesia in Face Lift

The tumescent technique injects large volumes of fluid with dilute anesthetic solution into the subcutaneous fat plane to facilitate dissection while providing anesthesia and producing vasoconstriction to reduce bleeding. The tumescent technique was adopted for face lifts by Brody, which he initially described in 1994 [32]. La Trenta has documented that the use of tumescence local anesthesia on face-lift surgery under IV sedation facilitates the subcutaneous dissection, creates a near bloodless surgical field, and decreases the incidence of hematoma formation [33]. Ramon et al. also showed that when high doses of diluted lidocaine with epinephrine (0.33 %, up to 6.3 mg/kg) were used in six prospective female patients undergoing elective face-lift surgery under IV sedation, there were no lidocaine-related side effects recorded [34].

Mesa and Vasconez showed that face lifts and neck lifts can be performed, wide awake, under local anesthesia using the tumescence technique, without the need of general anesthesia, IV sedation, or heavy oral sedation. In a prospective

study, 40 patients were enrolled to undergo face lift and neck lift under either local anesthesia or general anesthesia. Both groups of patients received diluted tumescent local anesthesia consisting of 0.25 % lidocaine and 1:400,000 epinephrine buffered with sodium bicarbonate in the surgical field (midface, lower face, and neck). Patients that elected surgery under wide-awake pure local anesthesia underwent the procedure without any intraoperative pain. None of the patients in either group presented clinical signs of lidocaine toxicity postoperatively [35, 36].

Regional Anesthesia in Plastic Surgery

Regional anesthesia supplement with sedation for breast surgery, either reconstructive or cosmetic plastic surgery has been successfully, but is an uncommon practice compared with general anesthesia [37, 38].

Thoracic epidural anesthesia has been shown to be effective in intra-op and postoperative pain control in breast augmentation. Lai et al. studied 30 consecutive patients undergoing submuscular breast augmentation under continuous thoracic epidural anesthesia [39]. His study found that all cases were successfully anesthetized, except one case (3 %) that had a partial analgesic effect and required supplemental general anesthesia. Perioperative complications included transient shivering (33 %), stuffy nose (20 %), nausea (7 %), and shortness of breath (13 %). These symptoms were alleviated after reassurance or light sedation and oxygen inhalation. Immediate postoperative pain of the operative site was effectively controlled by injection of local anesthetics through the epidural catheter. There were no serious side effects associated with this type of regional anesthesia for breast augmentation [39].

Paravertebral nerve bock (PVD) for breast augmentation has also been shown to be successful. Gardiner et al. evaluated the safety and efficacy of PVB (ropivacaine) compared with surgical field local anesthesia infiltration for pain control in breast augmentation patients. He found that PVB with ropivacaine is superior to direct surgical infiltration of ropivacaine for bilateral breast augmentation in same-day surgery [40].

Regional anesthesia without IV sedation or general anesthesia, has also been successfully used in breast augmentation [41]. Shimizu et al. evaluated the efficacy and safety of combined intercostal nerve block and tumescent anesthesia (without IV sedation) for breast augmentation in 35 prospective patients. In his study intercostal nerves innervating the T-3 to T-6 regions, were anesthetized using 0.5 % bupivacaine. Tumescent solutions consisting of lidocaine, epinephrine, and saline were injected around the mammary gland. Breast augmentation was conducted using silicone implants. The majority of patients (31/35) reported no pain during the procedure. No patient experienced pneumothorax or toxicity of local anesthetics [42].

Complications of Local and Regional Anesthesia in Plastic Surgery

Epidemiologic information about the incidence of local and regional anesthesia toxicity in plastic surgery is quite scarce. The following report provides information pertinent to the practice of plastic surgery.

Local anesthetic toxicity usually occurs for three main reasons: intra-arterial injection, intravenous injection, and absorption of local anesthetic from peripheral injection [43]. Intra-arterial injections are usually associated with regional anesthetic techniques in the head and neck region (interscalene block, cervical plexus block, ophthalmic blocks, blocks in the face and scalp region, dental blocks, and stellate ganglion blocks) and are usually characterized by a rapid onset of symptoms as the local anesthetic directly enters the cerebral circulation. Small quantities are sufficient to produce symptoms. Intravenous injection (inadvertent) usually occurs during the performance of epidural or caudal anesthesia. Bolus injections of local anesthetic used for these blocks, despite clearance by the pulmonary and hepatic tissues, are sufficient to produce blood levels high enough to cause central nervous system toxicity. Absorption of local anesthetic from peripheral injection, such as peripheral nerve block or subcutaneous tissue infiltration is the more common cause of toxicity in plastic surgery procedures. In these cases, the blood levels produced depend on the site of injection, the total dose of the local anesthetic agent, and the presence or absence of vasoconstrictors.

Central Neural Blockade Following Local and Regional Anesthesia in Plastic Surgery

Most toxic reactions of local and regional anesthesia involve the central nervous system. Initially, there is an excitatory phase manifesting as muscle twitching, first in the face and distal extremities, that progress to tremors and ultimately to generalized tonic–clonic convulsion. As the anesthetic levels in the CNS rise, a depressive phase ensues, evidenced by drowsiness, unconsciousness, and respiratory arrest [44].

Kairaluoma et al. reported the case of CNS toxicity after a single-injection paravertebral block (SPVP) with 0.5 % bupivacaine for breast surgery [45]. The patient developed convulsions after an SPVB without losing consciousness, which was aborted by a small dose of a benzodiazepine; the author suggested the adverse event was most likely caused by an accidental intravascular injection of part of the local anesthetic.

Toxicity of Long-Acting Local Anesthetics in Plastic Surgery

Bupivacaine, a long-acting local anesthetic, is known for having cardiotoxic effects when compared with short-acting local anesthetics like lidocaine [46]. Sudden cardiovascular collapse (ventricular fibrillation or ventricular· tachycardia, cardiac asystole, or complete heart block with P waves only) that most of the time it is refractory to resuscitative measures has occurred almost immediately after rapid intravascular injection of the local anesthetic agent [46, 47].

Ropivacaine, a long-acting local anesthetic, is known to be less cardiotoxic than bupivacaine [48]. Complications about the use of ropivacaine and bupivacaine in plastic surgery are scarce. Fayman et al. compared the use of bupivacaine and ropivacaine for infiltration anesthesia for bilateral breast surgery. In his study he found that women undergoing either breast reduction or submuscular breast augmentation that underwent infiltration with either bupivacaine or ropivacaine for postoperative pain control did not present complications associated with the use of either local anesthetic [49]. Additionally, in terms of analgesia, they found that overall analgesia achieved with bupivacaine and ropivacaine infiltrations was not statistically different.

A prospective double-blind study was conducted to compare the analgesic properties of levobupivacaine and ropivacaine in a bilaterally symmetrical mastopexy model, which demonstrated that both anesthetics provided satisfactory analgesia for at least 10 h, and none was associated with local anesthetic-related toxicity [50].

Cardiotoxicity of Local Anesthetics in Plastic Surgery

Cardiovascular collapse from accidental local anesthetic toxicity is a rare but catastrophic complication of regional anesthesia. The long-acting amide local anesthetics bupivacaine, levobupivacaine, and ropivacaine have differential cardiac toxicity, but all are capable of causing death with accidental overdose [51]. Bupivacaine, levobupivacaine, and ropivacaine are three long-acting amide-based local anesthetics most commonly used in clinical practice.

Of all the amide local anesthetics, bupivacaine exhibits the most cardiotoxicity, which is often the result of a sudden increase of its concentration in the plasma. There is increasing evidence in the anesthesia literature supporting the use of lipid therapy to treat bupivacaine- and ropivacaine-induced toxicity after failure of established resuscitation measures [52]. However, published reports regarding local anesthetic-induced cardiac collapse in esthetic surgery are rare.

Overall, available data suggest that although systemic toxic reactions and cardiotoxicity to long-acting local anesthetics such as bupivacaine, ropivacaine, and levobupivacaine remain significant risks, these problems appear to have evolved to a level where they are comparable to other significant risks of regional techniques, especially in plastic surgery [43].

Vascular Complications of Local and Regional Anesthesia in Plastic Surgery

Major arteries and sizable arteries and arterioles could be punctured while injecting local or regional anesthesia for plastic surgery. Knowledge of the vascular anatomy of the area treated is paramount to avoid accidental vascular complications. The overall incidence of inadvertent vascular puncture and hematoma formation after paravertebral nerve blockade is 6.8 % and 2.4 %, respectively [53]. For local anesthesia administration the data is scarce.

In plastic surgery, the incidence of vascular complications secondary to local or regional anesthesia is very low. In general, the incidence of a meta-analysis of randomized controlled trials about the efficacy and safety of paravertebral blocks in breast surgery by Schnabel et al. showed that none of the trials evaluated reported any patients with vascular puncture or nerve damage [54].

Horner Syndrome Following Local and Regional Anesthesia in Plastic Surgery

Horner syndrome, the development of the classic triad of miosis, partial ptosis, and loss of hemifacial sweating (anhidrosis) secondary to the blockade of the sympathetic pathways that supply to the eye has been reported during local anesthesia administration in plastic surgery. Schnabel et al. in a meta-analysis of fifteen randomized controlled trials (published between 1999 and 2009) found the incidence of Horner's syndrome after paravertebral blocks in breast surgery was present but low [54]. In a trial testing of single-injection paravertebral block (SPVB) for breast surgery, only one developed Horner's syndrome. In another randomize trial for multiple-injection paravertebral nerve block (MPVB) for breast surgery, 11 patients developed Horner's syndrome [55]. Burlacu and Buggy also reported a case of Horner's syndrome in breast plastic surgery. A patient undergoing left mastectomy and immediate latissimus dorsi breast reconstruction under combined paravertebral block and general anesthesia developed left-sided Horner syndrome postoperatively [56].

Failure of Local Anesthesia and Regional Anesthesia in Plastic Surgery

Between local and regional anesthesia, the highest incidence of failure occurs following regional anesthesia. With infiltration the local anesthesia in the surgical field, most of the time the surgical field is completely anesthetized and therefore the failure is minimal. In regional anesthesia since success depends on multiple factors like location of the injection close to the nerve, etc., the failure rate has been reported in general to be between 5 and 20 %. Cooter and Gardiner evaluated the efficacy of paravertebral block in 100 ambulatory patients undergoing submuscular breast augmentation (172 single-level paravertebral blocks, 72 bilateral blocks and sedation). Their technique consisted of a single-injection paravertebral block at T4 level using a loss of resistance technique. They reported a failure rate of 13 % for surgical anesthesia and 6 % for postoperative analgesia [57].

Michael and Eko also evaluated the effectiveness of rib block for pain control in patients undergoing abdominoplasty outpatient surgery. They compared the outcomes of patients undergoing abdominoplasty under general anesthesia ($n = 9$) vs. rib blocks placed by the surgeon and supplemental intravenous anesthesia with additional airway control by laryngeal mask as needed ($n = 29$). In their study, three of the 29 rib block patients required inhalation anesthesia because of rib block failure (failure rate of 10 %) [21]. Hidalgo has also described the use of rib blocks for breast augmentation with mixed results [58, 59].

Nerve Injury Following Local and Regional Anesthesia in Plastic Surgery

Nerve injury following local anesthesia injection in general procedures has been reported in the literature [60]. However, recent data on the incidence of nerve injury after local anesthesia injection for plastic surgery is sparse. A meta-analysis of randomized controlled trials about the efficacy and safety of paravertebral blocks in breast surgery by Schnabe showed that none of the trials evaluated reported any patients with nerve damage [54].

Porter evaluated the safety and efficacy of regional anesthesia for hand surgery. He did a prospective audit out of 153 consecutive regional anesthetics for hand surgery, using intravenous regional anesthesia (IVRA), axillary block, or multiple peripheral nerve blocks. He found that surgery was carried out successfully in 147 patients. All patients but two (1.3 %) complained of paresthesia after regional nerve blocks. The rest of the patients had no nerve block-related side effects in the upper limb [61].

Plastic surgery of the hand and forearm is frequently performed on ambulatory basis. When blocks/regional blocks are performed on these patients, they should be warned both verbally and on written instructions about unknowingly injury to the anesthetized limb (e.g., touching a hot surface like stove, iron, or heater). They should also be specifically warned about caution when lying on the anesthetized extremity to avoid pressure sores and other injuries.

Accidental Injection of the Wrong Local Anesthetic Solution in Plastic Surgery

Accidental injection of the wrong anesthetic solution doesn't happen frequently in plastic surgery. Fortunately, reports of accidental injections of the wrong solution are rare. However, some reports have shown devastating consequences for the patient. Chapman has reported one case of skin and soft tissue necrosis in a 24-year-old healthy patient after tumescent liposuction of the lateral tight (subtrochanteric regions). The patient was inadvertently injected with tumescence solution made with hypertonic saline (sodium chloride 3 %), rather than normal saline. The patient initially complained of pain in the right thigh that subsequently resulted in skin and subcutaneous tissue necrosis. The defect required management with several reconstructive surgeries and the patient was left with a permanent scar [62]. Kerfant et al. also reported the case of 34-year-old woman who experienced inadvertent subcutaneous injection of hypertonic saline solution during body fat harvesting [63].

Pneumothorax After Local/Regional Anesthesia in Plastic Surgery (Breast Surgery)

Pneumothorax could be a frightening complication after local or regional block, especially in elective cosmetic plastic surgery. An episode of coughing or sudden inspiratory effort while performing the block may indicate that the pleura has been penetrated and the lung punctured. Symptoms and signs may not develop for hours and patients may not be symptomatic until a 20 % pneumothorax is present. A pneumothorax of 25 % or greater usually requires a chest tune placement.

A pneumothorax could happen during a chest local anesthesia infiltration or rib block for postoperative pain control purposes while under IV sedation or general anesthesia. Kaye et al. reported the case of an intraoperative tension pneumothorax in a young healthy woman undergoing breast augmentation under general anesthesia, secondary to local anesthesia administration for postoperative pain control [64]. A 32-year-old, 60 kg, woman without any significant medical history, underwent a bilateral breast augmentation and rhinoplasty. She underwent a routine general endotracheal anesthetic. Prior to the surgical incision, the surgeon infiltrated the breast with lidocaine with epinephrine. Six hours into the surgical procedure, the patient developed hemodynamic compromise

and was diagnosed with tension pneumothorax, which was treated emergently with a 14-gauge angiocatheter placed intrapleurally. Osborn and Stevenson also reported the incidence of pneumothorax during breast augmentation secondary to needle puncture during local infiltration. In a survey sent to 363 members of the California Society of Plastic Surgeons in 2001, the results showed that out of 83 pneumothoraxes reported, 37 % were secondary to needle puncture at the time of local injection [65]. Schnabel et al. also reported in a meta-analysis that pneumothorax occurs during paravertebral block in breast plastic surgery. They found the incidence was very low. Of 15 patients, only one patient was reported to develop accidental pneumothorax after paravertebral block in breast surgery [54, 66].

If ambulatory plastic surgery patients are being given chest wall local anesthesia and/or rib blocks, they should be warned in advance about the risk of pneumothorax, and given instructions (verbally and written) on how to proceed should symptoms develop.

In summary, the occurrence of pneumothorax after infiltration of local anesthesia in the chest wall or rib block, in plastic surgery procedures of the chest like breast surgery, is rare.

Complications of Local Anesthesia in Face Lift

Complications of local anesthesia in face lift and neck surgery in plastic surgery are very rare but have been reported. Ramirez and Galdino published a case report of unilateral superficial skin loss when using tumescent local anesthesia technique during a face lift and neck lift [67]. In their report, a 59-year-old female that underwent cervicofacial rhytidectomy under IV sedation was infiltrated with local anesthesia in the operative field. The midface, lower face, and neck were infiltrated with 300 cc of 0.25 % xylocaine with 1:400,000 epinephrine solution in the subcutaneous plane using the tumescent technique with a blunt needle and 10 cc syringes (150 cc each side). The author reported that in several areas of the right jaw line, there was evidence of a "peau d'orange" appearance of the skin, indicating a subdermal or intradermal injection. This finding was not evident in the contralateral side. During follow up 24 h of surgery, a large area of intense ecchymosis was observed in the right facial flap, thought to be due to a small interstitial hematoma that required no surgical management. Three days later, they noticed the ecchymosis had progressed to blistering over the skin in the pretragal and tragal areas and two other small, nonadjacent areas on the right jaw line. The areas of blistering had progressed from intermediate to almost full-thickness skin necrosis. The contralateral side did not have any changes indicating vascular compromise. The surgical wound had to be opened and managed with dressing changes and allograft skin grafts. Once the wounds were healed, the patient underwent revisional surgery with satisfactory esthetic outcome. The author suggested the complications observed were potentially secondary to the infiltration of the tumescent local anesthetic. They proposed that factors like time between the injection and surgical incision and undermining, hydrostatic pressure in the skin that reveals a definitive peau d'orange appearance, and the vasoconstrictive effect of epinephrine could all have been factors implicated in the development of the complication.

Allergic Reactions of Local Anesthetics in Plastic Surgery

Allergic reactions to local anesthetics are more common with ester-type local anesthetics than with amide-class agents. The metabolic product of ester local anesthetics is PABA (para-aminobenzoic), which is highly allergenic [68, 69]. When an allergic reaction to an amide local anesthetic occurs, it is usually due to preservatives such as methylparabens and metabisulfite, and not the local anesthetic agent itself. Symptoms of the allergic reactions fall into either type I anaphylactic and/or type IV delayed hypersensitivity responses. Symptoms include erythema, pruritus, urticaria, facial swelling, nausea, vomiting, coughing, wheezing, dyspnea, cyanosis, laryngeal edema, abdominal cramps, and diarrhea. For anaphylaxis it is essential to maintain the patient's airway and deliver oxygen following the BLS and ACLA guides [70, 71]. Administration of epinephrine 0.5 mg (5 ml in 1:10,000 solution) intravenously repeated every 5–10 min is the treatment of choice [69]. Reports of allergic reactions to local anesthetics in plastic surgery are lacking very likely due to the widespread use of lidocaine as main agent for local and regional anesthesia, which is known to have nonallergic side effects.

Complications of Local Anesthesia Infusion Pain Pumps in Plastic Surgery

The use of an infusion pain pump that delivers local anesthetics with catheters in a local wound has increased in the plastic surgery specialty [72]. Autologous breast reconstruction with deep inferior epigastric perforator (DIEP) and transverse rectus abdominis myocutaneous (TRAM) flaps may cause severe abdominal donor site morbidity; and infusion devices delivering local anesthetic are suggested to improve postoperative analgesia [73]. Several published studies have shown that the use of local anesthetic pain catheters for abdominal donor sites in microsurgical breast reconstruction, abdominal surgery (abdominoplasty, etc.) might be associated with a decreased use of narcotics and antiemetic medicaments and shorter hospital stay [72].

Heller et al. in a prospective, randomized, double-blind trial competed the effectiveness and safety of local anesthetic infusion and intravenous narcotic patient-controlled anesthesia pump for pain management in 48 patients that underwent free TRAM flap breast reconstruction [74]. The authors reported that patients with continuous infusion used lower mean doses of patient-controlled opioid during the first 2 postoperative days and transitioned earlier to oral opioids than did control patients. They also showed that there were no technical problems or complications related to the continuous infusion pump catheters and no adverse effects related to bupivacaine use.

Although pain pumps have been shown to be effective in controlling postoperative pain after abdominal plastic surgery, there was a believe that seroma formation, common in these plastic surgery procedures, could be associated with the use of pain pumps [75]. Smith et al. performed a study to elucidate the veracity of this assumption among plastic surgeons. The authors performed a retrospective chart review to evaluate all patients (n = 159) who underwent abdominal procedures (abdominoplasty, panniculectomy, and transverse rectus abdominis myocutaneous flap harvest) over a 3-year period. They found the overall seroma formation rate was 11.3 % (18 of 159 patients. The incidence of seroma was 11.0 % (11 of 100) in patients with pain pump use versus 11.9 % (7 of 59) in those who did not use a pain pump. The authors concluded there was no correlation between increased rate of seroma formation and use of a continuous-infusion local anesthetic pain pump system in their study population [76].

Toxicity of Topical Anesthetics in Plastic Surgery

When used appropriately, topical anesthetic creams are safe and effective even for plastic surgery purposes. Although topical application of an anesthetic usually produces minimal systemic effects, circumstances in which the skin is more permeable than usual allow the drug to be absorbed systemically, thereby producing adverse effects normally associated with parenteral administration [77].

Factors that increase the risk of toxicity with topical include application of the product over a large area, long duration of use, use of a product containing a high dose of anesthetic, application to skin that is not intact (as in the presence of rash or abrasion), skin vasodilatation (allowing a greater flow of blood near the surface of the skin) which can result from heating the skin by covering it with plastic, heating pad, or applying the drug immediately after exercise. Age is also a factor that affects the risk of toxicity. The skin of children and older adults is more permeable than that of young and middle-aged adults. The use of high dose use over a large area and the presence of vasodilatation very likely have led to the deaths of the young female patients after application of the topical anesthetics [77].

However, a problem can arise when anesthetic creams are compounded in formulas in nonstandard doses. In 2001, a 22-year-old college student died from lidocaine toxicity after she applied a 10 % lidocaine and 10 % tetracaine cream from her waist to her feet for her laser hair removal. She was not given instructions on how to apply the cream and there was no prescription written by a physician. The cream had been compounded and marked “for office use only” [78].

Deaths Related with Local and Regional Anesthesia in Plastic Surgery

Death associated with the use of local and regional anesthesia in plastic surgery are very rare but have been reported. They are usually related with the use of high doses of local anesthesia. Rao et al. studied the incidence of deaths associated with liposuction that included lidocaine in the tumescence solution in death-notifications records of the Office of Chief Medical Examiner of the City of New York between 1993 and 1996 [1]. Of the 1001 deaths certified as due to therapeutic complications, five of them related to liposuction. All five occurred during or after tumescent liposuction. The causes of the deaths were examined. Each patient underwent a complete autopsy, including appropriate examination and collection of blood from the heart. The amount of lidocaine each patient received was calculated from the volume and concentration of lidocaine in the infusate (tumescence solution), or the total number of milligrams of lidocaine infused, if available in the medical record. In that report, all death related cases were infiltrated with tumescent solutions: (patient 1) hypotension and cardiac arrest; (patient 2) intraop wide complex infranodal bradycardia and asystole ventricular fibrillation; (patient 3) severe pulmonary edema secondary to fluid overload; (patient 4) pulseless electrical activity in the immediate post-operative period associated with deep venous thrombosis of the left calf with saddle and distal pulmonary thromboemboli. Among these patients, postmortem evaluation showed a lidocaine blood concentration of 5.3 mg/L, 2 mg/L, and 2.9 mg/L on patient 1, 2, and 4, respectively. Patient 3 did not undergo toxicologic analysis for lidocaine. The authors concluded that tumescent liposuction can be fatal, perhaps in part because of lidocaine toxicity or lidocaine-related drug interactions [1]. However, a direct correlation of lidocaine toxicity as the main cause of death in this retrospective report is lacking.

Prevention of Local Anesthetic Systemic Toxicity in Plastic Surgery

Multiple published manuscripts have recommended several practical tips or steps to prevent systemic toxicity during

local anesthetic administration in plastic surgery [79, 80]. These are the most common recommendations:

- Use the lowest dose necessary to induce local anesthesia
- If using high doses, always calculate the maximum dose based on patient's lean body weight
- Avoid intravenous infusion by exercising careful technique and by aspirating before injection.
- Use epinephrine unless contraindicated (this allows to maximize the intensity and effect of the duration of the local anesthetic when compared with plain local agent)
- Employ nerve blocks when possible.
- Before reinjecting an area, allow sufficient time for the anesthetic to work, particularly when using an agent with a slow onset of action.
- When anesthetizing a large area, use the lowest effective concentration of anesthetic.
- Use lidocaine whenever possible

Although proper technique and adherence to safe dosage guidelines can prevent local anesthesia toxicity, unrecognized intravascular injections can still occur despite negative aspiration tests. ECG monitoring is a useful indicator of bupivacaine toxicity. An increase in the blood concentration of bupivacaine is associated with decreased R wave amplitude and increased QRS complex before changes in blood pressure are evident. Bupivacaine toxicity may manifest itself with changes in blood pressure only when a significant decrease in cardiac output (40 % decrease) occurs [81].

General Considerations for the Treatment of Toxic Reactions of Local Anesthetic in Plastic Surgery

CNS toxicity treatment should follow the BLS (Basic Life Support) and ACLS (Advanced Cardiac Life Support) guidelines [70, 71, 82]. Patients should be placed in the recovery position. The airway should be maintained and supplemental oxygen should be administered when available. Ventilatory and cardiac support should be administered if necessary. Intravenous administration of short-acting benzodiazepines is recommended to control seizures [83]. For more details of the specifics about general management of toxic reactions of local anesthetics, please refer to the general chapters of this book.

Conclusion

This is an attempt to provide comprehensive review of complications following local and regional anesthesia in plastic surgery, describe safety considerations, and management of the adverse events. Although the overall incidence of complications following local and regional anesthesia in plastic surgery is low, they could be stressful and sometimes devastating especially in cosmetic patients. Most complications of local and regional anesthesia in plastic surgery are avoidable. Knowledge of the anatomy, proper technique, and awareness of the possible complications should allow the practitioner administering the local and/or regional anesthesia to have an uneventful anesthesia in plastic surgery patients. Patients should always be informed about the potential complications and acknowledgment of them should be documented when obtaining informed consent. Avoiding local anesthetic toxicity is primarily based on good practice, and anticipation of problems before they occur (an ounce of prevention is worth a pound of cure!).

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Part VI

Morbidity Studies: International Perspective

Development and Methodology of a Registry of Regional Anaesthesia

26

Michael J. Barrington

Key Points

- Prospectively collecting regional anaesthesia procedure-related data allows monitoring of quality of care and identification of problematic practices that may lead to complications or adverse events.
- Monitoring the quality and safety of regional anaesthesia is of paramount importance for informed patient consent and clinical decision-making.
- Serious, adverse events are infrequent or rare in regional anaesthesia, therefore documenting them requires large patient samples.
- Proactively monitoring for adverse events in new healthcare processes is recommended, one example being ultrasound-guided peripheral nerve blockade. In the 2000s this emerged as a significant potential advance in clinical practice popularizing peripheral nerve blockade globally.
- With periodic updates to practice guidelines and the ever-changing development of new approaches and technologies, use of a regional anaesthesia registry or database allows practitioners to make comparative analysis across time.
- Clinical registries and databases facilitate qualitative, evidence-based assessment of practice, allowing less reliance on expert consensus or practice based on outdated dogma. Registries can also overcome limitations of cost and frequent lack of statistical powering associated with randomized clinical trials.
- Registries/databases should be designed to collect as complete a dataset relating to the procedure as possible, including patient demographics, surgical information, anaesthetic type and dosage, and clinical effectiveness outcomes. Data recording and entry methods should be standardized and simple to use.

Abbreviations

ARAC	The Australasian Regional Anaesthesia Collaboration
ASRA	The American Society of Regional Anesthesia and Pain Medicine
AURORA	The Australian and New Zealand Registry of Regional Anaesthesia
IOM	United States Institute of Medicine
IRORA	The International Registry of Regional Anesthesia
LAST	Local anesthetic systemic toxicity
PNB	Peripheral nerve blockade
PNI	Postoperative nerve injury
RCTs	Randomized controlled trials

Introduction

In 1999, the United States Institute of Medicine (IOM) report of healthcare—*To Err is Human*—indicated that the need to improve quality and safety in healthcare was substantial [1]. The IOM report has contributed to increased awareness on human error and adverse outcomes in healthcare. The report extrapolated the results of two studies and the number of annual hospital admissions in the USA, to controversially extrapolate that deaths caused by medical error exceeded the eighth leading cause of deaths in the USA [2]. The IOM committee recommended that healthcare organizations: (1) Develop research tools that enhance the knowledge base about safety; (2) Establish voluntary (and mandatory) reporting to identify and learn from errors; (3) Raise the standards

M.J. Barrington, PhD, MBBS, FANZCA (✉)
Department of Anaesthesia and Acute Pain Medicine,
St. Vincent's Hospital, Melbourne, Fitzroy, Melbourne, Australia

Faculty of Medicine, Dentistry and Health Sciences,
Melbourne Medical School, University of Melbourne,
Parkville, VIC, Australia
e-mail: Michael.barrington@svha.org.au

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_26

and expectations in safety through the actions of its professional groups; (4) Create safety systems resulting in safe practice at the delivery level; (5) Build and maintain a culture of safety; (6) Provide leadership and a blame-free environment; (7) Proactively monitor for adverse events and (8) Continually engineer patient safety into healthcare processes. The IOM report is often quoted as a sentinel publication on healthcare safety. It has likely motivated healthcare organizations to increase their resources available to address healthcare safety and quality. Improving the safety and quality of healthcare has proved to be an extremely challenging problem and the problems that the IOM addresses are not confined to one geographical region [3, 4].

The public's perception of the risks associated with anaesthesia is primarily related to the extremely rare risk of death due to general anaesthesia. This perceived safety is at least in part related to the low risk of anaesthetic-related mortality obtained from studies with variable methodologies. In addition to these traditional epidemiological studies on morbidity and mortality [5, 6], other mechanisms used to obtain information about problems that occurred during or in association with an episode of anaesthesia care include closed-claims analyses [7], medical defence reports, retrospective medical record analysis and incident reporting and monitoring studies [8]. Finally, anecdotes and experience add to the list of methods used to obtain information about potential problems.

Monitoring the quality and safety of regional anaesthesia is of paramount importance for informed patient consent, clinical decision-making and because regional anaesthesia is often considered an alternative anaesthetic technique by many patients and anaesthesiologists. Anaesthesiologists may recommend regional anaesthesia to their patients but their preconceived beliefs may influence how receptive they are to regional anaesthesia. Explaining serious risks associated with general anaesthesia is straightforward, as the patient will often consider them inevitable and very rare if they were to occur. When a new set of benefits and complications (related to regional anaesthesia) are provided to patients, an additional burden is placed on the clinician. The challenges of providing this information were revealed in a 2008 survey of the American Society of Regional Anesthesia and Pain Medicine (ASRA) members [9]. The survey respondents reported widely varying incidences of serious risks. This was proposed as being related to the existence of only a few studies on the subject and the methodological limitations including self-reporting [10], and reviews of insurance claims [11]. The authors of the survey commented on the importance of accurate numerical disclosure of risks during the informed patient consent process. They commented that this would include disclosure of complications that may occur rarely but have a significant effect on the patient. Although considered rare, neurologic and other serious complications following peripheral nerve blockade (PNB) can be devastating to the patient and fall into this category (material risk). The authors commented that to obtain reliable incidence data on infrequent outcomes, a prohibitively large number of patients would be required.

Postoperative nerve injury (PNI) is often presumed to be a risk unique to regional anaesthesia; however, nerve injury associated with PNB may be related to perioperative nerve injury of diverse etiologies [12, 13]. The risk adverse anaesthesiologist is aware that PNI is often linked to regional anaesthesia. If general anaesthesia alone is utilized for a surgical procedure, the focus on an anaesthetic aetiology for PNI is likely to be lessened [14].

Fortunately regardless of aetiology, the most serious adverse events occur with relative rarity. However, an adverse event that occurs infrequently is still important to the patient, but also in terms of how our colleagues and the public view our specialty. It is demanding to obtain reliable incidence data on events that occur infrequently. In 2008, in an American Society of Regional Anesthesia (ASRA) practice advisory on neurologic complications of regional anaesthesia and pain medicine, Neal commented on how the relative rarity of complications made it difficult to obtain reliable incidence data and how: "*randomized controlled trials and other tools of evidenced-based medicine hardly ever existed on the subject and that they would be unlikely to do so in the future*" [15]. In 2010, following a review of published cases of local anesthetic systemic toxicity (LAST) over a 30-year period, the authors commented: "*we lack a precise and accurate portrayal of the clinical spectrum of LAST and its optimal treatment. This deficiency begs for the development of a prospective data collection tool in the form of a robust, comprehensive registry of LAST events designed to avoid the many shortcomings of retrospective literature review*" [16].

Monitoring the quality and safety of regional anaesthesia is also important because clinical practice is continually evolving. A significant example of this has been the shift from neuraxial to peripheral regional anaesthesia. Also, significant clinical and technological advances have occurred. Amongst these, the most significant has been the widespread use of ultrasound imaging for PNB. Ultrasound-guided PNB has emerged as a significant potential advance in clinical practice [17, 18]. The chief utility of ultrasound-guided PNB is the ability to image nerves, nerve plexuses, needles, local anaesthetic injectate and to avoid structures such as blood vessels. However, new technology that significantly changes clinical practice does not automatically mean that a technique will be safer or even be more effective compared to existing techniques in routine practice. All new technologies, devices and drugs that patients are exposed to should be assessed for safety and effectiveness. Because of the infrequency or rarity with which serious complications related to regional anaesthesia occur, large patient cohorts are required to reliably estimate the incidence of these complications.

The Australasian Regional Anaesthesia Collaboration

The precursor to the International Registry, the Australasian Regional Anaesthesia Collaboration (ARAC), was developed in 2006–2007 so that a multicentre clinical registry could be formed to explore aspects of quality and safety of PNB. This registry would provide the epidemiological tool to capture the "prohibitively" large sample sizes necessary to determine the incidences of infrequently occurring complications. The registry would identify patterns and trends in clinical practice.

In 2006–2007 when ARAC was developed there were several dynamics changing clinical practice:

1. The perception that neuraxial anaesthesia was associated with a greater risk of serious morbidity than previously recognized.
2. Evidence-based medicine supported PNB as being as efficacious as epidural analgesia (for lower limb orthopaedic surgery) with a lower incidence of side effects. Therefore PNB was being increasingly utilized worldwide.
3. The emergence of ultrasound guidance was popularizing PNB across a wider cohort of anaesthetists. One significant factor that contributed to the increased popularity of PNB in Victoria, Australia was the local emergence of ultrasound-guided PNB, driven in 2006, by a New Technology Grant that was awarded to 18 public hospitals for the purchase of 18 portable ultrasound machines. The grant was awarded for the specific purpose of ultrasound-guided PNB. As part of that deployment of new technology, anaesthetists from each of the 18 hospitals received centralized didactic, hands-on training in sonography (humans) and nerve blocks (live anaesthetized porcine model). All 18 hospitals were approached to participate in ARAC.

In 2006–2007, there were no safety data on ultrasound-guided PNB. ARAC was established so that data describing the quality and safety of PNB performed using both traditional and ultrasound-guided techniques could be collected and analysed from thousands of patients. Having reliable, contemporary incidence data is critical for informed consent and clinical decision-making. It is for these reasons, and the lack of published morbidity outcomes following ultrasound-guided PNB, that adverse events were given a priority. Having accurate denominator data was critical for this purpose; therefore a registry methodology was utilized.

The Registry Imperative

> "*There are widespread gaps in our ability to rigorously define best practices. An astonishing number of recommended practices are based on expert consensus*".

The above quote is from an editorial titled The Registry Imperative, in the journal *Anesthesiology* in 2009, on the importance of clinical registries in defining contemporary care in anaesthesia [19]. The editor's comments stem from the American Society of Anesthesiologists lengthy experience in the development of practice parameters and guidelines. Overall it is estimated that only 15–20 % of medical practices are based on rigorous scientific data that establishes their effectiveness [19].

Harvard Business School's Michael Porter is an expert in competition and strategy and has written on the problems that our healthcare systems face [20]. Although Porter's commentary is directed towards the United States Health Care system, many healthcare systems face the same fundamental problem—lack of competition and value. Porter argues that systematic measurement and dissemination of health outcomes should be mandatory for all medical conditions and that good outcome measures are vital feedback indicating what works and what does not. Monitoring what we do and measuring our results and what happens to our patients are essential for improvements in quality of care. Every thriving sector of the economy harnesses this kind of information to spur learning. Healthcare is the outlier [20]. Porter claims that comprehensive outcomes and results data will improve performance and efficiency. The systematic assessment of clinical results used by the American College of Surgeons National Surgical Quality Improvement Program is the type of project that Porter argues should be routine for every medical condition [20–22].

Definition of a Clinical Registry

At a basic level the concept of a registry is simple, a place where records are kept. Clinical registries systematically and uniformly collect information from people who undergo a procedure, are diagnosed with a disease or use a healthcare resource [23]. The American Heart Association defines a clinical registry as a prospective observational database of a clinical condition, procedure, therapy or population, in which there are no registry-mandated approaches to therapy and relatively few inclusion and exclusion criteria [24]. This is very different to the conduct of a controlled clinical trial where often, rigid filters in the form of inclusion and exclusion criteria are applied before sampling can occur. This process of exclusion generates internal validity, often at the expense of diminished generalizability. Many randomized controlled trials (RCTs) are industry sponsored where the primary motivation is financial. Despite these limitations, the RCT is the gold standard for determining if a therapy is efficacious. The focus of clinical registries is to capture real-world clinical practice, for example, native hospital behaviour, in large patient populations independent of the environment of a controlled clinical trial.

Registries are important "powerhouses" for driving clinical research and measuring adverse events and clinical outcomes [19–22]. Clinical registries are important for monitoring and benchmarking the quality of clinical care and are critical for clinical practice improvement [23]. Clinical registries can serve multiple functions such as public health surveillance, vehicles for quality improvement, performance assessment, evaluation of trends in clinical practice and to monitor the safety and effectiveness of a drug or device in phase four studies [24, 25]. Determining if best practice and evidence-based guidelines are being adhered to or alternatively if the results of RCTs apply in routine practice (effectiveness study) are further valid uses. There are many examples where the results of RCT were not reproduced outside of the study environment. For example, in a RCT of endarterectomy for asymptomatic carotid artery stenosis, the risk of stroke was 1:1000. However, in a subsequent effectiveness study, the risk of stroke increased to 1:100 and it was the real-life observational study that determined that the therapeutic benefits were significantly reduced when the entry criteria were removed [26].

Clinical registries also play an important role in measuring healthcare delivery including access to clinical services by, for example, socio-economically disadvantaged groups, or underuse or overuse of a therapy.

Advantages and Limitations of Clinical Registries

Registries are patient-level clinical databases and have been shown to be more reliable than administrative data at predicting outcomes [27]. Furthermore, the results of registries are considered more valid by both patients and physicians. Although, outcome measures, as valid as they are as measures of quality, do not point to the processes that must be fixed in order to improve results. In the New York Cardiac Surgery Reporting System, performance data potentially motivated hospitals identified as being outliers with poor performance, but did not motivate others to improve their performance from mediocre to excellent. The Cardiac Surgery Reporting System has been criticized for encouraging hospitals to exaggerate the presence of serious risk factors or not operate on high-risk patients [28, 29]. While some registries evaluate outcomes compared to a comparison group, the majority do not have a control group. Registries, because they contain uncontrolled observational measurements, hold a higher risk for unrecognized bias and incorrect conclusions about cause and effect than more rigorous designs. This stems from the influence that unmeasured or unknown confounders may have on the results [30]. The analysis of an observational dataset is often more complex than that required for a RCT. The controlled clinical trial aims to randomize a sufficiently large sample to eliminate significant baseline differences between study groups and reduce bias from confounders. RCTs represent the gold standard for evidence of causality. The analysis of observational datasets may establish association but not causality; however, this type of finding may be significant when large samples are involved. The large sample size will add to the credibility of the finding. The results of observational studies are generally considered exploratory, non-definitive and generate a hypothesis to be tested in a subsequent RCT. However, this may be an impractical paradigm when one realizes that serious outcomes may occur so infrequently that the conduct of a subsequent RCT may require such large patient numbers that it would be logistically impractical. Take for example the safety profile of the lipid soluble local anaesthetic enantiomer ropivacaine. In animal studies, it is clear that ropivacaine reduces cardiac toxicity compared with bupivacaine. However, in clinical practice that benefit may be theoretical and diminished with dose reduction (of bupivacaine), likely to occur with ultrasound-guided regional anaesthetic techniques [31]. Is the routine use of ropivacaine safer than bupivacaine? This is a question that would be logistically impractical in a RCT but could likely be addressed in an observational study. An example is the study by Mangano that investigated the safety of the serine protein inhibitor antifibrinolytic agent aprotinin, used to reduce bleeding following cardiac surgery [32]. Prior to this study, several RCTs (up to 45) had demonstrated the efficacy of aprotinin, but none had identified that aprotinin was associated with serious end-organ damage [32]. Excluding high-risk patients is commonly applied to phase three controlled clinical trials to reduce the number of adverse effects however, in the post-marketing phase; a therapy is often applied to a more heterogeneous patient population. The indications of a new drug, for example, may be extended without the same initial intensity of evaluation. Registries are ideally suited to perform post-approval phase four trials and post-marketing surveillance.

Registries are less expensive than RCTs and have the advantage of being ongoing data collection exercises providing insights into long-term efficacy and safety that a single trial may not be able to detect. Time series data can validate earlier findings and detect trends in practice. Patterns in time series data contain important information that other traditional statistical methods reliant on averages or summary statistics can mask. Improvement is a temporal event and incorrect claims of improvement or efficacy become apparent with time [30]. The practice of medicine moves quickly and the original clinical environment of a trial may no longer exist by the time its results are being applied. A registry, because of its longevity, is more flexible in these regards.

In summary, clinical trials are often underpowered to detect differences in outcomes that occur infrequently and external validity may be compromised by strict exclusion criteria. Registries are able to collect data from larger number of patients with minimal exclusion criteria that often reflect

Table 26.1 Examples of clinical registries or similar projects

Registry	Outcomes	Comments
American College of Surgeons National Surgical Quality Improvement Program	Operative morbidity and mortality	Developed risk models for specific complications [21]
The Society of Thoracic Surgeons, National Database	Morbidity and mortality following cardiac surgery	Has been credited with improving outcomes following cardiac surgery [35]
New York State Cardiac Surgery Reporting System	Risk-adjusted outcomes following coronary artery bypass surgery	Decreases in risk-adjusted mortality, cessation of cardiac surgery by low-volume, high-mortality surgeons, several hospital-specific quality improvement programmes have been initiated [36]
SWEDEHEART	ST-elevation myocardial infarction	Decrease in short- and long-term mortality, data entered to a web-based interface [37]
The Danish Knee Arthroplasty Register	Quality outcomes including implant survival	Large epidemiological studies performed to study trends as well as risk factors for poor clinical outcome [38]
Swedish rheumatology registries	Long-term safety and cost	Longitudinal studies address issues not well evaluated in controlled clinical trials [39]
French registries in rheumatoid arthritis and autoimmune diseases	Nationwide study to investigate the safety of biological agents	Higher risk of tuberculosis, Legionella pneumophila, lymphoma [40]
The VASCUNET Registry	Compared vascular surgical practice	Significant variations in practice [41]
20-year cohort study on total knee arthroplasty	Perioperative nerve injury	Nerve injury not associated with regional anaesthesia [42]
Registry of ultrasound-guided regional anaesthesia shoulder surgery	Neurologic	Low incidence of neurologic symptoms, none permanent
	Respiratory (single-centre study)	Incidence of dyspnoea (7–10 %), hoarseness (22–31 %) [43]
Clinical registry of peripheral nerve blockade	Neurologic	Neurologic symptoms, 0.09 at 6 months [44]
	LAST (single-centre study)	
Registry of shoulder surgery in sitting position with interscalene nerve block	Postoperative stroke (single-centre study)	One ischemic stroke at 24 h [45]
Pediatric Regional Anesthesia Network (PRAN)	Neurologic (multicentre study)	Low rate of complications [46]
Multicenter Perioperative Outcomes Group Research Consortium (MPOG)	Epidural hematoma requiring laminectomy	One event per 22,189 placements to 1 event per 4330 placements (95 % CI) [47]

ongoing real-life practice. Examples of registries or projects with similar methodology from surgery, internal medicine and anaesthesiology are tabulated in Table 26.1 [21, 28, 33–44].

Challenges in Managing a Clinical Registry

There are no formal requirements for the conduct of managing a clinical registry although there are operational documents referenced in peer-reviewed articles. An example is a 2010 editorial [23], that references (citation number [15] of the editorial) the Australian Commission on Safety and Quality in Health Care, Operating principles and Technical standards for Australian clinical quality registries. The registry imperative is evolving and perhaps this is indicated by the comprehensive policy document published in 2011 by the American Heart Association, in the journal *Circulation* [24]. This is in contrast to the long-standing existence of documents that clearly outline how to design, execute and report the results of a RCT [45, 46].

Registries aim to have complete, or almost complete, capture of all eligible procedures, thereby minimizing selection and enrolment bias [23]. Capturing a complete, or near complete, patient population with sequential enrolment is the goal. Registries operate as "business as usual", with no cherry picking of good results and include both good and bad outcomes. Other challenges include providing timely feedback to collaborators, privacy issues, management of a large dataset, and access to individuals with appropriate statistical or epidemiological expertise, funding and intellectual rights in the case of multicentre involvement.

Data Elements, Definitions and Quality Control

The data elements that registries collect need to be carefully considered and should be epidemiologically sound, meaning that the data should be simple, objective and reproducible. Examples of appropriate data to collect include patient demo-

graphics, surgical characteristics and anaesthetic type and dosage, other practice patterns and clinical effectiveness outcomes. The data elements need not be static, but rather change according to the important clinical questions that need to be addressed. The dataset for a registry should be simple and only data that are required to address the question or issue of interest should be collected. Logistically the data should be simple enough that physicians can efficiently enter information in a database in the context of a busy clinical practice.

For ARAC, data were recorded relating to the performance and effectiveness of PNB, adverse effects and complications. These data included a unique patient code, date of procedure, operation type, needle bevel type, local anaesthetic and dose, level of sedation and block success. PNB type was recorded: interscalene, periclavicular, axillary, distal humeral/forearm, femoral/fascia iliaca, sciatic, other peripheral lower limb nerves and trunk blocks. The technology used to locate plexus/nerves was recorded: ultrasound alone, nerve stimulator alone, ultrasound and nerve stimulator and other. The definitions used for this project were available online at www.regional.anaesthesia.org.au. The timing of follow-up for potential neurologic complications was either at 7–10 days or 6 weeks postoperatively, depending on practice location and time period. Patients were not considered to be uncontactable by phone until four attempts had been made at different times and using alternative phone numbers, including a mobile number if available. To detect potential neurologic complications patients were asked a standardized set of questions: Do you have any numbness? Do you have any tingling? Do you have any abnormal sensations? Do you have any pain? Do you have any weakness? These questions were asked in relation to the operative limb, and if the patient responded with "yes" to any of the questions, then further queries were made taking into account the anatomy relevant to the surgery and the PNB. Symptoms that were immediately adjacent to the wound, consistent with normal tissue healing or the initial trauma were not considered relevant in terms of anaesthesia being a causal factor. Symptoms that clearly were not related to the PNB were not considered significant. For patients with ambiguous symptoms or complaints, repeat contact was made with the patient. Triggers for referral to a neurologist were new onset of motor and/or sensory deficit; non-resolving paraesthesia; pain; allodynia; or dysaesthesia and any concern expressed by the surgical team regarding the potential for a PNB-related neurologic deficit. Assessment by the neurologist included history, examination, documentation and investigation. Investigations included electrodiagnostic tests [nerve conduction studies and/or an electromyogram], imaging [computed tomography, magnetic resonance imaging] and blood tests.

Data quality control was enhanced by the following methods:

1. Valid outcome definitions—for key data items, explicit definitions were given and were available online, and their existence and importance were communicated to collaborators.
2. Timing of data collection—the practitioner performing the procedure collected the initial data close to the point of care in theatre. The early postoperative data were collected directly from the patients on the wards or by phone.
3. Training of data collectors—this was undertaken to communicate the goals of the project and familiarize personnel with the required methods of data collection.
4. Electronic database—this was utilized throughout the project and for key data; drop-down menus were utilized.
5. Standardized data collection form—standardized data collection forms were generated for postoperative follow-up and included the neurologic questionnaire.
6. Missing data or unrealistic data—this was dealt with in a proactive manner taking into account the resources available. Because missing follow-up data was a threat to the validity of the key outcome, neurologic complications, this was a priority in monthly reports and other communications. Regular spot checks were made and queries sent back to local hospital collaborators. During analysis, the database was screened for erroneous and unrealistic data. Depending on the data type, the following methods were utilized: (A) Obviously erroneous non-essential data or combinations of data were eliminated (e.g. unrealistic combinations of height and weight), (B) Statistical techniques that were less sensitive to outliers were utilized for summary statistics and (C) Key outcomes such as major complications were confirmed with site collaborators.

When ARAC was completed, there was no other large-scale investigation into the safety of ultrasound-guided PNB [47]. The web-based interface utilized in ARAC facilitated ease of data entry, multicentre collaboration and collection of data from a large patient cohort. This project set up the foundation to develop a larger, more comprehensive clinical registry.

Development of an International Registry of Regional Anesthesia

To further develop the registry a comprehensive new online interface (www.anesthesiaregistry.org) and secure remote database were created. The new online interface had features that enhanced its quality including improved security, ease of use and functionality, improved reporting, rules enforcement, audit trail of changes to data and improved data quality control (for example, context specific drop-down menus and criteria based entry). Because the new interface was more complex, specific training was implemented for data collectors and collaborators so as to familiarize them with the new interface at www.anaesthesiaregistry.org. A broader range of

outcomes was incorporated including clinical effectiveness outcomes, patient-rated outcomes, wrong-site block and respiratory complications. Development of the registry included expanding the patient cohort available for analysis and refinement of outcomes measuring clinical effectiveness. Additional patient and block related fields and patient-rated outcomes were included in the new online interface, introduced into practice on June 1st 2011.

Additional postoperative outcomes were also introduced before the new online interface was introduced. The change in project name [The Australian and New Zealand Registry of Regional Anaesthesia (AURORA) and subsequently to the International Registry of Regional Anesthesia (IRORA)] provided a method to more effectively communicate the project's key requirements. The previous interface operated with a high level of reliability, however development of a new interface and formation of a new remote server was timely. The larger registry reported on a wider range of outcome and potential risk factors for the safety of PNB, and also to confirm (or refute) the initial results with ongoing data collection.

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Australia: Results of a Multicenter Registry of Regional Anesthesia

27

Michael J. Barrington

Key Points

- The primary goal of this registry was to determine the quality and safety of our current routine practice of peripheral nerve blockade.
- This chapter presents a summary of results from the Australasian Regional Anaesthesia Collaboration and the Australian and New Zealand Registry of Regional Anaesthesia.
- Results of the Australasian Regional Anesthesia Collaboration showed an incidence of 0.4/1000 peripheral nerve blocks for neurologic injury related to the block (out of 8189 blocks). Incidence of local anesthetic toxicity was 0.98/1000.
- Results of the Australian and New Zealand Registry of Regional Anaesthesia revealed incidences of peripheral nerve block-related late and long-term neurological deficits were 0.6 and 0.3 per 1000 blocks, respectively. Incidence of local anesthetic toxicity was 0.87/1000.
- Patients with postoperative neurologic features were more likely to have a cause unrelated to peripheral nerve blockade.
- The results presented from this registry demonstrate that the incidence of serious permanent neurologic complications attributable to peripheral nerve block is rare.
- The risk of local anesthetic systemic toxicity was reduced with ultrasound guidance and increased body weight. Local anesthetic dosage and site of injection were predictors of local anesthetic systemic toxicity.
- Incidence of post-block respiratory impairment was relatively higher (3.4/1000). Other complications, such as wrong-site blocks and pneumothorax, while rare, were nevertheless captured by the registry.

Abbreviations

ARAC	Australasian Regional Anaesthesia Collaboration
AURORA	The Australian and New Zealand Registry of Regional Anaesthesia
LAST	Local anesthetic systemic toxicity
PNB	Peripheral nerve blockade
PNI	Postoperative Nerve Injury

Neurological Complications

Postoperative neurologic complications are potentially debilitating and can result in functional impairment, decreased quality of life, and chronic pain. Neurologic complications cause significant stress for patients and health professionals and are a common cause of medical litigation [1]. When general anesthesia is utilized, there may be little focus on the anesthetic technique as being causative. When postoperative neurology occurs following regional anesthesia, the etiological focus is often directed towards the anesthetic technique, despite there being patient, surgical risk factors, or other potential mechanisms to explain the neurologic findings [2]. Anesthesiologists are often inadequately prepared to manage these scenarios and the etiology of postoperative neurology may well be assigned to the regional anesthetic by default.

PNI has a diverse and complex etiology being associated with a range of perioperative processes, anesthesia, and surgery [2]. There are well-known higher risk scenarios such as obstetrics and vulnerable anatomical structures such as the common peroneal and ulnar nerves [3–5]. Distinguishing

M.J. Barrington, PhD, MBBS, FANZCA (✉)
Department of Anaesthesia and Acute Pain Medicine,
St. Vincent's Hospital, Melbourne, Fitzroy, Melbourne, Australia

Faculty of Medicine, Dentistry and Health Sciences,
Melbourne Medical School, University of Melbourne,
Parkville, VIC, Australia
e-mail: Michael.barrington@svha.org.au

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_27

patients, surgical, anesthesia, and other potential etiological factors is demanding, and in some situations the exact cause remains speculative. Mechanisms for PNI include mechanical, stretch, compression, ischemia, inflammation, toxicity, and metabolic. PNB may expose patients to the risk of needle or catheter-induced mechanical trauma, neural ischemia, and local anesthetic neurotoxicity. Furthermore, a limb rendered insensate from any type of anesthesia will blunt the protective reflexes in the periphery. Presenting features of nerve injury include paresthesia, dysesthesia, neuropathic pain, and weakness. These clinical features may overlap with the recovery process following major surgery. Without careful evaluation, patient's postoperative neurologic features can be incorrectly attributed to regional anesthesia. The potential for these scenarios are similar to obstetric studies, where regional anesthesia is often blamed but rarely responsible [3].

Preliminary Results of the Australasian Regional Anaesthesia Collaboration

The development and methodology of this project has been described previously and in Chap. 26 [6]. A key feature is that all patients who received PNB for anesthesia and/or analgesia at each participating centre had their PNB recorded and were systematically followed up for neurologic and other complications.

During the study period 2006 to May 30 2008, ARAC captured 6950 patients who received 8189 PNBs. Of the 6950 patients, 6069 patients were successfully followed up. In these 6069 patients, there were a total of 7156 episodes of PNB forming the denominator for late neurologic complications. Thirty patients (0.5 %) had clinical features requiring referral for neurologic assessment. Three out of the 30 patients referred met the criteria for nerve injury due to PNB, giving an incidence of 0.4 per 1000 PNB's (95 % CI = 0.08–1.1:1000). The remainder of the patients referred for neurologic assessment (27/30) had postoperative symptoms/signs that were unrelated to PNB. Patients who met the criteria for referral to a neurologist were nine times more likely to have a cause unrelated to PNB than they were to have symptoms/signs attributable to PNB. PNI has multiple contributory factors. The estimates of both immediate and delayed complications according to nerve localization techniques are listed in Table 27.1 [6].

Data quality control methods developed during this study period included hospital-specific random and systematic checks comparing database content with medical records and audits to ensure all cases were captured (e.g., operating list or notes compared with database entry). In addition, monthly audits (for follow-up rates and trends indicating data collection issues) and spot checks were performed to identify and correct missing data. Investigators received feedback regarding any data quality issues. Key project requirements were communicated regularly with investigators and data collectors using individual and conferences phone calls, emails, personal correspondence, newsletters, and written material. Other strengths of this project included:

1. Systematic postoperative contact with patients, proactively seeking complications. A systematic approach to capturing complications is associated with more reliable capture of complications compared to a passive approach [7]. Without this approach, there is a risk of either over-diagnosing or missing complications.
2. A defined follow-up and neurologic referral and investigative pathway [6]. The project also utilized a standardized questionnaire for detecting patients with potential complications.
3. Clear definition and verification of all key outcomes—clear definitions for nerve injury due to PNB and other adverse events were utilized so as to improve reliability of the results.

Table 27.1 Immediate and delayed complications according to nerve localization technique

	Nerve localization technique			
Complication	Nerve stimulation ($N = 2507$)	Ultrasound ($N = 5141$)	Other ($N = 541$)	Total ($N = 8189$)
Local anesthetic toxicity	1.2 (0.25–3.5)	0.8 (0.2–2.0)†	1.8 (0.05–10.3)	0.98 (0.42–1.9)
Inadvertent vascular puncture††	13.9 (8.2–21.9)	5.1 (3.0–8.1)*	2.3 (0.06–12.8)	7.2 (5.1–10.0)
Unintended paresthesia††	10.8 (5.9–18.1)	20.5 (15.9–25.9)†	2.3 (0.06–12.8)	16.8 (13.4–20.8)
Late neurologic deficit	0.8 (0.1–2.9)	0.2 (0.005–1.1)†	–	0.4 (0.08–1.1)
Long-term neurologic deficit	0.4 (0.01–2.2)	0.2 (0.05–1.1)†	–	0.2 (0.03–0.9)

Ultrasound includes ultrasound used as the sole technology and combined ultrasound and nerve stimulation. Other comprises techniques not employing nerve stimulation or ultrasound technology. Data are presented as *n* per 1000 PNB (95 % CI). Source: Barrington MJ, Watts SA, Gledhill SR, et al.: Preliminary results of the Australasian Regional Anaesthesia Collaboration: a prospective audit of more than 7000 peripheral nerve and plexus blocks for neurologic and other complications. *Reg Anesth Pain Med* 2009; 34: 534–541

†Not statistically significant

††Reduced total cohort ($N = 4991$), for nerve stimulation ($N = 1297$), ultrasound ($N = 3260$), and other ($N = 434$)

*Indicates a statistically significant difference ($P = 0.001$; Poisson regression) between ultrasound and nerve stimulation and other techniques

4. Robust neurologic evaluation—it was only by evaluating patients with a focused history and examination, electro diagnostic tests and imaging studies that we were able to separate PNB causes of injury from those unrelated to PNB. In total, 26 out of 30 patients had electro diagnostic tests and 10 patients had magnetic resonance imaging.
5. Web-based central database—all practitioners utilized the same database with the same fields. In addition, the outcome definitions were readily available on the online interface using context-sensitive links.
6. Anonymity—all results were presented without identifying the patient, anesthesiologist, or hospital.

Clearly, maintaining patient anonymity is essential in any case report. Maintaining anesthesiologist and hospital anonymity potentially improved compliance with the project.

This study had limitations and challenges that have been previously described [6]. Study limitations included the timing (1 week or 6 weeks) of and proportion of patient follow-up (87 %). Follow-up at 6 weeks, as occurred in 34 % of our patients, may have missed nerve injury presenting in the early postoperative period but had resolved by time of contact. The incidence and time course of neurologic features has been well studied following shoulder surgery and interscalene blockade where early in the postoperative period the proportion of patients with neurologic features was temporarily high, with almost all patients having complete recovery [8, 9] The significance of early postoperative neurologic symptoms is important because the results of these studies are often interpreted as being PNB-related nerve injury [10]. In one study, minimal attempt was made to determine etiology, for example, there was no standardized neurologic investigative pathway that included electro diagnostic tests [9]. Candido concluded that symptoms in the C5–6 distribution were likely to represent complications related to interscalene block; however, distal mononeuropathies (e.g., in the ulnar nerve distribution) were unlikely to represent PNB-related nerve injury. Regarding proportion of patients successfully contacted, the author believes that patients with complications would actually be more likely than not to present back to their original hospital with a complaint. In addition, the denominator for the incidence of nerve damage was only calculated from the number of PNBs performed in the number of patients successfully contacted. It is for these reasons that we consider the denominator calculation and incidence accurate [6]. The numbers of some block types are low, and therefore we cannot calculate the incidence of injury for individual PNB types. The reliance on phoning patients (most commonly) rather than direct physical evaluation to detect potential complications is a study limitation. However, the resources required to assess in person every patient would have been prohibitive.

Results from the Australian and New Zealand Registry of Regional Anaesthesia

An important objective of continuing and developing the registry project was to obtain results from a larger patient cohort providing a more accurate estimate of the range in which the true incidence of PNB-related nerve injury value is likely to be. During the period of study January 2006 to May 2012, a total of 63 patients met a trigger for referral to neurology (new onset of motor/sensory deficit, non-resolving paresthesia, allodynia/dysesthesia, surgical referral) [11]. The most common presenting feature was a sensory deficit (most commonly paresthesia, followed by dysesthesia, allodynia) in the distribution of the PNB in 48 (76 %), followed by pain in 8 (13 %) and motor deficit in 6 (9.5 %), and in one patient the finding was incidental. Foot drop associated with knee arthroplasty was the most common motor presentation. Nine out of 63 patients referred had a defined diagnosis of generalized preoperative neuropathy confirmed with electro diagnostic testing. Postoperative investigations revealed that 20 patients had a specific mononeuropathy diagnosed distal to the site of PNB. Examples of these mononeuropathies were ulnar neuropathy localized to the elbow, median neuropathy localized to the wrist, radial neuropathy localized at the humerus, and common peroneal neuropathy localized to the fibular head.

There were a total of 11 patients with PNB-related nerve injury. There were five patients who had a mild femoral neuropathy following total knee arthroplasty and 4/5 patients were designated as having a PNB-related injury. From the 11 patients diagnosed with PNB-related deficits, four patients had preoperative chronic pain issues, one had peripheral vascular disease, three had a defined peripheral neuropathy, and six required a pneumatic tourniquet for their surgery. Four patients had more than one intraoperative risk factor (neuropathic pain, positioning, preoperative neuropathy, spinal canal stenosis, tourniquet, chronic pain, diabetic neuropathy, microvascular disease). The duration of postoperative deficit in the 11 patients with PNB-related nerve injury was: less than 6 months (n = 5); 6–12 months (n = 1) and greater than 12 months (n = 4). One patient with a complex medical history including a likely preexisting vasculitic neuropathy had a persisting motor deficit. Table 27.2 presents incidences of late and long-term neurologic complications from ARAC, AURORA, and ARAC/AURORA combined. Table 27.3 presents incidences of neurologic complications for specific PNB types. When brachial plexus, femoral, and sciatic blocks are included as the denominator (19,353 PNB), the incidences of PNB-related late and long-term neurological deficits are 0.6 (0.28–1.01) and 0.30 (0.11–0.67) [n per 1000 PNB, 95 % Confidence Interval], respectively. Long-term neurologic deficit defined as the criteria for late neurologic deficit having been met, and with persistence of symptoms for greater than 6 months after onset [11]. At the time of writing this chapter, the author is analyzing a larger cohort including patients recruited to May 2014.

Table 27.2 Incidences of late and long-term neurologic complications from ARAC, AURORA, and ARAC/AURORA combined

	Late neurologic deficit	Long-term neurologic deficit
ARAC		
Ultrasound (*N* = 5141)	1	1
	0.2 (0.005–1.1)	0.2 (0.005–1.1)
No ultrasound (*N* = 3048)	2	1
	0.7 (0.08–2.4)	0.3 (0.008–1.8)
Total (*N* = 8189)	3	2
	0.4 (0.08–1.1)	0.2 (0.03–0.9)
AURORA		
Ultrasound (*N* = 17,831)	7	3
	0.4 (0.16–0.8)	0.2 (0.03–0.5)
No ultrasound (*N* = 3563)	1	1
	0.3 (0.007–1.6)	0.3 (0.007–1.6)
Total (*N* = 21,646)	8	4
	0.4 (0.2–0.7)	0.2 (0.05–0.5)
ARAC/AURORA combined		
Ultrasound (*N* = 22,972)	8	4
	0.3 (0.2–0.7)	0.2 (0.05–0.4)
No ultrasound (*N* = 6611)	3	2
	0.5 (0.09–1.3)	0.3 (0.04–1.1)
Total = 29,835	11	6
	0.4 (0.2–0.7)	0.2 (0.07–0.4)

ARAC indicates Australasian Regional Anaesthesia Collaboration (2006 to May 30 2008), *AURORA* Australian and New Zealand Registry of Regional Anesthesia (June 1 2008 to May 30 2012), *PNB* indicates peripheral nerve or plexus block, and *N* the total number in each PNB category. Results expressed as number of events, *n* per 1000, (95 % Confidence Interval). Late neurologic deficits related to anesthesia were defined as a new onset of sensory and/or motor deficit consistent with a nerve/plexus distribution without other identifiable cause, and one of the following: electrophysiological evidence of nerve damage; new neurologic signs; new onset of neuropathic pain in a nerve distribution area; paresthesia in relevant nerve/plexus distribution area. Long-term neurologic deficit was defined as the criteria for late neurologic deficit having been met, and with persistence of symptoms greater than 6 months after onset. No technology designated in 252. Source: Barrington, M. J. (2012). The quality and safety of peripheral regional anesthesia. Ph.D. thesis, Department of Anatomy and Neuroscience, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Table 27.3 Incidence of neurologic complications for specific PNB

	N	Late neurologic deficit		Long-term neurologic deficit	
PNB type		*n*	Incidence	*n*	Incidence
Brachial plexus	8872	2	0.22 (0.27–0.81)	1	0.11 (0.003–0.63)
Femoral	6564	4	0.91 (0.33–1.99)	2	0.30 (0.04–1.11)
Sciatic	3917	3	0.8 (0.16–2.23)	3	0.8 (0.16–2.23)
Total	19,353	11	0.6 (0.28–1.01)	6	0.30 (0.11–0.67)

PNB indicates peripheral nerve or plexus block; *N* = total number in each PNB category; Incidence, *n* per 1000, 95 % Confidence Interval. Late neurologic deficits related to anesthesia defined as a new onset of sensory and/or motor deficit consistent with a nerve/plexus distribution without other identifiable cause, and one of the following: electrophysiological evidence of nerve damage; new neurologic signs; new onset of neuropathic pain in a nerve distribution area; paresthesia in relevant nerve/plexus distribution area. Long-term neurologic deficit defined as the criteria for late neurologic deficit having been met, and with persistence of symptoms for greater than 6 months after onset. Source: Barrington, M. J. (2012). The quality and safety of peripheral regional anesthesia. Ph.D. thesis, Department of Anatomy and Neuroscience, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Local Anesthetic Systemic Toxicity

LAST is a well-known and feared complication of local anesthetic administration that may lead to circulatory collapse with lethal effects. The awareness of LAST amongst clinicians has increased recently with advances in its treatment with lipid emulsion therapy, case reports of LAST, and practice advisories [12]. There is substantial variability in the clinical presentation and timing of LAST. LAST is thought to occur infrequently, so there are very few studies that systematically collect data on the subject. Reliance on case reports is problematic because they are not connected to a denominator to calculate incidence. Furthermore, the

events described in case reports are often remarkable or different from the usual. Before the commencement of this registry study, there were no incidence data on LAST during ultrasound-guided PNB.

Preliminary Results of the Australasian Regional Anaesthesia Collaboration

From ARAC, the incidence of LAST was 0.98 per 1000 blocks, Table 27.1 [6]. LAST occurred despite the utilization of ultrasound guidance in 63 % of PNB and in 50 % of LAST events. Real-time imaging of the needle and vascular structures provides a mechanism to avoid inadvertent vascular puncture. In this study and in a recently published meta-analysis, there was a reduced risk of vascular puncture using ultrasound guidance compared to nerve stimulation [13]. Despite this, LAST has been reported with ultrasound-guided PNB in case reports and in this registry study [14]. There was no statistically significant difference in the incidence of LAST in patients who had PNB performed with ultrasound compared to those who did not utilize ultrasound technology, Table 27.1 [6]. Despite the relatively large sample size, the rarity of LAST may have meant there was insufficient power to determine a significant difference between ultrasound-guided and other techniques.

Results from the Australian and New Zealand Registry of Regional Anaesthesia

The period of study for this multicenter study involving 20 hospitals was from January 2007 to May 2012 inclusive. The primary outcome was local anesthetic systemic toxicity comprising minor, major, and cardiac arrest (due to toxicity) events determined using standardized definitions. The study population comprised 20,021 patients who received 25,336 PNBs. Fourteen thousand eight hundred and sixty patients received 1 block, 5033 received 2 blocks, 102 received 3 blocks, and 26 received 4 blocks. There were 22 episodes of LAST (13, minor; 8, major; and 1, cardiac arrest). There were 12 episodes of LAST (8, minor; 4, major) with PNB performed with ultrasound (N = 20,401) and 10 episodes of LAST (5, minor; 4, major; and 1, cardiac arrest) with PNB not performed with ultrasound (N = 4745). The patient who suffered cardiac arrest was having a paravertebral block inserted. The clinical features were consistent with direct intravascular injection of local anesthetic rather than neuraxial spread. The patient was successfully resuscitated with airway management, advanced cardiac life support, and lipid emulsion therapy. Twenty patients with LAST episodes received one block and two patients received two blocks [15].

Overall, the incidence of LAST was 0.87 per 1000 PNB (95 % CI, 0.54–1.3:1000). The incidences of LAST per 1000 PNB, at different sites of PNB were upper limb [1.75 (95 % CI, 0.93–2.99)], paravertebral; [3.62 (95 % CI, 1.33–7.86)], lower limb [0.24 (95 % CI, 0.05–0.71)], and trunk [0.00 95 % CI, (0–0.94)].

Ultrasound guidance was associated with a reduced incidence of LAST following PNB. All univariate and multiple multivariable analyses resulted in identical conclusions. The point estimate for the odds ratio for LAST with ultrasound guidance, compared to no ultrasound use ranged from 0.19 to 0.25 and the P values from 0.001 to 0.007 depending on the model utilized. That is, the results of this analysis indicated that the risk of LAST was reduced by over 75 % with ultrasound guidance. This study indicates that paravertebral and upper limb blocks were associated with an increased risk of LAST compared to lower limb and trunk blocks. Increasing local anesthetic dose per weight and local anesthetic dose were independent predictors of LAST, increasing the risk of LAST. Low patient weight increased the risk of LAST. It is relevant to note that the importance of both the site of injection and local anesthetic dose have been thought to be relevant risk factors for LAST for almost 100 years [16].

Respiratory Outcomes, Wrong-Site Block, Other Outcomes and Trends

The results of this registry initially indicated that the incidence of pneumothorax to be 0.98 (0.12–3.53) [2049 interscalene, supraclavicular, and infraclavicular blocks], per 1000 PNB (95 % CI) [denominator]. One episode of pneumothorax from this current study had symptoms that were subtle and delayed. This mode of presentation may result in underdiagnosis of pneumothorax. The upper 95 % CI of 3.53 per 1000 PNB was not significantly different to results obtained with landmarks techniques. We have since explored this topic (presenting features, risk, and training) in more detail. The estimate of pneumothorax risk following supraclavicular blockade was 0.4 (0.01–2.3) [2384 supraclavicular blocks], per 1000 PNB (95 % CI) [17].

Phrenic nerve block is a common side effect of the interscalene and supraclavicular approaches to the brachial plexus block. Ultrasound guidance results in a reduced incidence of phrenic nerve paresis compared to nerve stimulator techniques using the same doses of local anesthetic following interscalene or supraclavicular brachial plexus blocks [18, 19]. In this current study, the incidence of respiratory compromise was 3.4 (1.72–6.16) [3197 interscalene and supraclavicular PNB], per 1000 PNB (95 % CI) [denominator] [11]. Episodes of respiratory compromise secondary to phrenic nerve blockade occurred with ultrasound guidance; however, more traditional dosages of local anesthetic were utilized (Table 27.4).

Table 27.4 Respiratory distress following interscalene or supraclavicular block

PNB	Ultrasound-guided	LA type and dose	Comments
ISB	Yes	Ropi 112 mg	Respiratory distress in PACU, elevated hemidiaphragm on radiograph, required observation overnight in PACU
ISB	Yes	Ropi 200 mg	Respiratory distress, surgery cancelled, observed in ICU overnight
ISB	Yes	Ropi 300 mg	Mild dyspnea
ISB	Yes	Ropi 150 mg	Respiratory distress, surgery cancelled, noninvasive ventilation for 6 h
ISB	No	Ropi 150 mg	PNB inserted asleep, difficult anatomy, required ventilation in postoperative period, possible neuraxial spread
ISB	Yes	Ropi 150 mg	Dyspnea post PNB, proceeded with surgery
SCB	Yes	Lido 100 mg	Dyspnea post PNB
		Ropi 150 mg	
SCB	Yes	Lido 300 mg	Severe dyspnea post PNB
SCB	Yes	Ropi 150 mg	Dyspnea post PNB, proceeded with surgery
		Lido 200 mg	
SCB	Yes	Lido 400 mg	–
		Ropi 35 mg	
SCB	Yes	Lido 400 mg	Required noninvasive ventilation
		Ropi -unknown	

Data from patients recruited from 1 June 2008 to May 31 2012, who received 1660 interscalene and 1537 supraclavicular blocks. *PNB* indicates peripheral nerve or plexus block type, *ISB* interscalene block, *SCB* supraclavicular block, *LA* local anesthetic, *Ropi* ropivacaine, *Lido* lidocaine, *PACU* Post Anesthesia Care Unit, *ICU* Intensive Care Unit. Source: Barrington, M. J. (2012). The quality and safety of peripheral regional anesthesia. Ph.D. thesis, Department of Anatomy and Neuroscience, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Table 27.5 Details of wrong-site PNBs

PNB	Ultrasound-guided	Sedation	Contributing factors
FNB	No	Moderate	At end of operation patient moved from operating table to bed for PNB
FNB	Yes	Unresponsive	Due to haste, site mark not visible
FNB	No	Alert	No time-out, distracted with teaching
FNB	Yes	Alert	–
FNB	No	Light	Language, inexperience
PVB	No	Light	–

PNB indicates peripheral nerve or plexus block type, *FNB* femoral nerve block, *PVB* paravertebral block. Period of data collection from 1 June 2008 to May 31 2012 including 16,959 patients and 21,646 PNBs. Source: Barrington, M. J. (2012). The quality and safety of peripheral regional anesthesia. Ph.D. thesis, Department of Anatomy and Neuroscience, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Wrong-site block is a preventable event, and fortunately the baseline incidence from this study is rare. Despite the infrequency of its occurrence, it is increasingly accepted that it should be completely avoidable with good clinical practices and checklists. The incidence of wrong-site blocks was 0.28 (0.10–0.60) [21,646], per 1000 PNB (95 % CI) [denominator], and these events are tabulated in Table 27.5. Femoral nerve block comprised 5/6 of wrong-site blocks; therefore, the incidence of wrong-site blocks for that PNB is 0.82 per 1000 (0.27–1.9), 95 % CI. Haste, distraction, inexperience, no time-out, site mark not visible and language all appear to be potential contributory factors [11]. More recently, wrong-site blocks were utilized as an outcome to identify targets for quality improvement [20]. The incidence of wrong-site blocks in Australia and New Zealand was estimated to be 0.04 % (7 events from a denominator of 19, 268 PNB).

Wrong-site blocks emphasize the importance of having systems in place to ensure that critical processes occur [21]. In particular, having systems that do not rely on memory, having prompts and changing our mindset from autonomous thinking to that of a disciplined physician following standard process [22]. A similar theme is highlighted in surgery, where checklists and cues for effective communication are associated with improved outcomes [23].

Summary

PNB-related nerve injury is a subset of PNI that has a diverse and complex etiology being associated with a range of perioperative processes, anesthesia, and surgery. Patients with postoperative neurologic features were most likely to have a cause unrelated to PNB. This registry utilized a proactive approach involving systematic postoperative contact and assessment of all patients with suspected nerve injury. These current results indicate that the incidences of long-term and late PNB-related nerve injury are 0.3 and 0.6 per 1000 PNB, respectively. The results of AURORA indicate that ultrasound guidance is associated with a reduced risk of LAST. Importantly, this study comprising 25,336 PNB provided statistical evidence, for the first time, that ultrasound guidance may improve safety because it was associated with a reduced risk of LAST following PNB. However, despite the relative infrequency (0.87 per 1000 PNB) with which it occurs, LAST is an important cause of morbidity following PNB, ongoing vigilance is required and it is important to recognize that one technique in isolation will not prevent this complication. The pneumothorax risk overall was initially estimated to be 0.98 per 1000, however following supraclavicular blockade is 0.4 per 1000. Wrong-site block still occurs (estimate of 0.3–0.4 per 1000 PNB) providing an opportunity to improve processes.

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Canada: Medical Legal Aspects of Regional Anesthesia Practice

28

Kari G. Smedstad and Brendan T. Finucane

Key Points

- Legal action against anesthesiologists in Canada rarely results in a court decision; in these cases, approximately 2/3 of the decisions were in favor of the physician. Most litigious claims stem from the use of newer anticoagulants, incorrect dosage of medications, incorrect medication given, allergies, and issues surrounding informed consent.
- The portion of medical legal actions related to regional anesthesia has increased in recent years. Recent reports show that 80 % were dismissed and 10 % were settled. Most regional anesthesia claims (75 %) are related to complications of neuraxial blocks, 1/3 of which are obstetric cases.
- The Canadian Medical Protective Association is a physician-funded entity that pays current and past claims and assists with a variety of issues related to legal action lodged against physicians. The most recent analysis of the CMPA database revealed 77 cases related to regional anesthesia over a 20-year period. Twenty-five involved epidurals, 11 involved spinal anesthesia, and the remainder involved various pain blocks and peripheral nerve blocks. The majority (60/77) of these cases were dismissed.
- Forty-one obstetric cases were analyzed from the CMPA database; several of these involved serious complications, including death. Litigation costs associated with obstetric claims vary but can be in the millions of dollars range, in situations with catastrophic outcomes or a compromised baby.

K.G. Smedstad, MB, ChB, FRCPC (✉)
Department of Anesthesia, McMaster University, Hamilton, ON, Canada
e-mail: ksmedsted@shaw.ca

B.T. Finucane, MB, BCh, BAO, FRCA, FRCPC
Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada
e-mail: bfinucane6@gmail.com

Introduction

Regional anesthesia is used frequently in Canadian operating rooms, labor suites, and pain clinics. Complications are not frequent but do occur. Measures of complications are published reports, anecdotal evidence, and medical legal actions. This chapter describes the latter in the Canadian setting.

In Canada, all anesthesia services are provided by physicians. All legal actions against physicians are defended by the Canadian Medical Protective Association (CMPA). The CMPA is a Canada-wide medical mutual defense association for physicians. It is not an insurance company. Established in 1901, the CMPA is funded and operated on a not-for-profit basis by physicians and for physicians. More than 65,000 Canadian physicians are members of the CMPA, comprising about 95 % of doctors licensed to practice in Canada. The medical legal situation in Canada is unique, and one cannot discuss litigation against anesthesiologists without describing briefly how the CMPA functions [1].

Membership fees are set annually through a review of experience with claims and costs. The fees and income from investments fund a reserve to handle the cost of present and future claims. The CMPA is fully funded to pay for all claims related to the current and past years. Because the organization operates on an occurrence basis, members are eligible to receive assistance regardless of when a claim is made, including protection in retirement and against a member's estate. This protection also ensures that compensation is available for injured patients when they are eligible to receive a settlement or court award. The CMPA defense philosophy holds professional integrity first and foremost. The association will vigorously defend a member as long as there is good expert support for their medical care. Cases are not settled against physicians in Canada because of expedience or cost savings.

The CMPA Risk Management Services provides seminars and educational sessions for physicians of all specialties across Canada. Statistics and analyses of closed claims can

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_28

be made available for study and educational purposes within the framework of the educational mission of the organization. Thus, the results published in this chapter are comprehensive and accurate. A review of closed claims in regional anesthesia in Canada has previously been published [2]. The cases that form the basis of this discussion have been updated to include closed claims from 1990 to 2002[a] and more recent closed claims from 2008 to 2012[b].

Legal Actions Against Anesthesiologists in Canada

The risk of a legal action against an anesthesiologist in Canada is similar to the risk for the average physician (1.5 %). Approximately 1 in 65 anesthesiologists were sued every year up to 2003. The risk of legal action involving anesthesiologists in Canada declined to approximately 30 cases per year between the years 2008 and 2012, down from 45 cases per year prior to the last reporting period.When threatened about a legal action or worried about a bad outcome or occurrence, anesthesiologists contact the CMPA and receive help with a variety of matters. These include advice, help with hospital privileges, complaints to provincial/territorial regulatory authorities, involvement in coroner's inquests, billing matters, and civil and criminal legal action related to the professional practice of medicine. Thus, only a very small proportion of files opened relate to civil legal actions. To put the figures related to regional anesthesia in context, the statistical review for 2003 shows that CMPA opened 15,127 new files, of which 1117 were legal actions. Only a small proportion of these cases actually proceed to trial [3].

In 2003 there were 39 new legal actions commenced involving anesthesiologists. Most legal actions against anesthesiologists arise from general anesthesia cases. In the 5 year period between 2008 and 2012, 147 legal actions were filed involving anesthesiologists in Canada, 64 % were dismissed, 27 % were settled out of court and 9 % required court decisions. Upon review of the cases that required a court decision, 65 % were in favor of the physician and 35 % the plaintiff. The most common sources of litigation involved newer anticoagulants, incorrect dosage of medications, incorrect medication given, allergies and problems with informed consent. In the reporting period between 1990 and 1997, 80 % of the actions against anesthesiologists involved general anesthesia and 20 % regional and a small percentage of these (13 %) involve obstetric anesthesia (Fig. 28.1). In the most recent reporting period (2008–2012) 50 % of legal actions involved regional anesthesia and 50 % general.

In Canada, about 60 % of cases that arise from anesthesia practice are dismissed, and approximately 30 % of claims against anesthesiologists are settled. Cases are settled when expert support is lacking. Experts are peers who are familiar with the practice of anesthesiology relevant to the claim. The remaining 10 % go to trial. When going to court, anesthesiologists win about 75 % of cases, but the courts find against the doctor in the remaining 25 %. CMPA protection provides no limit to the cost of legal help which the member is eligible to receive. Similarly, there is no dollar limit on damages paid to patients, but structured settlements are encouraged.

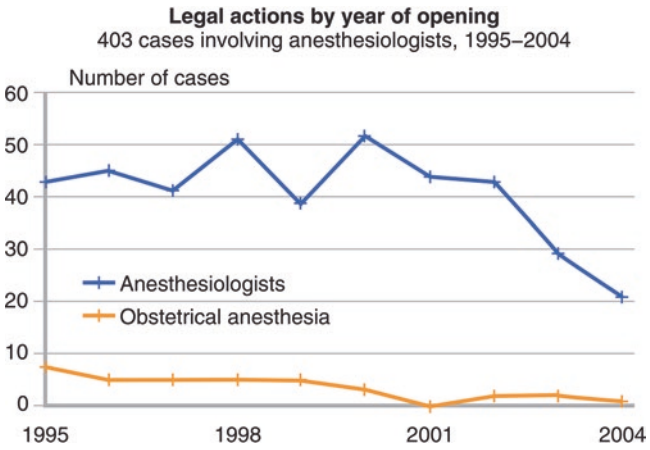

Fig. 28.1 Anesthesia-related legal actions in Canada decreased over a decade or so between 1995 and 2004. Legal actions related to Obstetric anesthesia are miniscule by comparison over the same period

Disabilities and Legal Outcome

Not all harm suffered by patients during anesthesia is attributable to negligent anesthetic care. Therefore, the severity of physical disabilities suffered by patients may not be related to the legal outcome of claims. Physical disabilities for the purpose of legal action in Canada can be classified as: minor: pain, scarring; major: disabilities that interfere with the activities of daily living; catastrophic: resulting in severe neurologic impairment; and death.

Legal outcomes are divided into four categories: (1) consent dismissal—plaintiff(s) withdraws or abandons the legal action before trial. (2) Settlement—legal action is resolved by way of a payment by CMPA on behalf of the defendant member before trial. (3) Judgment for the defendant—the court decides in favor of the defendant at trial (case won). (4) Judgment for the plaintiff at trial (case lost).

Claims Experience in Regional Anesthesia

Until recently 20 % of medical legal actions in anesthesia were related to regional anesthesia. In the most recent reporting period (2008–2012), 50 % of the actions were related to regional anesthesia, including pain procedures and obstetric regional cases. The legal outcome was overall better in these

cases than litigation related to general anesthesia—in that 80 % were dismissed and only 10 % were settled. Should the case go to court, the outcome is the same: 7 of 10 cases are decided in favor of the defendant.

If the patient experiences a complication, even resulting in a significant disability, but there is no fault in the standard of care, the case is usually dismissed or won in Canada. Vigorous defense of doctors who practice within the standard of care results in fewer lawsuits. Good plaintiffs' lawyers in Canada know this, and most investigate the validity of a claim before taking the case.

Neuraxial blocks (spinal and epidural) comprise the majority of cases that lead to medical legal difficulties (75 %), and this trend has not changed in more than 30 years. In the most recent report (2008–2012) one third of the complications related to neuraxial block involved obstetric patients. Peripheral nerve blocks also give rise to complications that may trigger complaints and lawsuits. Regional anesthesia is increasingly used in postoperative pain management, and recently we have seen cases arise from both acute and chronic pain management. Major risk factors associated with neuraxial block include: obesity, pre-existing anatomic deformity and anti-coagulation.

Cases arising after spinal and epidural anesthesia can fall into any one of the four categories of outcome. Paraplegia is a catastrophic outcome. Postdural puncture headache (PDPH) is a relatively "minor" outcome but can seriously impact the family when protracted. To date, no such case has been settled against a Canadian anesthesiologist. In contrast, in the vast majority of cases of paraplegia resulting from an epidural anesthetic, the legal outcome was unfavorable to the physician.

Overall, the patient outcome from malpractice claims related to regional anesthesia was similar to that of all anesthesia claims, with a slightly higher percentage of patients suffering minor or major disabilities, but fewer catastrophic outcomes and deaths.

Analysis of Regional Anesthesia Claims over a 20-Year Period

The CMPA database allowed for analysis of closed claims related to litigation against anesthesia practitioners who performed regional anesthesia in Canada. The cases closed in the years 1990–2002, but the actual medical care or procedures that gave rise to these claims happened from 1977 to 2000. The average claim can take between 3 and 4 years to process and complete. Data from the most recent reporting period (2008–2012) have not yet been fully analyzed at this time.

There were 77 cases related to regional anesthesia performed in operating suites or pain clinics across the country. The procedures were for intraoperative anesthesia, postoperative pain relief, or treatment of chronic pain. In addition, there were 41 cases arising from obstetric anesthesia and analgesia in the same period. These will be discussed separately.

Patients who sue doctors or hospitals do so for many reasons, but usually litigation arises when the patient or the family believes that the outcome of the procedure has caused damage. Unsatisfactory outcome will not in itself lead to legal actions; there are usually a number of factors that may influence the patient or family to launch a legal complaint. These include communication failure, lack of consent, permanent disability, unexpected catastrophic outcome, or death.

Neuraxial Blocks

Epidural or spinal analgesia and anesthesia is frequently used in the operating setting and in the pain clinic. We do not know how many such procedures are performed daily in Canada, but the trend is to use neuraxial blocks as an adjuvant to anesthesia for thoracic, abdominal, and lower body surgery. Spinal anesthesia is frequently used for pelvic and urologic procedures. Combined spinal and epidural anesthesia is also used frequently. The denominator is therefore probably very large, and the number of cases leading to legal problems very small. We cannot put a number on this ratio.

Epidural Blocks

There were 25 cases involving epidural injections. Of these, nine were epidural steroid injections, three epidural blocks for chronic pain relief, seven cases of epidural catheters inserted for postoperative pain relief, and six cases of epidural anesthesia for surgery. The complications associated with these epidural procedures varied widely. There was one broken catheter, where the tip could not be found. Other minor outcomes (see above) were two cases of PDPH and one case of lipolysis of the back. Numbness, temporary weakness, and ongoing back pain led to complaints in some cases. One patient complained of awareness! There was a case of "vasomotor instability" and one case of intravascular injection with seizures. Viral hepatitis, contracted months after the epidural, led to a complaint against the anesthesiologist. Two patients developed foot-drop, one after an epidural steroid injection and one after attempted epidural for hernia repair. Total or high spinal anesthesia necessitating resuscitation occurred in three cases, one after an epidural steroid injection and two after epidural analgesia for postoperative pain relief. Even though one of these patients had a cardiac arrest, the resuscitation was successful in all cases, and no permanent sequelae resulted. All the cases mentioned above were dismissed.

More serious outcomes were four cases of paraplegia and one case of organic brain damage. These cases are instructive, in that all except one case were settled on behalf of the doctors involved because they could not be defended. However, one case of paraplegia was dismissed, because the lesion occurred well above the insertion site of the epidural and the etiology of the cord damage could not be ascertained. The four cases that could not be defended hinged on lack of consent for the procedure, lack of monitoring during hypotensive anesthesia, and use of a non-approved drug for epidural injection. In the fourth case, the epidural steroid injection was not related to the development of paraplegia; it resulted from a sequestered disc, but the case could not be defended because the doctors involved did not adequately assess the patient before going ahead with the injection. There were no deaths in the epidural group.

Spinal Anesthesia

Eleven legal actions arose from spinal anesthesia for surgery. That is a remarkably small number over a 20-year period considering the commonality of spinal anesthesia. All these actions were dismissed. Two complaints were for PDPH. Persistent back pain or sciatica occurred in several cases; one of these was thought to be attributable to aseptic meningitis, the others to preexisting conditions. One complainant had multiple attempts at insertion of the spinal needle. One patient developed persistent tinnitus and hearing loss. There was one case of cauda equina syndrome of unproven origin, and a complaint of leg weakness that presented 6 months after the spinal anesthetic and was found to be caused by disc disease.

Only one case had a serious outcome, namely, paraplegia as a result of a cord bleed. The patient was anti-coagulated, and the bleed occurred 12 days postoperatively and was thought to be spontaneous and not related to the spinal anesthetic.

Other Types of Anesthetic Blocks

The remaining 41 cases span the spectrum of anesthesia pain management. Seven cases were associated with cataract surgery, in which anesthesia staff performed retrobulbar or peribulbar blocks. Global perforation occurred in five cases, two were settled, and two won in court. There was one case of vitreous hemorrhage and one of acute glaucoma postoperatively. Both were dismissed.

There were eight cases of sympathetic plexus blocks, including celiac plexus (1), stellate ganglion (4), and lumbar sympathetic chain (3). A phenol neurolytic block of the celiac plexus, resulting in paraplegia, was settled. Also settled was a case of paraplegia and incontinence resulting from a neurolytic lumbar sympathetic block. The other cases arose from pneumothorax, septicemia, or pain issues, some preexisting, and these were all dismissed.

Four cases involved damage to nerves: sacral nerve-root, femoral, obturator, and ulnar. Two were neurolytic blocks with phenol or alcohol, both resulting in paralysis. These were settled. Two cases arose from persistent or aggravated pain; these were dismissed.

Intercostal nerve blocks caused complications in four actions, two for serious injuries and two for pneumothorax. One patient fainted and sustained fractures; this case was settled. One patient with a preexisting condition developed aspiration pneumonia after the procedure and died. This case was won in court.

Regional blocks of the brachial plexus, paravertebral nerves, and supraclavicular plexus caused pneumothorax. All were dismissed.

Injection of the cervical plexus of nerves for chronic neck pain caused three legal actions, two of them dismissed. In both cases, the patient had dyspnea and temporary paralysis, treated with appropriate airway management and resuscitation. The third patient developed cardiac arrest and sustained permanent neurologic damage. The case was settled because of inadequate resuscitation and failure to monitor appropriately.

Two cases arose from acupuncture treatment, and both centered on consent discussions. One case was settled, the other dismissed. A patient developed pneumothorax from trigger-point injections, and again the case was dismissed. Thus, all 11 cases of pneumothorax as a complication of different regional blocks were dismissed.

In the miscellaneous category, a case of septic arthritis from an intraarticular injection of steroid was dismissed. After the insertion of a spinal cord stimulator, the patient developed weakness and hemiparesis, which was found to be related to the preexisting condition and thus dismissed.

Bier block for surgery of the upper limb is frequently used. Two legal cases came to light. One case had a catastrophic outcome because the local anesthetic was mistakenly diluted with concentrated saline, resulting in serious tissue damage. This case was settled. The other case alleged development of sympathetic dystrophy; this allegation was dismissed.

Three cases of facet joint injections led to legal actions. One patient had dural puncture and worse pain, one patient developed a paraspinal abscess, and the third had seizures after an inadvertent intra-arterial injection. Two cases were dismissed, the third won in court. This case went to court because of deficient discussion of material risk.

Obstetric Anesthesia and Analgesia

The annual number of legal actions from obstetric anesthesia has been stable since 1980. During that time, obstetric analgesia including epidural and combined spinal-epidural

analgesia has become more prevalent, and there has been a change to regional anesthesia for operative delivery [4]. The prevalence of epidural analgesia for labor is about 30 % overall in Canada [5].

We analyzed 41 cases from CMPA's closed files. Thirty-one cases were dismissed, five settled, four won in court, and one case judged against the physician. There were ten incidents of PDPH, all dismissed. Accidental total spinal anesthesia occurred in two cases. One was dismissed, the other had a catastrophic outcome and the case was settled on the grounds that the care was inadequate. Two sheared epidural catheters led to complaints that were dismissed. Four instances of nerve root irritation or damage were also dismissed, as were all six cases in which the patient complained of pain, either during cesarean delivery or after the delivery.

One case of pain in labor received much attention in the national and international press, and this case was won in court [6].

Preexisting conditions can lead to medical legal actions. A patient who was found to have neurologic deficits was diagnosed with syringomyelia, unrelated to epidural pain relief in labor. Another patient developed a post-delivery cavernous sinus thrombosis. Dense hemiplegia 3 days after delivery was found to result from cerebral hemorrhage secondary to pregnancy-induced hypertension. These cases were dismissed, as were two others, one related to consent discussion and one to the wrong drug injected, but without sequelae.

Two patients developed epidural abscesses after labor analgesia. Both resulted in neurologic deficits. One case was settled, the other dismissed when the action was not pursued.

There were three cases of amniotic fluid embolism leading to major or catastrophic outcome or death. The cases in the two former categories were both won in court [7]. The case of the patient who died was settled, because vigilance was found wanting. That settlement was shared between anesthesia and obstetrics.

Remaining in the "catastrophic" outcome category were two cases of paraplegia and one of hypotension causing perinatal asphyxia. One case of paraplegia was settled, the other was the only case in this entire series of regional anesthesia legal cases that was lost in court. Although the paraplegia was thought to be caused by a decrease in blood pressure and lack of blood supply to the fetus during cesarean delivery, the judge found the anesthesia staff liable because of inadequate monitoring and record keeping.

A last case was also related to hypotension in labor after epidural analgesia. Lack of monitoring, lack of adequate fluid therapy, and failure to appreciate the effect on the fetus resulted in a large settlement for lifetime care of the child. One patient died. Death was not deemed related to the anesthetic.

Cost of Litigation

Medical legal actions are costly for the plaintiff and for the defense. The cost of the 77 regional anesthesia claims discussed above depended on the outcome. Sixty cases were dismissed. The average cost of a dismissed case was 13,000 Canadian dollars. There were 12 settled cases. The cost of settling a case averaged $520,000. The high cost reflects the serious disabilities in some of these cases. Five cases went to court and were won in favor of the doctor with an average cost of $110,000. No regional anesthesia cases were lost in court.

Obstetric anesthesia costs differ somewhat. Although there are few cases, the cost may be very high if the case includes care for a compromised baby. The average of the settled cases in regional obstetric anesthesia was $190,000, but one claim for a compromised baby was for 4.6 million dollars. The mean cost for the cases that were won in court was almost double that of the regional claims, around $190,000. Dismissing the cases in obstetric anesthesia costs around $15,000, which is similar to the regional claims. If a case is lost in court, as was one case in the obstetric anesthesia series, the cost may run into millions of dollars, reflecting catastrophic outcome.

The costs of CMPA fees have increased significantly for many "high risk" specialists in Canada. At the top of the scale are obstetricians, followed closely by neurosurgeons and orthopedic surgeons. The costs have remained relatively stable for anesthesia practitioners over the last 25 years, reflecting the risk-management initiatives taken in our specialty, particularly with regard to airway management and monitoring. Doctors in Canada are reimbursed by the provincial governments for most of their malpractice premiums.

Legal Issues

What can we learn from these cases? We should not practice "defensive medicine." We should practice regional anesthesia to the best of our ability, keeping up to date, and performing according to the standard of care that is expected of a trained anesthesiologist. We cannot avoid getting sued occasionally even if all goes well. As can be seen from the cases discussed, minor complications can lead to legal action even if no bad outcome results. But we can minimize the risk of lawsuits.

Consent discussion: We know what the common risks are in regional anesthesia. We are obligated to mention common risks and serious risks regardless of frequency when discussing a procedure. It is estimated that the risk of dural puncture and PDPH is about 1 % in teaching hospitals [8]. Similarly, pneumothorax is a known complication of many different blocks, and this should be mentioned in the consent discussion. Questions have been raised regarding the consent for

obstetric anesthesia. This has been well explained in two publications in recent years [9, 10]. Material risk should be put in the context of the planned procedure, bearing in mind that paralysis and nerve damage is exceedingly rare but can occur. This is particularly important when performing neurolytic blocks. As is seen from our series, most cases are dismissed when the consent discussion was adequate.

Record keeping is very important. To properly defend a legal claim, the CMPA must depend on the written record. In all cases, the record should be complete and legible! The consent discussion can be mentioned briefly, or ticked off on a preprinted record.

If an unexpected or untoward outcome has occurred, it is wise to write a note in the chart. This should be factual and state the procedure, the clinical findings and outcome, and the plan for further action. The best defense is a complete clinical record. Take note of pre-existing conditions. Certain patients are more prone to complications from regional anesthesia, for instance, those with diabetes or obesity and abnormal anatomy. We are aware of the problems associated with anticoagulation, and are very vigilant about blocks in such patients. It is interesting that there were no legal cases associated with epidural hematomas related to the performance of blocks. Only one case occurred, and that was found to be spontaneous. Patients with neurologic diseases such as amyotrophic lateral sclerosis and Klippel-Feil deformity presented in this series. It is important to note the presence of such abnormalities. Similarly, take note of common conditions such as scoliosis and previous back surgery. These patients are more likely to present difficulties with regional anesthesia.

Monitoring vital signs before and during procedures is clearly part of the standard of care. It is very difficult to defend the practitioner if monitoring is inadequate. Monitoring should be documented. Know what to do if complications arise. Regional anesthesia should be performed in an environment where resuscitation can be properly performed.

Inappropriate drugs are sometimes administered by mistake. Usually this is a systems failure, and hospitals are working hard to provide safeguards to minimize this risk. We are accustomed to checking all drugs before we give them, but should a mistake be made, it must be documented and the patient must be followed adequately. It is also necessary to disclose such errors, to prevent recurrence and ensure adequate care in follow-up.

Conclusion

We have discussed 77 cases of regional anesthesia and 41 obstetric anesthesia legal actions which comprise the closed claims that occurred in Canada in the time period 1980–2002.

In the reporting period between 2008 and 2012, 147 actions were filed against anesthesiologists for all types of anesthesia errors. Sixty four percent were dismissed, 27 % were settled and 9 % were tried in court. Two thirds of these actions were decided in favor of the defendant and one third in favor of the plaintiff. In this recent reporting period, the number of actions against anesthesiologists declined from 45 cases per year to 30 and the number of regional anesthesia cases equaled the number of cases involving general anesthesia. The complications that led to legal action are those that are frequently associated with regional anesthesia. Although rare, legal action cannot always be avoided, but a favorable outcome of the action is influenced by good practice. That includes appropriate consent discussion, good record keeping, good communication strategies, and adherence to the standard of care.

Acknowledgement Information provided by Ross Berringer MD (ABEM) MCFP (EM), Acting Senior Physician Risk Manager CMPA[a,b].

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France: Regional Anesthesia Morbidity Study

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Dan Benhamou

Key Points

- The French SOS regional anesthesia (RA) service supplies clinical assistance to anesthesiologists facing a complication, collects information on complications, and provides advice on difficult cases prior to administration of anesthesia. Of over 158,083 blocks performed over a 10-month period, 56 major complications were identified by the SOS RA service.
- Limitations of such a database are biased or under-reporting, difficulty in attributing a complication to regional anesthesia, and having a sample size large enough to allow meaningful analysis.
- A systems analysis approach allows one to identify potential contributing factors to complications in regional anesthesia, including skill and experience of the anesthesiologist, lack of standardized aims and protocols, and failure to follow up and identify complications in a timely manner.

Introduction

Regional anesthesia is both an old and a new technique. It is now a well-established technique of anesthesia and its use has increased very much during the last 20 years [1]. Providing estimates of the incidence of the various complications related to regional anesthesia is not a new concern. In two classic studies, each assessing a large number of spinal blocks, Dripps and Vandam assessed the risk associated with the use of procaine and tetracaine in 10,098 patients [2], whereas Phillips et al. monitored 10,440 patients after lidocaine spinal anesthesia [3]. The main message of these prospective studies was that complications related to spinal anesthesia are very rare. Such results and the numerous advantages associated with regional anesthesia have contributed to the perception that regional anesthesia is "safe" and this has translated into an increasing number of regional anesthesia procedures performed worldwide. However, one should be very careful before extrapolating these old results to our current practice.

The comparison cannot probably be made not only because of methodological concerns and but also because of tremendous quantitative and technical changes during this 30-year period. This factor also restricts our ability to conduct meta-analysis studies [4]. Unfortunately, the number of recent prospective studies assessing the incidence of severe complications related to regional anesthesia is low, and this is particularly true when peripheral nerve blocks are concerned. Severe complications are rare and this is the main factor explaining the low number of studies. Indeed, the number of monitored procedures has to be very large in order to estimate the level of risk with sufficient statistical power [5]. In the case of rare events, other approaches that have been developed in other fields of research need to be used to understand and to control the risk associated with regional anesthesia techniques [6, 7].

SOS Regional Anesthesia Service

In 1996 a large epidemiologic study evaluating the incidence of serious complications associated with regional anesthesia and evaluating their characteristics, was published in *Anesthesiology* [8]. In 1998, a completely new service, entitled SOS Regional Anesthesia (RA) Service, was established [9]. This service first included a hot line and three experts (Pr Samii, Pr Ecoffey, and Pr Benhamou) rotated each week to respond to any question asked by participants on regional anesthesia at any time (even at night if necessary) and 7 days

D. Benhamou, MD (✉)
Département d'Anesthésie et Réanimation, Groupe Hospitalier et Université Paris Sud, le Kremlin Bicêtre, Orsay, France
e-mail: dan.benhamou@aphp.fr

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_29

a week (even Sunday if necessary). SOS RA Service had four main goals: (1) to provide an online clinical help for the practitioner facing a severe complication, (2) to obtain immediately relevant clinical information for every complication reported (and obviate the loss of pertinent information related to late collection as this occurred in the first survey), (3) to provide advice on difficult clinical cases before any anesthesia is given (generally at the time of the preanesthetic visit), (4) to estimate the incidence of complications from a prospective declaration of all regional techniques performed by practitioners who had subscribed to the service. The SOS RA Service works currently according to the three first initial goals as the calculation of incident rates was not maintained after the first 10-month period because of the complexity related to exhaustive case collection. Even with this deficiency, this expert system remains highly demanded by practitioners (one phone call each day as a mean) and is very useful for detecting the emergence of "new" complications. From the voluntary participation of 487 anesthesiologists who performed 158,083 regional blocks in a 10-month period, 56 major complications (including four deaths) were reported in the SOS RA survey.

Cardiac Arrest

The incidence of cardiac arrest that occurred after spinal anesthesia was 2.7/10,000. Interestingly, the clinical situations associated with cardiac arrests were homogeneous because bradycardia was recorded before each cardiac arrest that occurred during spinal anesthesia, and cardiac arrest causing death occurred in the course of a central block performed during hip surgery in an elderly patient. Spinal anesthesia is mainly a vasoplegic process and crystalloid preloading has a limited protective effect [10]. The use of vasoactive drugs, mainly drugs with a potent alpha effect, are needed. This has been well demonstrated in obstetrics [11], a situation in which the dose of local anesthetic used has to spread over a large metameric distribution (up to T4–T5). As bradycardia is an important warning sign, surveillance is important. During cesarean delivery, heart rate is known to be a surrogate factor of cardiac output and bradycardia occurs more often with phenylephrine than with ephedrine [11]. Bradycardia should be treated immediately by reducing the infusion rate, adding ephedrine or atropine if blood pressure is low [11]. Since cardiac arrests may occur later, attention should be maintained throughout the procedure, especially when high block is used or when additional contributing factors can be encountered during the procedure. The factors involved in cardiac arrest occurring during central blocks are numerous and the risk probably increases from the beginning of the procedure until it ends. Factors causing hemodynamic instability superimpose on those previously present. In cardiac arrests that occur "later," additional factors that add to an already unstable situation, include sympathetic blockade and hemorrhage. Special attention should therefore be given to correct each factor that might contribute to decompensation.

One case of cardiac arrest and two respiratory complications (not leading to cardiac arrest) occurred during a lumbar plexus block performed via the posterior approach and the incidence of 80/10,000 seen after posterior lumbar plexus block is obviously much higher than after spinal anesthesia. Complications are related to cephalad diffusion of the local anesthetic in the epidural or intrathecal space [12]. Although it was difficult to draw any definite conclusion regarding this block, French anesthesiologists were warned against the high rate of complications that was found with the posterior lumbar plexus block and advised to manage this block with at least the same vigilance as for a central block [13].

Local Anesthetic Systemic Toxicity (LAST)

In the main SOS-RA survey [9], local anesthetic systemic toxicity consisted of seizures only, without cardiac toxicity. The results suggested a decreased rate of local anesthetic-induced systemic toxicity when compared with the first survey [8] although methodological differences between the two studies preclude any definitive conclusion. If this result proves to be true, the low incidence of toxic systemic complications may be related to better physician information, improved practice patterns (lower doses, slow injection, test dose, fractionated injection …), and the introduction of ropivacaine in clinical practice (at the time the first study was performed, ropivacaine was not available in France). In the face of these reassuring results, two important points were emphasized at that time: (a) the most important factor for increased safety is to maintain a high level of vigilance even if ropivacaine was introduced to prevent systemic toxicity [14], (b) the "good" prognosis of these complications (neither cardiac arrest nor death were reported) could become worse if such complications occur outside the operating theater (i.e., in case of postoperative analgesia on the wards). A few years after, however, case reports describing cardiac arrest were published [15]. Although the safety of ropivacaine can be questioned after the report of these cardiac arrests, it should be noted that both patients were easily resuscitated, a characteristic that is obviously different from bupivacaine. This also shows that the absence of adverse events in large surveys cannot lead to the conclusion that the incidence is zero. Calculation of the incidence of rare complications thus remains difficult and might be underestimated, again suggesting that epidemiologic surveys are not the only way to study rare events.

A recent prospective survey performed under the auspices of SOS-RA was aimed at gaining information related to complications associated with ultrasound guided axillary plexus blocks [16]. This was believed to be useful as initial large-scale studies failed to clearly demonstrate a reduced incidence of LAST [17]. Of 27,031 blocks performed, the incidence of systemic toxicity of local anesthetic was very low at 1.5 per 10,000 [16]. This incidence was in agreement with other recently performed studies and also confirms that ultrasound guidance probably reduces the risk of LAST although this technique does not nullify the risk [18–20]. Interestingly, there was no systemic toxicity from local anesthetic due to delayed absorption from the tissues [16]. Inadvertent vascular puncture may not be reduced with ultrasound guidance but may be associated with a reduced dose of local anesthetic administered thereby reducing the risk of delayed LAST [21].

Another issue which has recently attracted attention is the occurrence of seizures or cardiac arrest in patients who had undergone TAP block. In most of these reports, women of relatively small height and weight and bilateral TAP blocks using relatively large doses of local anesthetic were involved, reminding us that these muscle planes are highly vascularized [22, 23].

Neurologic Complications

In the main SOS-RA survey, lidocaine spinal anesthesia was associated with more neurologic complications than bupivacaine spinal anesthesia (14.4 versus 2.2/10,000) [9]. Most neurologic complications were transient. These results about transient neurologic symptoms and neurologic toxicity of lidocaine contributed to the declining use of intrathecal lidocaine in France.

Among 12 complications that occurred after peripheral nerve blocks [9], 9 were observed in patients in whom a nerve stimulator had been used, demonstrating that nerve stimulation is not a definitive guarantee against neurologic complications. Moreover, the exact incidence of neurologic complications after nerve stimulation (versus other techniques) cannot be calculated from this study because of the low number of cases. In cases reported in our files since 1998, inadequate patient positioning and/or non-cooperative patients, insufficient physician experience, insufficient patient information on the procedure, excessive sedation, or a non-gentle technique are often critical factors that contribute to increased risk of neurologic complications. Obviously, these factors hold true also when a nerve stimulator is used. The use of nerve stimulation was already accepted in European institutions and a relatively new debate emerged related to the significance of a paresthesia occurring during puncture. This debate is far from being closed. Experts using ultrasound guidance have, for example, added to the discussion by reporting several cases in which the needle had made physical contact with a nerve, but no paresthesia was felt by the patient [24]. Others have also shown that intraneural injection can follow a puncture in which nerve stimulation has been used without any warning sign [25].

In the recent SOS-RA survey evaluating ultrasound-guided axillary plexus blocks, an incidence of neurological complications of 0.37/10,000 was observed [16]. This figure was much lower that what we had previously observed (2/10,000) [9]. One should pay attention to the fact that in the present survey, this incidence was calculated before hospital discharge, i.e. in the very early period after the block. As the incidence of neurological complications decreases with time, this result is extremely encouraging and in agreement with studies which evaluated the ability of ultrasound to decrease the incidence of postoperative nerve complications [26]. Orebaugh et al. have indeed shown a decreased incidence with ultrasound-guided blocks as compared to nerve stimulation guided blocks [19]. Unfortunately it is difficult to precisely compare these results with ours as Orebaugh et al. only reported the incidence of long lasting nerve injuries.

Sites et al. [20] reported an incidence of nerve complications after ultrasound guided nerve blocks lasting more than 5 days of 1.8/1000, which is a nearly 50 times greater incidence than in the French recent report [16]. It is thus still too early to conclude on whether the risk of neurological injury has really decreased since the introduction of ultrasound guidance. The French results may have been obtained by chance or alternatively may represent a more “mature” regional anesthesia system in which skills necessary to perform ultrasound have been acquired by the majority of physicians. Indeed data provided by Sites et al. were recorded between 2003 and 2011 and it is possible that their results represent more a learning period than the incidence that would have been obtained with skilled physicians [20].

Limitations of Reporting Systems

Reporting systems designed to study rare events encounter several difficulties. In order to collect sufficient information, these studies must be more broadly based and ideally should be nationwide (or even at a multinational level as already done in studies related to aviation safety). At present, voluntary declaration is often the solution used to gather information about complications associated with regional anesthesia. Because there is no “black box” system, an obvious bias of underreporting exists and different sources of information have to probably be merged. However, voluntary declaration has some advantages to improve safety culture and to conduct in-depth causal analysis because results are often debated at the proximity level of the medical unit. Because

of the difficulty in gathering cases, investigators are tempted to pool the reported cases, with the risk of pooling very different patient populations or pooling very different regional anesthesia populations. It is now clear that the obstetric population should be studied separately. A recently published study in more than 100,000 central neuraxial blocks performed for major joint surgery demonstrated that major complications (including epidural hematoma) were observed at a much higher incidence in non-obstetric cases [27]. One significant problem is the difficulty in attributing a complication to regional anesthesia. On one hand, it is important to define if the complication is related or not to regional anesthesia, particularly for insurance judgment. One clinically significant and frequent situation is obstetric nerve injuries. Regional anesthesia is often blamed first whereas the relative incidences of complications related to the procedure or delivery are five to tenfold higher. On the other hand, reducing the analysis of cases to the single question of causal relation, limits our view and conclusions that could be drawn, to avoid future complications. Compartment syndromes are severe complications occurring after lower limb orthopedic surgery, in particular if a cast is needed. In several cases reported to the SOS RA Service, it was clear that an intense postoperative analgesia, often associated with motor blockade, was a factor of bad prognosis, delaying the diagnosis of this complication and masking breakthrough pain that would have occurred with a lower concentration of the local anesthetic [28]. In these cases, the main question is not, "Is this complication related or not to regional anesthesia?" but "What happened?" To explore in depth the last question, all staff involved (anesthesiologists, surgeons, nurses) should analyze together facts that contributed to the incident. Another challenge to improve safety is to enlarge our point of view. Looking at published data surprisingly shows that very few cases associated with human errors have been recorded. To explain these findings, it can be hypothesized either that the incidence of such complications is very low or that a classification bias exists (i.e., complications as consequences of human being considered as unrelated to regional anesthesia technique). Drug injection errors continue to be regularly reported to SOS RA Service. Fortunately, most of these cases had a good prognosis but some of the patients had after-effects. All of the wrongly injected drugs were usually located on the anesthetic tray near the syringes containing the local anesthetic drugs.

A Systems Analysis Approach

To explore more widely the causes of complications, we have to keep in mind that behind the outcome is the process of care and that a complication can be considered as a window on the healthcare system. We thus have to move from the "What happened?" question to "Why did it happen?" [5] This requires a change of our investigation tools. The systems analysis used by Vincent is a typical example of methods to investigate in depth a complication, and especially to study system errors [7]. This approach remains useful for extremely rare events whereas the epidemiologic approach does not work because of the difficulty (or impossibility) of gathering enough similar cases to obtain sufficient statistical power.

Using Vincent's methods for analyzing several cases reported to SOS RA Service, we identified several root causes specific to regional anesthesia. Four of them were noticed often:

1. An important dispersion in "how to do" the block within a single group of anesthesiologists: Many techniques or drugs are often available for a given block procedure. The anesthesia technique changes according to the anesthesiologist's preferences or experience. And this large dispersion could be considered a latent factor leading to human errors [29].
2. Insufficiently defined aims and protocols: A regional anesthesia technique can be performed for both anesthesia allowing a surgical procedure and/or postoperative analgesia [4]. However, there are some differences (type of drugs, drugs concentration, sites of puncture, etc.) that may lead to differences of outcomes. This can be a source of confusion and sometimes of mistakes (i.e., a too high concentration of a local anesthetic used for postoperative analgesia leading to side effects that will occur during the patient stay on the ward or at home).
3. Prolonged effects of regional anesthesia: The long duration of postoperative analgesia is often an argument in favor of the use of regional anesthesia. However, after the patient has left the operating theater to go on the ward or at home, the medical and nursing organization should be prepared to care for these prolonged anesthetic effects. For example, the timing at which neurologic complications become apparent is often delayed. In several cases reported to the SOS RA Service, neurologic complications were discovered long after the block was performed and only after discontinuation of a continuous infusion. This has been seen to occur also in institutions where anesthesiologists are highly trained and where surgeons have a high confidence toward RA but where monitoring and nurses' training are not adequately organized to allow for rapid diagnosis of complications. It is as if physicians do place a greater emphasis on performing the block than on organizing the postoperative surveillance.
4. Regional anesthesia is a technique: As with all techniques, regional anesthesia needs first to be learned (in particular, excellent knowledge of anatomy is critical) and this initial training period should be associated with

adequate supervision. The next step is a stabilization period of how to do in order to avoid unnecessary changes without real benefit for the patient. It is still too often that physicians try for the first time in their next patient a new block for which the technique was described (as being easy to do, safe—a conclusion often reached after several hundred performed procedures—and with a high rate of success) by an enthusiastic speaker in a meeting that they had recently attended.

5. Regional anesthesia is a technique that can fail. Whereas it is considered that general anesthesia always works (although awareness has not a negligible incidence), it is clear that regional anesthesia can fail. In several cases associated with insufficient anesthesia reported to us, the poor outcome was related to the lack of preoperative definition of an alternative anesthesia strategy.

The interest of such approaches is to identify common causes (each of them leading to different types of complications). Controlling the side effects of one cause is a way to manage the risk related to regional anesthesia, often decreasing the risk of several types of complications.

Conclusion

Large epidemiologic studies remain necessary. Many strategies such as improved training, use of safer devices and drugs, technologic innovation, and use of quality improvement programs have been implemented to control the risks of RA. This probably explains why severe complications are now very rare in healthy patients (e.g., obstetric patients). In particular for "rare events," other approaches are available to explore complications and increase safety culture.

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Nordic Countries: Principles of Safe Practice in Local and Regional Anesthesia

30

Mikko T. Pitkänen

Key Points

- All the Nordic countries have a public, primarily tax-paid healthcare system. Also the legal arrangements to deal with complaints are similar. All countries have patient insurance schemes in order to regulate patient rights to economic compensation when injuries have been inflicted by medical staff.
- Patient Insurance Centre promotes patient safety by carrying out research, making calculations, and compiling statistics. This database has produced studies of anesthesia complications at least in Denmark and Finland.
- Studies of Danish Patient Insurance Association data show that, over an 8-year period, approximately 400,000 anesthesia procedures were performed and, of these, 916 claims were made, with 132 resulting in financial compensation from regional anesthesia procedures. Additionally, 24 cases over a 9-year period were found to result in death following a regional anesthesia procedure. In both studies, all major complications followed neuraxial blockade.
- In Sweden, Dr. Moen and colleagues published a broadly referred article on severe neuraxial complications which were collected from the information in the Swedish health care system.
- A study of anesthesia complications in Sweden demonstrated the disparity in reporting complications between patient insurance databases and anesthesia departments. Finnish studies reveal that the activity of reporting claims increased when the insurance system was relatively new but is now stabilized, likely resulting in more reliable data.

M.T. Pitkänen, MD, PhD (✉)
Department of Anesthesia, Orton Invalid Foundation, Helsinki, Finland
e-mail: mikko.pitkanen@orton.fi

Introduction

Fortunately, serious complications involving regional anesthesia occur rarely. Therefore, large databases are needed for morbidity studies. That is the main reason that these studies are usually retrospective multicenter trials. It is difficult to ensure that all complications will be registered. Likewise, often the accuracy of the denominator can be questioned. On the other hand, there have been excellent prospective nationwide studies where these problems have been eliminated [1, 2].

All the Nordic countries have a public, primarily tax-paid health care system. Also the legal arrangements to deal with complaints are similar. All countries have patient insurance schemes in order to regulate patient rights to economic compensation when injuries have been attributed to the medical staff.

Cases of medical malpractice are peer reviewed and handled by special institutions, not ordinary criminal courts. The schemes are based on what can best be characterized as "no fault" liability. There are patient ombudsmen or similar institutions that help patients to handle their complications. For instance, the Finnish Patient Insurance Centre (PIC) handles all personal injuries that occur in connection with health care activities in accordance with the Patient Injuries Act. A prerequisite for compensation is that an experienced medical professional could have performed a different procedure in the examination or treatment situation in question, thereby avoiding the injury. The economic compensation is granted without the necessity of finding a guilty party. The majority of rejected claims are due to the fact that regardless of appropriate treatment, the injury could not have been entirely avoided. It is not always possible to achieve satisfactory treatment results, for example, due to the serious nature of an illness or trauma. PIC promotes patient safety by carrying out research, making calculations, and compiling statistics. Its members include all insurance companies granting patient insurance policies in Finland. The reporting of complications is encouraged and thus a database is constructed. It can be

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_30

assumed that most major complications are recorded. This database has produced studies of anesthesia complications at least in Denmark and Finland.

Hove and colleagues have published two studies in the anesthesia literature from Danish Patient Insurance Association's (PIA) material [3, 4]. In the first study, they evaluated the files of patients who were given financial compensation because of an injury caused by an anesthetic procedure [3]. They evaluated the type of injuries, anesthetic procedure, and finally the size of financial compensation. The material was collected between 1996 and 2002. It was estimated that annually 400,000 anesthetic procedures were performed in Denmark. During that period, 916 anesthesia-related claims were made. Of those, 374 resulted in financial compensation. Out of these 374, regional anesthesia procedure was performed in 132 cases. Permanent nerve injury resulting in pain, incontinence, or motor function impairment was the most common serious complication. There were also some cases with paraplegia. Interestingly, only one epidural hematoma was registered. They examined separately patients, who each received more than 150,000 Euros in compensation. Out of these 13 patients, eight had received spinal anesthesia or epidural anesthesia with or without general anesthesia. Paralysis or reduced power of the legs was the most common symptom in these patients. Exact mechanisms of these complications are not revealed. In three cases, hypotension was suspected.

In the other study, Hove et al. studied the material from the Danish PIA between 1996 and 2004 for deaths related to anesthesia [4]. They found 24 cases where the patient's death was considered to result from the anesthetic procedure. Out of these in three cases epidural analgesia was used in combination with general anesthesia, once epidural analgesia was used for pain treatment and once spinal anesthesia. The reasons for death were abscesses in two cases, total spinal damage to medulla spinalis, and drug error once.

In these Danish studies, all major complications had occurred after neuraxial block. There were no cases after peripheral blocks or local anesthetic systemic toxicity (LAST).

In Finland, two studies on serious complications after neuraxial blocks have been issued from the material of Finnish patient insurance claims. The first study was published in 1997 and it is from the material 1987–1993 [5]. The latter is from the material 2000–2009, published in 2013 [6].

Some differences can be observed when these two studies with a similar method of data collection are compared (Table 30.1). Some of the changes in the numbers must be caused by changes in anesthesia practice between those periods. The number of claims has markedly increased between these two studies; however, the incidence of serious complications has remained, broadly speaking, unchanged. In the earlier study material, only one casualty (cardiac arrest) was observed compared to six in the new material (two after paraplegia, two drug errors, one infection, and one total spinal).

Table 30.1 Major morbidity in Finnish Patient Insurance Center Material Studies (number of cases, spinal/epidural)

	Aromaa et al. [5]	Pitkänen et al. [6]
Cardiac arrest	2/0	0/0
Total spinal anesthesia	0	0/2
Neurologic complication	19/4	7/17
Infection	4/2	7/6
Acute toxicity	0/2	0
Drug error	0/1	0/2

The calculation of incidences when trusting the patient insurance claims can be unreliable. Even though the patient insurance system should be well known and ombudsmen in the hospitals help patients with claims, all complications will not be registered. This is well expressed in a retrospective study by Moen et al., where they gathered information from the Swedish health care system [7]. The study was based on a mailed enquiry to anesthesia departments confirmed through search of adequate administrative files dealing with malpractice or insurance matters. They found 127 complications, including 33 hematomas. Only two out of these 33 hematomas were found in the Swedish patient insurance claims.

On the other hand, when we compare the Finnish studies we can see that there has been a marked increase in the activity of reporting claims. During the period 2000–2009, the annual number of claims has been stable, at about 8000. During the period 1987–1993 when the insurance system was relatively new, the annual number of claims rose from 2500 to 5700. Therefore, we can assume that the increase in claims has produced more reliable results.

Moen et al.'s study is from severe neurologic complications after central neuraxial blockades in Sweden 1990–1999 [7]. At that time the population in Sweden was approximately 8.8 million. In the 10-year period, they found 127 severe complications: spinal hematoma (33 cases), cauda equine syndrome (32 cases), meningitis (29 cases), epidural abscess (13 cases), and miscellaneous (20 cases). Only serious neurologic complications were included in that study. Less serious and transient complications or those attributed to systemic local anesthetic toxicity and cardiovascular side effects were not covered. They succeeded in acquiring a comprehensive retrospective study in serious neurologic complications. The number of complications as well as the denominators in their study seems to be accurately achieved. There are several interesting results which can be compared between these three studies. The numbers of neuraxial anesthesia procedures per capita are rather similar (Table 30.2).

Table 30.2 Morbidity after neuraxial blocks, Nordic studies

	Moen et al. Sweden [7]	Aromaa et al. Finland [5]	Pitkänen et al. Finland [6]
Study period (year)	1990–1999	1987–1993	2000–2009
Population	8,800,000	5,100,000	5,300,000
Spinal anesthesia	1,260,000	550,000	840,000
Epidural anesthesia	450,000	170,000	520,000 (incl CSE)

CSE combined spinal and epidural anesthesia

Table 30.3 Spinal hematomas (number of patients)

Operation, anesthesia method	Moen et al. Sweden [7]	Aromaa et al. Finland [5]	Pitkänen et al. Finland [6]
Knee arthroplasty, epidural	6	1	4
Hip arthroplasty, epidural	1		1
Hip fracture spinal	5	1	
Obstetrics epidural	1		
Cesarean section, spinal	1		
Other operations, epidural	17	2	7
Other spinal	2	1	1
Total	33	5	13
Treatment and result			
Laminectomy	12	1	8
Recovery	6	2	1

Spinal Hematomas

Hematoma after neuraxial block occurs most commonly in epidural space. It can appear also subarachnoidally and even subdurally (between dura and arachnoidea). Moen et al. and Aromaa et al. did not differentiate the anatomical location [5, 7]. Moen et al. used the term spinal hematoma, which can be assumed to mean all hematomas [7]. In Pitkänen et al.'s study, there were nine epidural, two subdural, and two subarachnoid hematomas in the lumbar area [6]. The spinal hematomas are presented in Table 30.3. In Finland, the number of hematomas increased between the two studies; however, the relative number is smaller than in the Swedish study.

In 1990s, the problem of thrombosis prophylaxis with neuraxial anesthesia was questioned because of several epidural hematomas. Since then guidelines for safe use of neuraxial block and thrombosis prophylaxis have been published by several associations (SSAI, ASRA, and ESA) [8–10]. However, in Moen et al.'s study, one-third of spinal hematomas occurred in patients receiving thrombosis prophylaxis according to the current guidelines in the absence of any previously known risk factor [7]. Likewise in Pitkänen et al.'s study 10/13 hematoma patients had thrombosis prophylaxis and in four out of these ten the current guidelines were followed [6].

Infections

Epidural abscess after neuraxial block was found in 13 patients from Sweden [7], 12 after epidural analgesia. In these patients, the epidural catheter had been in situ between 2 days and 5 weeks. Six of these thirteen had laminectomy. Seven out of these thirteen recovered. Pitkänen found only four abscesses, all after epidural which had been in place between 4 days and 2 weeks [6]. Two patients had laminectomy but all recovered. In Aromaa's study, only two abscesses were reported [5]. According to these numbers, the prognosis of spinal abscess is better than that of hematoma.

Meningitis was found in 29 cases in the Swedish study [7]. Spinal anesthesia had been used in 24 patients. Six patients did not recover completely. Aromaa et al. found four cases with meningitis, all except one recovered [5]. Similar results were reported from Pitkänen et al., there were seven cases of meningitis after spinal and one after epidural anesthesia, all

recovered [6]. In that material, there was also one fatality and that patient had developed cerebral and spinal abscesses. The symptoms started with headache 2 months after spinal anesthesia.

Neuraxial Morbidity, Conclusion

Most complications were seen after orthopedic surgery. Similarly epidural block was more often related to complications than spinal block. In all three studies, spinal stenosis was a risk factor. Moen et al. calculated that the risk for spinal hematoma in a female patient subjected to knee arthroplasty was as high as 1:3600 [7]. In contrast to this, the risk of that same complication is 1:200,000 in obstetric patients who were subjected to central neuraxial blockade.

The retrospective studies are already old when published. The treatment protocols change rapidly. From the Nordic studies we can see that there was an increase in the frequency of epidural hematomas after orthopedic surgery most probably because of active thrombosis prophylaxis and lack of proper guidelines [8]. It is important to observe that hematomas occur even though the guidelines are followed. The use of epidural analgesia in orthopedic surgery has diminished and the incidence of epidural hematomas seems to have decreased.

Local Anesthetic Systemic Toxicity

All the previously mentioned studies have concentrated on severe complications after neuraxial blocks. Peripheral blocks and LAST have not been included. Recently, a survey of severe local anesthetic toxicity from Finland was published [11]. It is based on a structured electronic questionnaire to Finnish public hospitals in 2014.

The total number of cases of LAST was 15 in the time period between 2011 and 2013. Fourteen developed central nervous system toxicity symptoms and only one cardiac symptoms. All patients recovered without sequelae. After excluding spinal anesthesia, the total incidence of LAST occurring in regional anesthesia was 15:211,700, i.e., 1:14,100. Lipid emulsion for treatment of LAST was given to five patients, including the one with cardiac symptoms.

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United Kingdom: Recent Advances in the Safety and Prevention of Regional Anesthesia Complications

31

Graeme A. McLeod

Key Points

- The National Institute of Academic Anesthesia's Health Services Research Centre (HSRC) was formed in 2011 and coordinates national audit, quality improvement and research activity investigating the influence of perioperative care, anesthesia, and critical care on patient morbidity and safety. The National Patient Safety Alerting System alerts health personnel of drug- or device-related risks.
- Complications that are the focus of UK regional anesthesia include inadvertent intravenous injection of local anesthetic, wrong site blocks, efficacy and side effects of central neuraxial blocks, and regional anesthesia for hip fracture surgery.
- In 2014, the HSRC conducted a national survey of 260 UK hospitals in order to provide a national benchmark for patient satisfaction and patient-reported awareness after anesthesia against which hospitals could measure their own performance.

Abbreviations

AAGBI	Association of Anaesthetists of Great Britain and Ireland
ASAP	Anaesthesia Sprint Audit of Practice
CNB	Central Neuraxial Block
CSE	Combined Spinal–Epidural
HSRC	Health Services Research Centre
NAP	National Audit Project
NaPSAS	National Patient Safety Alerting System
NHS	National Health Service
NIAA	National Institute of Academic Anesthesia
NPSA	National Patient Safety Agency
NRLS	National Reporting and Learning System
RCoA	Royal College of Anaesthetists
SALG	Safe Anaesthesia Liaison Group
SNAP	Sprint National Anesthesia Project
UK	United Kingdom

G.A. McLeod, FRCA, FFPMRCA, MD (✉)
Division of Neuroscience, Institute of Academic Anaesthesia, Medical Research Institute, Ninewells Hospital & University of Dundee School of Medicine, Dundee, Scotland, UK
e-mail: g.a.mcleod@dundee.ac.uk

Introduction

This review discusses the efforts made by UK anesthetists to reduce patient morbidity by making regional anesthesia procedures safer. However, beforehand, it is first necessary to understand the political backdrop in the UK that has recently placed patient safety at the forefront of healthcare delivery.

The overriding impetus to improve patient outcome in the UK has been driven by the report of the Francis inquiry into poor patient care at Mid Staffordshire National Health Service (NHS) Foundation Trust in England that exposed excessive morbidity and mortality alongside a highly negative clinical and managerial culture [1]. Poor healthcare delivery was not attributed to any individual but to a total "systems failure," and led the Prime Minister, David Cameron, to publicly state his desire "*to make zero harm a reality in our National Health Service (NHS)*" [2]. The ensuing Berwick report recommended developing a healthcare culture that was open, transparent, and honest, with an emphasis on objectivity and clinical reflection, in order to inform and educate staff, and in doing so reduced avoidable morbidity [3].

Recently, two anesthesiologists were recently charged with manslaughter by gross negligence over the death of a woman in Kent, who died after giving birth by emergency caesarean section [4]. The Maidstone and Tunbridge Wells NHS Trust, which runs the hospital, was charged with corporate manslaughter and represented the first time that this charge had been taken against a hospital in the UK using

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_31

the Corporate Manslaughter and Corporate Homicide Act, 2008 [5]. Its objective was to make organizations more accountable in the event of death occurring in the workplace, and to make senior managers more accountable for all areas of health and safety within a hospital including the organization and management of individuals tasked with patient care.

NHS England now centrally coordinates all "safety" activity. The National Reporting and Learning System (NRLS) [6], the most comprehensive database of patient safety information in the world, was retained with NHS reorganization, but a new National Patient Safety Alerting System (NaPSAS) was created in order to inform all health personnel of drug- or device-related risk [7]. Hospital safety performance is now published and a list of "never events" has been created. This includes wrong site surgery and, as of 1st April 2015, wrong site regional anesthesia.

Thus, initiatives within UK regional anesthesia must be seen within a wider context, and regarded as the contribution of a single subspecialty to a highly complex "systems" problem that requires coordinated, multidisciplinary input from all clinical and nonclinical healthcare professionals. The national coordination of safety data from reorganization of NHS England has facilitated that subspecialties may take a UK approach to reducing patient morbidity.

Regional anesthesia in the UK has focused on the following clinical problems: (1) inadvertent local anesthetic injection; (2) wrong site blocks; (3) the efficacy and side effects of thoracic epidural anesthesia and analgesia; and (4) the role of regional anesthesia in hip fracture surgery. The publication of the Berwick report has provided an opportunity for anesthesiologists to participate actively within a safety-focused and outcomes-driven health service.

Inadvertent Local Anesthetic Injection

The design of medical devices should follow the established principle of "safety under single fault conditions," i.e., a single fault should not result in an unacceptable risk. Yet in 2015, it is still possible to inject epidural or perineural drugs intravenously and vice versa using standard syringes and needles. In UK anesthetic practice between 2001 and 2004, three deaths occurred secondary to accidental intravenous infusion of bupivacaine. A review of reports made to the National Patient Safety Agency (NPSA) over 17 months between 2005 and 2006 revealed 346 incidents associated with epidural practice [8]. Most of these resulted in little harm, but included six incidents where epidural drugs were injected intravenously. NPSA advice was to use preprepared drug as much as possible, clearly label all infusions and syringes and color code infusion devices for specific intravenous and epidural use [9]. Despite this guidance, an NPSA safety alert in 2011 reported a fourth fatal wrong route injection of epidural drug from February 2007, and 18 wrong route epidural and 4 wrong route regional anesthesia injections between 2008 and 2009 [10]. The NPSA recommended that all intrathecal and epidural injections be conducted using non-Luer syringes and needles before a deadline of 1 April 2012.

However, widespread introduction into clinical practice has been delayed because of concerns about the technical performance of new devices. An ISO-standard non-Luer connector for neuraxial applications is being developed—"Small-bore connectors for liquids and gases in healthcare applications ISO 80369 part 6"—but the timescale for clinical introduction may not be until 2016 [11].

Manufacturing delays have been attributed to balancing fail-safe design with clinical applicability. In a study by Onia et al., 49 clinicians evaluated the acceptability and performance characteristics of a BD UniVia-6 Safety Connector system (BD, New Jersey) tested on an artificial back model [12]. Clinicians agreed that the safety system was clinically acceptable and that the safety system prevented or reduced the risk of misconnection between a standard syringe and a safety spinal needle. However, two in five clinicians highlighted cross-connectivity issues between a safety syringe intended for spinal injection and an intravenous Luer device. Their findings contrasted with that of Cook et al. investigating Neurax® and Spinalok® non-Luer spinal needles and syringe systems on a bench model [13]. These non-Luer devices were regarded as less usable than the conventional system and demonstrated several cross-connectivity issues. Kinsella et al. identified major technical problems in up to one third of patients when non-Luer needles were used for spinal anesthesia including poor observation of cerebrospinal fluid in the hub and connection of the syringe to the spinal needle [14]. Of greatest concern was the failure to achieve spinal anesthesia in up to 7 % of patients.

The Chief Medical Officer for England foresaw these problems in 2002 and stated that: "we need to be certain that any potential new design solution is rigorously tested and, crucially, that by introducing new equipment to prevent one specific type of error, we do not, in turn, introduce new unforeseen risks to patients" [15]. Therefore, when new non-Luer devices are eventually introduced into practice, it will be essential for each hospital to restrict itself to one type of connector, and formally evaluate its introduction using parameters such as time to appearance of CSF in order to maintain patient safety [16].

Wrong Site Block

Wrong site procedures should not happen. They are regarded as "never events"—serious, largely preventable patient safety incidents that should not occur if the available preventative measures have been implemented [17]. Ironically, for

every patient in the UK, a modified version of the WHO Surgical Safety Checklist is completed before surgery but not after anaesthesia [18]. In the UK, the Safe Anaesthesia Liaison Group (SALG), comprising members from the Royal College of Anaesthetists (RCoA), NPSA, and Association of Anaesthetists of Great Britain & Ireland (AAGBI) identified 67 wrong block sites introduced an electronic online reporting system (Anesthetic eForm) [19].

An enquiry conducted by Nottingham University Hospitals NHS Trust in response to a cluster of five wrong-sided blocks during a 12-month period found that wrong-sided block occurred despite correct marking of the surgical site and performing a WHO check in all patients. Contributing factors to wrong-sided nerve blocks were distractions and social activity in the anesthetic room when conducting blocks; prolonged time between start of anesthesia and WHO sign in; and covering-up of the surgical mark with blankets in an attempt to keep the patient warm [19]. Distractions can occur easily within UK anesthetic rooms particularly when teaching medical students, anesthesiology trainees, or postgraduates from other disciplines engaged in regional anesthesia research. The author's own experience is that students less familiar with the environment of the operating room tend to be more demanding in time and attention. Three bioengineering masters students introduced into the surgical environment have fainted on separate occasions during conduct of regional anesthesia. Needless to say this automatically drew attention away from the patients and represented a serious risk to morbidity! Any procedural difficulty with increased duration of anesthesia, turning of the patient, and change in technique or absence of routine operating room personnel is likely to compound problems and potentially compromise safety and increase morbidity. Surgical sites are marked but are often distant and covered by blankets; paradoxically, few anesthetists mark their own block sites.

In response to their own enquiry, the Nottingham regional anesthesia team promoted a patient safety initiative called "Stop Before You Block" that has been implemented nationally [20]. Anesthetists and operating department personnel are requested to (Fig. 31.1):

1. Conduct WHO sign in before anesthesia. Any member of the team is encouraged to initiate this.
2. Define the STOP moment as that immediately before needle insertion. At this point in time the anesthesiologist and his/her assistant should select the correct site before needle insertion by confirming the surgical site and side of block. The following is recommended:
   (a) Visualizing the surgical arrow indicating site of surgery
   (b) Asking the patient to confirm the side of surgery (if conscious)
   (c) Double checking the consent form for operative side (if patient unconscious)

Fig. 31.1 Notice for anesthetists and anesthetic assistants

No reaudit of this initiative has yet been conducted but the results are eagerly anticipated.

Efficacy and Side Effects of Central Neuraxial Block

Over the last 20 years, numerous surveys of the efficacy of thoracic epidural analgesia have been conducted, often within single institutions. Taken together, the most striking clinical feature is the wide variation in pain experienced by patients in the days following major surgery. Early audits recognized that while some patients experienced both excellent pain relief and mobility, others endured severe pain, needing repeated but increasingly ineffective rescue medication. Recent work by Moore et al. describing the bimodal nature of postoperative pain relief gives credence to these findings [21].

The dilemma that many clinicians have, when deciding how to manage pain relief after surgery, is trying to balance the potential benefits of thoracic epidural analgesia, based on evidence and personal and local experience, against the risk of serious adverse events such as epidural hematoma, epidural abscess, and nerve damage.

The problem with local surveys is that, even when conducted over many years, they are unlikely to capture rare events.

Similarly, randomized controlled trials (RCTs), although providing the highest caliber of evidence, are invariably too small to quantify the incidence of serious side effects after thoracic epidural analgesia. Thus, both anesthetists and patients are denied valuable information that may guide clinical practice.

In view of this major limitation, anesthesiologists within the United Kingdom have concentrated, in the main, on conducting national audit projects (NAPs) with the purpose of identifying the incidence of rare complications of anesthesia otherwise impossible to quantify without a national survey. The choice of the third UK national audit project (NAP) was the "Major Complications of Central Neuraxial Block in the United Kingdom" [22]. NAP3 consisted of two parts: the first estimated the denominator, the number of central neuraxial blocks (CNBs) performed annually, and the second calculated the numerator, the incidence of complications over 12 months.

Denominator

Every anesthetic department in the UK was contacted and asked to appoint a coordinator. Over a 2-week period each coordinator documented the number of epidural, spinal, CNBs, CSEs, and caudal blocks inserted within the following categories: adult perioperative; obstetric; chronic pain; pediatric; and non-anesthetist. The 2-week sampling period represented a balance between precision and reliability of data capture. Projection to 52 weeks estimated the denominator as 707,455 central neuraxial blocks per year in the NHS.

Numerator

All major complications of CNBs performed over 12 months (vertebral canal abscess or hematoma, meningitis, nerve injury, spinal cord ischemia, fatal cardiovascular collapse, and wrong route errors) were reported. Each case was reviewed by an expert panel to assess causation, severity, and outcome. "Permanent" injury was defined as symptoms persisting for more than 6 months.

Eighty-four major complications were reported, of which 52 met the inclusion criteria at the time they were reported. Data were interpreted "pessimistically" and "optimistically." "Pessimistically" there were 30 permanent injuries and "optimistically" 14. The incidence of permanent injury due to CNB (expressed per 100,000 cases) was "pessimistically" 4.2 (95 % confidence interval 2.9–6.1) and "optimistically" 2.0 (1.1–3.3). "Pessimistically" there were 13 deaths or paraplegias, "optimistically" 5. The incidence of paraplegia or death was "pessimistically" 1.8 per 100,000 (1.0–3.1) and "optimistically" 0.7 (0–1.6). Two-thirds of initially disabling injuries resolved fully.

Strengths and Weaknesses

The strength of NAP3 was that it was relevant to patients, anesthetists, and the wider health service. Collection of data was robust and every case report was reviewed by a team of experts. Importantly, NAP3 has driven changes in practice and recommendations for good practice of thoracic epidural analgesia were published nationally in 2010 by a national collaboration of interested parties headed by the RCoA [23]. The weaknesses of NAP3 were the absence of good outcome controls and justification for the decisions of experts.

National Coordination

National Audit Projects are now organized and run by the Health Services Research Centre (HSRC) of the National Institute of Academic Anesthesia (NIAA) [24, 25]. In addition, the HSRC coordinates quality improvement initiatives and rapid or "sprint" audits of national practice, drawing in data from each acute hospital. Key to success of national data collection was the creation of a network of approximately 260 local anesthesiologists, or Quality Audit and Research Coordinators (QuARCs), responsible for coordinating local data collection, and acting as the interface between routine clinical anesthesia and the HSRC. The advantage of such an approach is that it has encouraged many trainees to participate in data collection for the first time and contribute to projects of national importance. Examples of national audits relevant to regional anesthesia include National Hip Fracture Database Anaesthesia Sprint Audit of Practice (ASAP) and Sprint National Anesthesia Project (SNAP) [26, 27].

The Role of Regional Anesthesia in Hip Fracture Surgery

The morbidity and mortality of hip fracture is very high. Patients are elderly and have concomitant, multiple, chronic illness. Mortality is approximately 8 % at 1 month and has ostensibly not changed in the last 30 years [28]. Therefore the National Hip Fracture Database ASAP was conducted as part of the UK National Clinical Audit program in 2013. A total of 16,904 patients were admitted with hip fracture to 184 hospitals over a 3-month period in 2013. Of those 97.6 % underwent anesthesia and operation. The most notable observations arising from the audit concerned the role of regional anesthesia; spinal anesthesia was associated with less hypotension compared to general anesthesia, and adjunct nerve block was administered to just over half of patients with a hip fracture. The audit recommended that nerve block should be offered to all patients with hip fracture; departments of anesthesia should develop evidence-based standardized

approaches to spinal anesthesia, administration of sedatives, oxygen and intrathecal opioids.

Patient Satisfaction

Anesthetic departments have few validated tools at their disposal to measure outcomes after either general or regional anesthesia. Therefore the HSRC conducted a national survey of 260 participating hospitals in order to provide a national benchmark for patient satisfaction and patient-reported awareness after anesthesia against which hospitals could measure their own performance. The "Sprint National Anesthesia Project" (SNAP) took place over 2 days in May 2014 and the results are awaited with great interest [26].

Conclusion

Morbidity secondary to regional anesthesia gained national prominence over 10 years ago after four accidental deaths due to intravenous injection of epidural local anesthetics. Since then, anesthesiologists within the UK have actively tried to reduce morbidity associated with regional anesthesia by making the process of nerve block and its postoperative management safer. Several studies have been conducted in the UK on non-Luer connectors and documented the potential benefits and side effects of these devices; an ISO directive is anticipated in 2016 and will change practice worldwide. As from this year, wrong site block is now regarded, like wrong side surgery, as a "never event" and a successful campaign to "Stop Before You Block" has been successfully run in the UK and at the European Society of Regional Anaesthesia. The Health Services Research Institute at the Institute of Academic Anaesthesia now coordinates national audit projects such as NAP3 that allow calculation of the approximate incidence of rare adverse events within regional anesthesia. Conversely, "SNAP" audits of national routine practice are also possible and the first has recently been conducted. I would anticipate that attempts to further reduce morbidity in UK regional anesthesia will be made by national collection of "Big Data," and linkage with other datasets such as cancer and pharmacy prescription data in order to drive change at a national level.

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United States: Complications Associated with Regional Anesthesia (An American Society of Anesthesiologists' Closed Claims Analysis)

32

Christopher Kent, Karen L. Posner, Lorri A. Lee, and Karen B. Domino

Key Points

- The American Society of Anesthesiology Closed Claims Project is designed to collect information about and analyze adverse events related to anesthesia. Over 10,500 claims in the database represent events that occurred in 1970–2013.
- From 2000 to 2013, 445 claims were made relating to regional anesthesia, with obstetric cases comprising about 1/3 of the total. The majority (71 %) of claims were related to neuraxial anesthesia.
- More cardiovascular and respiratory complications as well as permanent injury or death were reported among neuraxial block claims. Peripheral nerve block claims were more commonly associated with temporary neurologic impairments and local anesthetic systemic toxicity compared to neuraxial block cases.
- Neurologic injury, including direct needle trauma, was reported for both peripheral and central neuraxial blocks. Several claims related to peripheral nerve blocks were due to wrong-side blocks or administration of the block under general anesthesia.
- Standards for documentation of regional anesthesia procedures differ among institutions. Poor documentation may put the anesthesiologist at risk of lacking evidence that a procedure was performed according to practice standards or that patient consent was obtained properly.

Abbreviations

ASA	American Society of Anesthesiologists
ASRA	American Society of Regional Anesthesiologists
CPR	Cardio-pulmonary resuscitation
GA	General anesthesia
ISB	Interscalene block
LAST	Local anesthetic systemic toxicity

Introduction

The American Society of Anesthesiologists' (ASA) Closed Claims Project was initiated in 1984 in order to study adverse outcomes in anesthesia practice. Researchers with the project have systematically evaluated a database of closed malpractice claim files obtained through the voluntary participation of professional liability insurance companies in the United States [1]. The number of participating insurers has changed over time but the database has captured claims from all 50 states and a variety of practice settings, including physician-owned self-insured groups, academic practices, and anesthesiologists insured by private insurance companies. The participating organizations currently insure approximately 36 % of the practicing anesthesiologists in the United States. More than 10,500 claims for adverse outcomes that originated between 1970 and 2013 have been included in the database. Usually 2–5 years elapse between the occurrence of an adverse event and the closure of its associated claim, so there may be a significant time lag for analyses of specific events.

The claims are reviewed by practicing anesthesiologists who visit each insurance company office after having received instruction on how to use a standard data collection form to gather detailed case information. Claims with enough information to reconstruct the sequence of events and to attempt to determine the nature and causation of

C. Kent, MD • K.L. Posner, PhD
K.B. Domino, MD, MPH (✉)
Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA
e-mail: kentc02@uw.edu; posner@uw.edu; kdomino@uw.edu

L.A. Lee, MD
Department of Anesthesiology, Vanderbilt University, Nashville, TN, USA
e-mail: lleegas@aol.com

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_32

injury are included. Dental injury claims and claims without sufficient information are excluded from the database. The closed claims files usually contain relevant hospital and medical records, depositions from involved healthcare personnel, expert reviews, deposition summaries, outcome reports, and the cost of settlement or jury award. Reviewers assess the overall appropriateness of anesthetic care based on the standard of care at the time of the event and its contribution to the injury. A severity of injury score is assigned to each claim that is designated by the onsite reviewer using the insurance industry's ten-point scale, where 0 = no injury and 9 = death. A score of 1 represents emotional injury; 2–4 reflect temporary injuries; 5 reflect permanent, nondisabling injuries; and 6–8 reflect permanent and disabling injuries. Payment amounts represent payments by all defendants and are adjusted to 2014 dollar amounts. Average payments are reported as the median for payments made (excluding claims with no payment). In addition to their completion of the data sheet, the onsite reviewers provide a narrative summary of events. Data collection forms and narrative summaries are then sent to practicing anesthesiologists of the Closed Claims Project Committee in Seattle, Washington, U.S.A., where committee members review each claim. Data are then analyzed according to variables of interest including damaging event, patient demographics, procedure, severity of injury, etc.

The Closed Claims Project database allows for the analysis of rare adverse events that would only otherwise be captured by large multicenter long-term studies [2]. It is important to understand the limitations of the database and the ways in which the closed claims perspective on adverse anesthetic events is distorted by the lenses and filters of the medical malpractice system. The results of the Harvard Medical Practice Study have indicated that there is a poor correlation between the occurrence of patient injury due to medical negligence and the filing and outcome of malpractice claims [3]. Under the US system which operates predominantly on a contingency fee basis, lawyers approached by plaintiffs have to make a calculated judgment whether the likelihood and amount of a financial settlement in a verdict for the plaintiff will justify the time, effort, and initial expense that the legal team will have to carry until the claim is settled. This means that the subset of adverse anesthetic events associated with malpractice claims will almost certainly be skewed toward the inclusion of those with more severe adverse outcomes which are more likely to yield higher payments. Near misses and episodes of care where interventions successfully prevent a patient from experiencing a complication are not likely to appear in the database. Other limitations include the effect of outcome bias, the somewhat low inter-rater reliability for assessment of standard of care, and the lack of a definable denominator population for evaluating the incidence of complications [4–6].

Complications Associated with Regional Anesthesia

Data for the analysis of regional anesthesia claims in this chapter were derived from the Closed Claims Project database with claims originating from events occurring between the years 2000 and 2013. For purposes of analysis and comparison, inclusion criteria were any claim that involved regional anesthesia used for surgical anesthesia, postoperative pain management ("acute pain"), or obstetric procedures. Claims for chronic pain management and obstetric claims involving only injuries to the baby were excluded from this analysis. The final analysis contained 445 regional anesthesia claims.

Claims were categorized according to damaging events (mechanisms of injury) and complications (injuries). Primary damaging events are the predominant mechanism of injury for any claim. Broad categories for damaging events include respiratory system events, cardiovascular system events, regional block-related events, equipment problems, drug administration errors, other anesthesia events, surgical events or patient condition, and none or unknown events. Specific damaging events included in the broad category of regional block-related damaging events were unintentional intravascular injection or absorption of local anesthetic; shearing or breaking of an epidural catheter; high block; and inadequate analgesia from block, dural puncture, block needle trauma, and neuraxial cardiac arrest. Neuraxial cardiac arrest was defined as the sudden onset of severe bradycardia or cardiac arrest during neuraxial block with relatively stable hemodynamics preceding the event without an apparent alternative causation, nor apparent progression to a high block or total spinal.

Complications are the injuries for which the patient (plaintiff) is seeking compensation, and multiple complications may be involved in one claim. Death was considered the complication whenever it was associated with other injuries. Complications were categorized as nerve damage if there were clinical, anatomic, or laboratory findings consistent with damage to discrete elements of the spinal cord or peripheral nervous system [7]. Low back pain or muscle aches without specific neuroanatomic lesions were categorized as other complications and were not included as nerve damage.

Overview

The patient and case characteristics are summarized in Table 32.1. Obstetric anesthesia cases (142) make up the single largest clinical case type among the neuraxial claims (45 %) and represent 32 % of all regional anesthesia claims. There were fewer total peripheral nerve block claims (128) than there

Table 32.1 Patient and case characteristics

	Neuraxial $n = 317$	PNB $n = 128$	p value	Total $n = 445$
Sex of patients				
Female	236 (74 %)	61 (48 %)	$p < 0.001$	297 (67 %)
Age in years ($n = 435$)				
Mean (SD)	46 (19)	52 (15)	$p = 0.001$	48 (18)
Pediatric (16 and under)	2 (1 %)	2 (2 %)	$p = 0.326$	4 (1 %)
ASA physical status ($n = 432$)				
ASA 1–2	181 (58 %)	92 (76 %)	$p = 0.001$	273 (63 %)
Emergency ($n = 441$)				
Yes	58 (18 %)	6 (5 %)	$p < 0.001$	64 (15 %)
Procedure scheduled as inpatient/outpatient ($n = 435$)				
Inpatient	287 (92 %)	30 (24 %)	$p < 0.001$	317 (73 %)
Outpatient	25 (8 %)	93 (76 %)		118 (27 %)
Category of anesthetic care				
Surgical	112 (35 %)	73 (57 %)	$p < 0.001$	185 (42 %)
Obstetrics	142 (45 %)	0 (0 %)		142 (32 %)
Acute pain	63 (20 %)	55 (43 %)		118 (27 %)

PNB peripheral nerve blocks, *ASA* American Society of Anesthesiologists
$N = 445$ unless otherwise specified. Claims with missing data excluded
p-values for differences between neuraxial and peripheral nerve block groups by Fisher's exact test for proportions and t-test for age

were obstetric claims. The large number of obstetric claims had a significant influence on the age and gender of the subjects with neuraxial claims. There were very few claims involving pediatric subjects, with only two neuraxial and two peripheral nerve blocks in pediatric patients. Patients involved with peripheral nerve block claims were more commonly healthy (76 % ASA physical status 1–2) outpatients (76 %) than patients in neuraxial claims (58 % ASA 1–2, 92 % inpatient).

The specific distribution of the blocks associated with claims is summarized in Table 32.2. The most common neuraxial blocks in claims were lumbar epidural (44 % of neuraxial block claims) and spinal (36 %). Among peripheral nerve blocks, the most common were interscalene (45 % of peripheral block claims), followed by eye blocks (14 %), axillary blocks (12 %), and femoral blocks (12 %). It is difficult to know whether the frequency of the appearance of the individual block types mirrors the frequency with which these blocks were performed in clinical practice, but there are some indications that it does not. A national survey of practice patterns for peripheral nerve blocks published in 1998 indicated that anesthesiologists reported performing the following upper extremity blocks in decreasing order of frequency: axillary, interscalene, wrist, supraclavicular, elbow, infraclavicular while for the lower extremity the block order in descending frequency was ankle, femoral sciatic, popliteal [8]. If this study accurately reflects national practice and the pattern has not changed greatly over the ensuing years, it would suggest that interscalene block is a potentially higher risk block for injuries with malpractice claims, while ankle blocks appear to be lower risk relative to the frequency with which they are performed. The same consideration of malpractice risk relative to frequency of clinical volume may apply to eye blocks but it is even more difficult to capture data on the number of these blocks performed by anesthesiologists.

Table 32.2 Types of regional blocks

Neuraxial blocks ($n = 317$)	n (% of 317)
Lumbar epidural	140 (44 %)
Spinal	113 (36 %)
Spinal-lumbar epidural combination	31 (10 %)
Thoracic epidural	26 (8 %)
Caudal epidural	1 (0 %)
Cervical epidural	1 (0 %)
Unspecified epidural	5 (2 %)
Peripheral nerve blocks ($n = 128$)	n (% of 128)
Interscalene	58 (45 %)
Eye blocks	18 (14 %)
Retrobulbar	9 (7 %)
Peribulbar	7 (5 %)
Eye block, unspecified	2 (2 %)
Axillary	15 (12 %)
Femoral	15 (12 %)
Popliteal	7 (5 %)
Ankle	5 (4 %)
Brachial	3 (2 %)
Paravertebral	2 (2 %)
Bier block	2 (2 %)
Femoral/sciatic	1 (1 %)
Multiple techniques	2 (2 %)

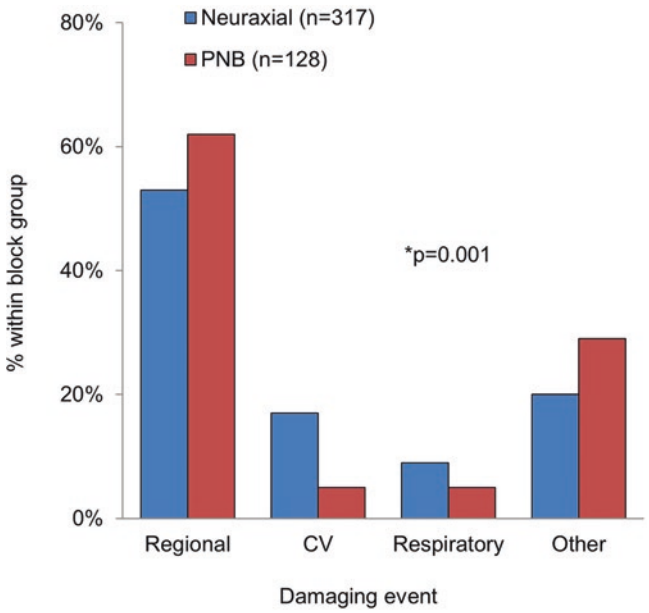

Fig. 32.1 Primary damaging events in neuraxial vs. peripheral nerve blocks. *PNB* peripheral nerve blocks, *CV* cardiovascular events. Events differed between groups ($p = 0.001$ by Fisher's exact test). Neuraxial blocks were associated with proportionately more cardiovascular and respiratory events

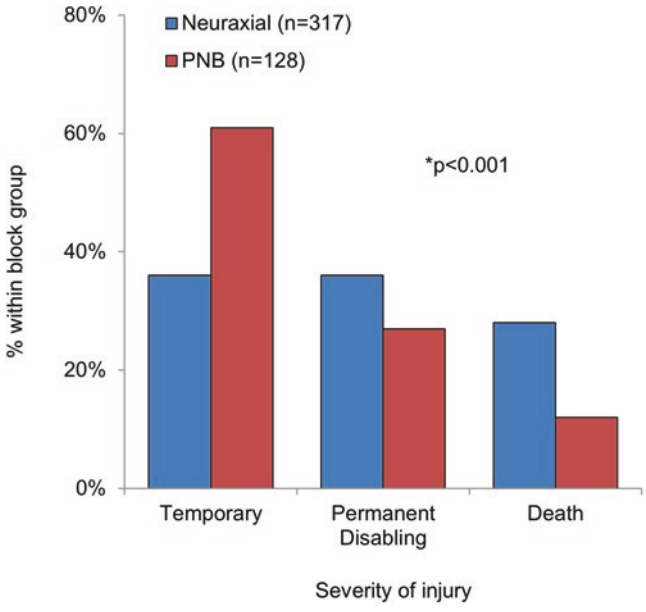

Fig. 32.2 Severity of injury in neuraxial vs. peripheral nerve blocks. *PNB* peripheral nerve blocks. Death was more commonly associated with neuraxial blocks, while temporary injuries were more commonly associated with PNB. Severity differed between groups ($p < 0.001$ by Fisher's exact test)

Table 32.3 Liability

	Neuraxial	PNB	*p* value	Total
Appropriate anesthesia care ($n = 405$)	177 (62 %)	77 (65 %)	$p = 0.652$	254 (63 %)
Claim paid ($n = 442$)	172 (55 %)	57 (45 %)	$p = 0.074$	229 (52 %)
Payment amount ($n = 229$)				
Median ($p < 0.01$)	$503,000	$248,000	$p < 0.001$	$382,000
Interquartile range	$173,000–$1,214,000	$20,000–$545,000		$117,000–$1,056,000

PNB Peripheral nerve block
$N = 445$ unless otherwise specified. Claims with missing data excluded
Payment amounts adjusted to 2014 dollars by CPI and rounded to nearest $1000.00
Payment median *p*-value by Mann–Whitney *U* Test between neuraxial and PNB groups
Appropriateness and claim paid *p*-values for differences between neuraxial and PNB groups by Fisher's exact test for proportions

A comparison (Fig. 32.1) of the damaging events between peripheral nerve blocks and neuraxial blocks indicates that, while regional anesthesia-related events were most common in both groups, there were proportionately more cardiovascular and respiratory damaging events in the neuraxial group than the peripheral nerve block claims. This finding may be related to the higher proportion of ASA 3–5 patients in the neuraxial group or due to the cardiovascular effects of a neuraxial block. Most (61 %) peripheral nerve block claims involved temporary or non-disabling injuries, while neuraxial claims had proportionately more permanent disabling injuries (36 % of neuraxial claims vs. 27 % peripheral nerve blocks) and death (28 % neuraxial vs. 12 % peripheral nerve blocks, Fig. 32.2). Only one-third (36 %) of neuraxial block claims had temporary injuries, which were predominately associated with obstetric claims (69 %).

Claims reviewers assessed the anesthesia care as appropriate in about two-thirds of both neuraxial (62 %) and peripheral nerve block claims (65 %, Table 32.3). Approximately half of all regional anesthesia claims resulted in payment. Payments for neuraxial blocks were significantly higher than for peripheral nerve blocks (median payment $503,000 vs. $248,000, respectively, p = 0.001, Table 32.3), which is likely related to the higher severity of injury associated with neuraxial blocks.

Neuraxial Cardiac Arrest

The problem of neuraxial cardiac arrest occupies a central place in the history of the Closed Claims Project as it was the subject of the first article and review of the database published in 1988 [2]. In another review of closed claims of regional anesthesia complications encompassing the 1980s and 1990s, there were 73 neuraxial cardiac arrest claims making it at that time the largest category of block-related regional anesthesia claims with death or brain damage [9]. In contrast, the review for this chapter covering events that occurred in the year 2000 or later contained 12 claims for neuraxial cardiac arrest in 13 years with two of those claims being severe bradycardic episodes that responded to pharmacologic treatment without progression to full arrest or requirement for chest compressions. Only one of the 12 claims in the recent review fit the most common pattern described in 1988 by Caplan et al. [2], that is, of an arrest occurring approximately 30 min after initiation of the anesthetic in a patient receiving moderate to heavy sedation. Three of the more recent claims were for arrests occurring during epidural anesthesia, while nine claims were associated with spinal anesthesia, one of which was due to the spinal component of a combined spinal epidural. In three claims, the arrest occurred within the first 5 min after the spinal was placed and in all of these cases the resuscitation was unsuccessful with death as the final outcome. The timing of the arrest relative to the initiation of the anesthetic in the remaining claims was quite variable with one occurring over 1 h into the procedure and another coinciding with placement of the dressing at the end of surgery. There were four deaths in the 12 claims and five patients had hypoxic–ischemic brain injury ranging from mild residual cognitive deficits to severe, disabling encephalopathy. It is likely that most episodes of bradycardia occurring during neuraxial anesthesia respond to single doses of ephedrine or anticholinergic medications, but in these claims there was a pattern of failure to respond to multiple repeated doses of these medications, raising the possibility that clinicians may need to consider an earlier transition to epinephrine when faced with bradycardia resistant to standard treatments. Six of the claims occurred in the setting of obstetric anesthesia, two of these arrests resulted in the death of the patients, two were associated with hypoxic–ischemic brain injury, and the other two had severe bradycardia without cardiac arrest and no long-term sequelae. The role of establishing and maintaining good rapport with patients is highlighted by these two claims as the records suggested that preexisting poor rapport was possibly a more significant trigger for the claim than the anxiety and discomfort that accompanied the brief, successfully treated arrhythmia. Payments for damages were made in six claims with a median payment of $383,250 (range $187,500–$2,211,000).

Two frequently suggested mechanisms to explain neuraxial cardiac arrest are as follows: (1) left ventricle hypovolemia causing a paradoxical bradycardic response via stretch/mechanoreceptors (the Bezold–Jarisch reflex); and (2) blockade of the cardiac accelerator fibers with high sympathetic blockade >T4 [10]. Baseline bradycardia and male gender have been identified as risk factors for severe bradycardia (<40 beats per minute) under neuraxial blockade, but these were not present in the claims in this review. Previous studies are consistent with the findings of this review in that bradycardia which may be a premonitory sign of impending arrest can be widely distributed throughout the time course of neuraxial anesthetics [11].

Although timely initiation of appropriate treatment for neuraxial cardiac arrest has been associated with full recovery in several case studies, many patients are refractory to rescue [12]. This refractoriness to treatment was explored in studies in dogs which demonstrated that the intense sympathetic blockade during spinal anesthesia decreases circulating blood volume and reduces coronary perfusion pressure, thereby rendering cardiopulmonary resuscitation (CPR) ineffective [13]. Moreover, other studies in dogs have shown that neuraxial anesthetic blockade prevents an increase in epinephrine and norepinephrine catecholamine levels during cardiac arrest compared with controls without neuraxial blockade [14]. Consequently, both severe vasodilatation and lack of an appropriate catecholamine response to stress make resuscitation during neuraxial cardiac arrest more difficult.

The apparent dramatic reduction in the number of neuraxial cardiac arrest claims in the database over the past three decades could have a number of explanations, however, given the difficulty of assessing trends in the undefined denominator population, any explanations of this phenomenon should be considered speculative. Several factors could have had an impact on the claims. There may be a reduction in the absolute number of neuraxial anesthetics being performed, particularly for nonobstetric anesthetics, where there has been an increase in peripheral nerve blocks and catheters over the last decade. Changes in anesthetic practices may have reduced the number of neuraxial cardiac arrests relative to the number of neuraxial anesthetics or improved the prevention, recognition, and effectiveness of the rescue therapy provided in neuraxial cardiac arrest. The report by Caplan et al. [2] advocated closer respiratory monitoring when sedation was used with neuraxial anesthesia, the earlier use of epinephrine in the treatment of sudden severe bradycardia with neuraxial anesthesia, and immediate treatment of cardiac arrest with a full resuscitation dose of epinephrine. Whether the dissemination of these ideas or whether other aspects of anesthetic practice contributing to improved patient safety reduced the frequency of malpractice claims for neuraxial cardiac arrest is unclear. Because patients who recover completely from neuraxial cardiac

arrests may be less likely to file malpractice claims, the success and failure rates of prompt resuscitation and monitoring cannot be determined from the apparent decrease in the number of claims in the database.

High Block/Total Spinal Block

There are instances where it can be difficult to clearly distinguish, both in the moment or retrospectively, between claims related to neuraxial cardiac arrest and those where cardiac arrest occurred in the setting of unusually high neuraxial block or total spinal anesthesia. As much as possible these claims should be differentiated and reviewed separately as the factors associated with these two complications appear to differ in significant ways. In the most recent review, there were 24 claims involving a high neuraxial block, evenly divided between those arising in obstetric and nonobstetric anesthesia practice.

Of the 12 claims for high block in obstetric practice, four occurred during the provision of labor analgesia while the other eight involved anesthesia for cesarean delivery. All of the claims associated with labor analgesia appeared to have involved unrecognized intrathecal injection. Two of the four labor analgesia obstetric claims involved the questionable practice of injecting local anesthetic through the epidural needle prior to placement of the catheter. The remaining two high blocks associated with labor analgesia cases resulted from injections through the epidural catheter, one with a lidocaine test dose and the other without use of a formal test dose. Among the high blocks associated with anesthesia for cesarean delivery, five occurred with dosing of an epidural and three in the setting of spinal anesthesia. Notable among these cases was an incident where an aspiration test that was negative for cerebrospinal fluid prior to a 10 mL injection of lidocaine was noted to be undeniably positive after it resulted in a total spinal. There is controversy, particularly in obstetric anesthetic practice, regarding what doses of local anesthetic represent appropriate test doses for the identification of an intrathecal catheter when an aspiration test is negative [15, 16]. Data from the limited number of pertinent cases in the database cannot add much clarity to this controversy. High neuraxial blocks occurred both in the setting of dose amounts consistent with historically accepted test doses and in instances where a negative aspiration test apparently gave a false sense of security before an unintended intrathecal injection of a large dose of local anesthetic.

One of the more vexing challenges in obstetric anesthesia arises when the existing labor epidural provides insufficient anesthesia for a cesarean section after injection of what would usually be an adequate dose of local anesthetic. If time permits, one of the options available to the anesthesiologist in this setting is the removal of the epidural and placement of a spinal anesthetic. However, the appropriate spinal local anesthetic dose in this context remains uncertain. In one of the claims in this review, a standard dose was used in a spinal after a failed epidural local anesthetic load, resulting in a high block leading to respiratory and cardiac arrest. In a major review of obstetrical complications, this practice was identified by D'Angelo et al. as having significant potential for dangerously high neuraxial blocks, as 20 % of the high blocks in their review occurred with spinals placed after failed epidurals [17].

In the nonobstetric setting there were six high blocks resulting from the placement of thoracic epidurals for analgesia, three claims in the setting of spinal anesthetics, three from lumbar epidurals, and two from peripheral nerve blocks (an interscalene and a paravertebral). The two high thoracic epidural blocks that were due to unrecognized intrathecal placement left the patients with residual neurologic injury to the spinal cord, a syrinx in one claim and cauda equina syndrome in the other. The importance of recommendations to avoid placing neuraxial blocks in adults who are unresponsive or poorly responsive due to sedation or general anesthesia is raised in this group of claims, as the syrinx of the spinal cord occurred in a patient whose epidural was placed under general anesthesia. The remaining high thoracic epidural blocks occurred largely in the setting of aggressive use of lidocaine boluses to rapidly achieve analgesia in postoperative and posttrauma patients who were vulnerable to the effects of a high thoracic sympathectomy. From the lack of intensity in the monitoring during the immediate postblock period, it appeared that the providers were unaware of and unprepared for the effect that a large dose of lidocaine could have when delivered as a bolus to the thoracic epidural space. In many of the high block claims, the combination of delayed recognition of a high block and the inability to simultaneously address both the apnea and hypotension accompanying this complication caused severe patient injuries. In some instances, delayed recognition was due to the fact that the anesthesiologist administered a dose of local anesthetic and then very shortly after that left the patient to attend to other tasks. The anesthesiologist was then belatedly aware of the problem only upon return from the distracting task or when alerted by nursing staff.

The claims associated with high neuraxial blocks resulted in severe injuries and frequently multimillion dollar payments for compensation. The closed claims reviewers found that care was less than appropriate in 20 of 24 claims. Payment was made in a very high proportion of claims (21 of 24) with a median payment of just over $1,161,000 (range from $110,000 to 16,000,000). These payments reflect the severity of the injuries, commonly death or brain injury (18 of 24). In addition, the newborn was also injured in one of these claims.

Local Anesthetic Systemic Toxicity

There were 13 claims associated with local anesthetic systemic toxicity (LAST) resulting from unintentional intravascular injection or rapid uptake into systemic circulation of a toxic dose of local anesthetic. Twelve of these claims occurred during the performance of peripheral nerve blocks and one with an epidural block. The injection of local anesthetic for labor analgesia in the epidural claim was temporally related to seizure onset, but assessment of causation was complicated by a diagnosis of preeclampsia prior to the initiation of the anesthetic. This pattern of association is markedly different from the review of claims occurring between 1980 and 1999 when all the LAST claims occurred with injection of local anesthetic for epidurals [9]. Changes in obstetric anesthesia practice, including withdrawal of 0.75 % bupivacaine in obstetrics and increased use of test doses and fractionated doses of local anesthetics, may account for the reduction in claims for LAST in obstetric anesthesia. All of the claims for LAST during peripheral nerve blocks in this review occurred during either interscalene (nine claims) or axillary blocks (three claims). This inversion in the frequency of LAST events relative to the projected frequency that interscalene and axillary blocks are performed in the US as advanced by Hadzic et al. [8] could reflect a higher risk for LAST events during the performance of interscalene blocks.

All of the claims involved adults. For adults, there is controversy regarding the value of simple weight-based dosing of local anesthetic/epinephrine mixtures that don't also incorporate the absorptive characteristic of the block site and patient-specific comorbidities into the choice of total local anesthetic dose [18]. The database cannot shed any clarifying light on this issue as there were no claims associated with a dose of local anesthetic exceeding any of the commonly cited weight-based dosing guidelines. In only one of the claims was the timing of the initial signs of toxicity relative to the injection suggestive to the reviewers that the episode occurred because of excessive extravascular local anesthetic absorption without substantial intravascular injection. In this instance, the bupivacaine dose was well under 2 mg/kg and seizure activity and cardiac arrest occurred several minutes after completion of the block. For all the remaining claims, the timing was most consistent with unrecognized, direct intravascular injection.

The increasing use of ultrasound guidance in the performance of peripheral nerve blocks could theoretically have had an impact on the occurrence of episodes of LAST particularly in the latter years of the time period studied in this review. A retrospective review by Orebaugh et al. suggested that the introduction of the use of ultrasound guidance in their institution statistically significantly reduced the episodes of LAST from one per 1000 to no episodes in over 9000 blocks [19]. Other case reports and database studies note that LAST can occur even with the use of ultrasound guidance [20–22]. In this review, one LAST claim involved the use of ultrasound in conjunction with nerve stimulation guidance, but the theoretical safety advantage gained by performing the block with ultrasound guidance was probably nullified by failure to use electrocardiographic, blood pressure, or pulse oximeter monitoring. Additionally, there was testimony alleging that intermittent aspiration during injection was not performed. Not surprisingly, given the small number of claims in the review, there were no obvious patterns to the manner in which the injections of local anesthetic were performed. There were claims where LAST had occurred in spite of the reported use of incremental dosing coupled with a delay for a monitoring period between dose increments, the use of intermittent aspiration, and the use of epinephrine in the local anesthetic mixture for detection of tachycardia. A common scenario in the performance of the block was the presence of an assistant, usually a nurse, injecting the local anesthetic under the direction of the anesthesiologist. Notably in at least two instances the assistant denied that intermittent aspiration was performed while the anesthesiologist maintained that it had been, the cause of this discrepancy is unclear, but imprecise communication between the anesthesiologist and assistant remains a potentially remediable issue.

The discovery of lipid rescue therapy (intravenously administered 20 % lipid emulsion) for the treatment of LAST could have had an impact on the severity of outcomes associated with these events. The first case reports documenting the successful use of lipid rescue in humans were published in 2006, and by 2010 a protocol for lipid rescue was included in an American Society of Regional Anesthesia (ASRA) practice advisory on LAST [23–25]. Six of the LAST events in this review occurred in 2007 or later when knowledge of and access to lipid rescue was at least theoretically available to the treating anesthesiologists. Lipid emulsion treatment was used in two cardiac arrests due to LAST in 2007 and 2008. In one instance, lipid emulsion was administered approximately 10 min after arrest but there never was a return to spontaneous circulation and death was declared after inability to separate from cardiopulmonary bypass. In the other claim where lipid emulsion treatment was used, return of circulation occurred after 25 min and the patient had residual cognitive deficits. Episodes of LAST with rapid reversal of toxicity with lipid emulsion therapy and sequelae-free resuscitation are unlikely to result in malpractice claims and therefore would not likely be captured in a closed claims analysis. However, it would appear that the development of two potentially important regional anesthesia safety innovations, i.e., lipid rescue therapy and ultrasound guidance, has not entirely eliminated the problem of LAST.

Claims resulting from LAST were associated with severe outcomes and correspondingly high payments for damages. There were two deaths in the immediate time period after cardiac arrest and two deaths in the days after the arrest when supportive care was withdrawn due to the severity of hypoxic–ischemic brain injury. Four other patients experienced varying degrees of cognitive deficits and neurologic injury due to cardiac arrest. Payments for damages were made in seven of 13 claims with an average payment of $494,000 (range $218,000–$1,100,000).

Nerve Injuries Associated with Peripheral Nerve Blocks

During the time period of this review from 2000 to 2013, the use of ultrasound guidance for the performance of peripheral nerve blocks largely supplanted the use of nerve stimulator and paresthesia techniques. The low incidence of block-related nerve injuries may make it difficult to demonstrate superiority of one technique over another. Surprisingly, ultrasound has created more uncertainty regarding the pathophysiology of block-related nerve injuries. Prior to the use of ultrasound, it was generally thought that the placement of a block needle too close to a nerve could result in mechanical injury to the nerve making it more susceptible to chemical toxicity from the local anesthetic and to the hydrostatic effects of an intraneural injection [26]. Ultrasound imaging has revealed that intraneural needle placement and injection is not infrequent, with well-documented instances of intraneural injection without any accompanying block-related nerve injury [27].

In this review there were two nerve injury claims where ultrasound was used, one interscalene block (ISB) involving temporary phrenic nerve weakness and one femoral block where ultrasound was combined with nerve stimulation in a patient who also had evidence of overlapping lumbar radiculopathy and no clear electrodiagnostic evidence of femoral neuropathy. If there is such a thing as a prototypical narrative for a peripheral nerve block-related nerve injury, one might expect this narrative to involve a block where the performance was associated with paresthesia and pain on needle placement or injection with subsequent electrodiagnostic confirmation of nerve injury at the block site. Very few of the claim narratives followed this pattern. Not uncommonly claims mirrored the complexity of the ultrasound-guided femoral block claim with confounding factors and no clear picture of causation. For example, claims were reported with accompanying cubital tunnel neuropathy findings in injuries attributed to axillary block, and in other claims there were indications of an isolated axillary nerve injury, which is mechanistically more likely to be related to the surgery, but this was attributed to the ISB. Once again ISB may have been over-represented in complications relative to the frequency of its use, as it was associated with 30 of the 59 nerve injury claims occurring with peripheral nerve blocks. There were ten claims following femoral blocks, seven claims with popliteal blocks, and nine claims involving axillary blocks. Payment was made in 25 % of the claims (14 of 59). The median payment of claim was $142,500 in the paid claims with a range of $10,100–$4,422,000.

Four claims for nerve injury were associated with wrong-sided blocks. The challenge of defending an anesthesiologist after performance of a wrong-sided block was evident in that payment was made for nerve injury in one of these claims in spite of the lack of evidence of any lasting injury. In two of the other wrong-sided block claims, it took a protracted defense and video evidence obtained by private investigators of the plaintiff engaging in normal physical activity to get the claims dismissed. Two of the wrong-sided blocks were popliteal blocks where changing sides during prone positioning was a factor leading to the errors. The necessity for unwavering adherence to a “time out” and other site verification processes with the involvement of nursing staff and surgical site marking to avoid this complication cannot be overemphasized.

There is controversy regarding the safety of peripheral nerve blocks performed in adults under general anesthesia (GA) [26]. There were six claims for injuries associated with blocks that were clearly performed under GA and one other claim where the documentation was suggestive but unclear regarding the timing of the block relative to the induction of GA. The closed claims reviewers felt that care was appropriate in the three lower extremity blocks under GA but not in the three claims where an ISB was performed under GA, which included a multimillion dollar claim where the ISB caused a spinal cord syrinx, arachnoiditis, and hydrocephalus. Payment was made in four of the six claims, which included all three of the ISB claims and one femoral block claim. The femoral nerve injury claim was probably tourniquet related, but the controversy surrounding blocks placed under GA was a factor that pushed the defense team toward settling the claim rather than continuing to defend it. Anesthesiologists who believe it is appropriate to perform peripheral nerve blocks while a patient is under GA can cite the apparent poor correlation between symptoms reported during the performance of a block and block-related nerve injury. Among the claims in the database there were nerve injuries that occurred in interactive patients in the absence of painful premonitory symptoms during the block and there are cases where patients reported symptoms but not in time to prevent a catastrophic nerve injury. Examples included a spinal cord syrinx after ISB and a brachial plexus injury after ISB where the occurrence of paresthesias during initial needle placement caused an injury, despite not injecting local anesthesia and aborting the block. Regardless of the lack of clarity in the evidence, it would appear that there is a body of

medicolegal opinion in the US that recommends against the performance of blocks under GA in adults, particularly ISBs.

There were a number of claims where "bystander" nerves were affected during performance of an ISB. Phrenic nerve paresis is generally thought of as being nothing more than a temporary side effect of interscalene and supraclavicular blocks with infrequent occasions when it can be a safety concern for patients who have pulmonary comorbidities. A case series by Kaufman et al. reporting on the surgical treatment of permanent or long-term phrenic nerve paresis suggested that this type of injury after ISB may occur more frequently than has been previously recognized [28]. In the closed claims database, phrenic nerve paresis represented almost one quarter (7 of 30) of the nerve injury claims associated with interscalene blocks. There were two claims filed for the distress and extra healthcare costs associated with episodes of temporary phrenic nerve paresis and five claims for well-documented long-term, perhaps permanent, phrenic nerve paresis. There was also a claim for long-term persistence of ptosis that accompanies Horner's syndrome and sympathetic plexus block which is also usually only a transient nuisance with ISB. There was also a claim with findings strongly suggestive for permanent superficial cervical plexus injury after ISB.

Injuries to the Neuraxis

There were 19 claims in which neuraxial hematoma was associated with injuries to the spinal cord. The associated block was an epidural in ten cases, spinal in seven, one case of a combined spinal/epidural, and one misdirected paravertebral. In eight of those claims, the clinical description and MRI findings suggest that the primary cause of the injury was direct needle trauma to the cord and any hematoma was most likely incidental and at most contributory to the injury rather than its primary cause. In past closed claims analyses, neuraxial anesthetics for vascular surgery procedures were associated with over half of the claims with neuraxial hematoma. The vascular surgery landscape has shifted such that there are increasingly more endovascular procedures. There may be a corresponding decline in the use of neuraxial anesthesia for vascular procedures. This may have contributed to the fact that in this review only three of the 19 hematomas occurred in association with vascular surgery procedures while almost half occurred in the setting of orthopedic surgery. In eight of the 19 claims, anticoagulant medications were administered preoperatively, intraoperatively, and/or postoperatively. The black box warning regarding the use of low-molecular-weight heparin and neuraxial blocks was issued in 1987 and the first ASRA consensus recommendations regarding anticoagulants and neuraxial blocks were published in 1998, so all of these claims occurred in the time period after information about the need for heightened vigilance around the use of neuraxial blocks with anticoagulation had been disseminated [29]. There were a number of claims where miscommunication and misunderstanding about the timing of the administration of anticoagulant medications, particularly clopidogrel (Plavix) and low-molecular-weight heparin, appears to have played a major role in the injury. There were three claims where a combination of non-pharmacologic coagulopathy and anticoagulant use contributed to the hematoma, one involving thrombocytopenia (90–110,000) and aspirin, another with thrombocytopenia (86–112,000) and clopidogrel, and one case that involved a patient receiving dialysis for chronic renal failure.

In the event of a vertebral canal hematoma, surgical decompression is recommended within 8 h of onset of neurologic symptoms in order to provide the best opportunity for recovery [29]. The timing of the appearance of specific symptoms was difficult to precisely determine in many cases in our review, making it challenging to know how much time elapsed between injury onset and decompression treatment. The majority of cases involved delays well beyond the 8 h window, including delays of 24–48 h. The factors contributing to delays included failure to be vigilant and investigate when motor block exceeded the usual expected duration, failure by nursing staff to communicate the presence of unusual motor block or incontinence to surgical or anesthetic teams, failure of acute pain teams to either visit or document a follow-up visit of patients with neuraxial catheters, and on at least two occasions, delays resulting from first obtaining a CT scan of the spine that was falsely reassuring before a diagnostic, confirmatory MRI was completed.

The possibility that there is a significant association between neuraxial regional anesthesia, spinal stenosis, and neurologic injury has been previously raised in literature examining complications after regional anesthesia [30]. A review by Hebl et al. indicated that there may be a higher than expected incidence of complications in patients with spinal stenosis with four recorded neurologic problems among the 187 patients with preexisting spinal stenosis who received a neuraxial block in their case series, an incidence of 2.1 % [31]. In our review of the 70 nonobstetric neuraxial anesthetic injury claims, spinal stenosis appeared either as a known preanesthetic diagnosis (one claim) or as a previously undocumented comorbidity revealed during the workup of a postanesthetic neurologic problem (six claims). These findings are generally similar to those reported by Moen et al. in a Swedish survey of severe neurologic complications occurring after central neuraxial blocks with 14 study subjects reported as having spinal stenosis among the 117 nonobstetric cases [32]. Only one of the 14 subjects in the Moen review had a known history of spinal stenosis prior to the occurrence of the complication of spinal cord injury. An ancillary project of the Framingham Heart study provides a reasonable

estimate of the prevalence of spinal stenosis in a population sample, using a restrictive definition of spinal stenosis the authors reported the prevalence of all types of spinal stenosis to be 8.4 % among adults 40–80 years old, rising to 14.3 % among those over age 60 [33]. The fact that the population prevalence of spinal stenosis among adults does not appear to be dramatically different from the proportion of subjects with spinal stenosis in a group of subjects with neuraxial block and spinal cord injury in this closed claims review might suggest that there is no strong relationship between spinal stenosis and neuraxial block complications leading to malpractice claims. Perhaps a more interesting aspect of the concern around the risk of injury with spinal stenosis is the essentially unexplained nature of the neurologic injuries in five of the seven claims. In these claims there were no signs of hematoma or needle to cord trauma or unusual symptoms during placement of the block. There were two claims where apparently otherwise uncomplicated epidurals were associated with findings indicative of spinal cord infarction. It is conceivable that spinal stenosis may create a poorly compliant space, making the spinal cord particularly vulnerable to the pressure and concentration effects of local anesthetic boluses. In a study of bolus epidural injections of 10 mL of lidocaine into the epidural space of subjects without known neuraxial pathology, the pressure in the epidural space increased between 4 and 40 mmHg and that pressure was transmitted to the intrathecal space at the same level [34]. In patients with spinal stenosis there is potentially an even greater pressure peak and a more sustained pressure response in the neuraxial space with local anesthetic boluses.

Direct needle trauma is a significant source of neuraxial neurologic injury. This can arise from unintentionally deep placement of an epidural needle or unintentionally high, that is too cephalad, placement of a needle for intrathecal block. In this review, many of these claims had MRI evidence of spinal cord trauma from direct needle contact. These claims were frequently associated with patient reports of pain or paresthesia on needle placement and injection, but this was not universally reported. Anatomic variability among patients in the location of the end of the spinal cord (T12 to L3) [35] has been previously reported but in only one claim in the review was the MRI finding of termination of the spinal cord at L2 felt to be a contributing factor. The more common contributing factor was the difficulty that anesthesiologists can have when relying on surface land marks to accurately identify at which vertebral level they are performing a block. Studies have documented variability in the iliac crest alignment with lumbar interspaces (L4-5 to L3-4) [36]. This anatomic variability in the height of the iliac crest relative to the lumbar vertebrae is likely one of the factors that contributed to the finding from a study by Broadbent et al., that anesthesiologists' identification of the lumbar interspace by palpation was accurate in only 29 % of patients where vertebral level was subsequently confirmed by an MRI scan [37]. Anesthesiologists in that study were one level higher (cephalad) than the correct location in half of the cases. In some instances, the labeled interspaces were up to four levels higher than the correct location. This finding is consistent with our closed claims review: the most extreme documentation recorded that the spinal needle was placed at L3-4, but MRI studies indicated needle tracks and trauma at T12. These findings support the principle that for spinal anesthesia or analgesia, the most caudad suitable interspace should be selected to reduce the potential for direct needle trauma to the cord, particularly in obese patients where landmarks may be difficult to palpate.

Eye Injuries in Regional Anesthesia Claims

The most common complication associated with ophthalmic regional anesthesia was perforation of the globe during performance of the block (nine claims). Four of these perforations occurred during the performance of a peribulbar block, three during retrobulbar blocks, and two during unspecified "eye" blocks. The setting for the majority of ophthalmic procedures over time has undergone a progressive shift from inpatient to outpatient settings. Techniques for the most common procedure, cataract extraction with intraocular lens implant, have improved to the extent that it has become feasible to provide topical anesthesia for many patients. Both of these trends have led to decreasing opportunities for anesthesiologists to obtain proficiency in peribulbar and retrobulbar anesthetic blocks during their training [38]. Training deficiencies combined with production demands played a very explicit role in two claims in the database, where the anesthesiologist was noted to have no formal training in performing peribulbar blocks, but took up the practice because it was deemed more efficient for the anesthesiologist to perform the block rather than having it done by an ophthalmologist. Eye injuries associated with blocks were predominately high severity with 13 of 18 of claims associated with permanent, disabling injury.

Claims for Regional Anesthesia: The Role of Consent and Communication

It is rare for a plaintiff to file a malpractice claim alleging there was absolutely no consent for a procedure, as this approach would constitute a basis for a criminal case for medical battery. In a malpractice claim that is built on a foundation of inadequate consent, the plaintiff has to demonstrate that harm was causally related to the consent process, that is, if certain risks or other information had been disclosed to the patient, more likely than not the patient would not have agreed to the procedure. The issue of inadequate consent may play a more prominent role in regional anesthesia malpractice

claims than in those that involve only general anesthesia. This arises from the concept, perhaps controversial for advocates of regional anesthesia, that regional anesthetic procedures have more of an "optional" aspect to them as either an alternative to general anesthesia or as an analgesic supplement to general anesthesia. For many conditions and surgeries refusing general anesthesia would mean refusal of the surgical procedure itself but this is rarely the case for regional anesthesia. An assertion that inadequate consent contributed to harm because the patient did not have the best information on which to make a decision is difficult to prove but may be more plausible when applied to regional anesthesia.

Standards for documentation of consent vary between jurisdictions and institutions. Some require separate written consent for anesthesia whereas in other jurisdictions consent for anesthesia can simply be appended to the signed surgical consent with a supplementary note by the anesthesiologist somewhere in the anesthetic record attesting that verbal consent was also obtained. A poorly documented consent process can be introduced by the plaintiff's legal team as evidence that the anesthesiologist was cavalier or inattentive. Alternatively, documentation of consent that appears to be substantially at odds with what the anesthesiologist states was done might become the focus of an attempt by the plaintiff's legal team to discredit the veracity of the anesthesiologist's testimony and entries into the medical record. There were six claims for peripheral nerve block injury and one claim for LAST where the closed claims reviewers indicated that the lack of documentation of informed consent played a pivotal role in a ruling against the defendant anesthesiologist or in the need for a protracted defense before dismissal of a claim. There were many reports where the patient alleged lack of consent because they did not recall the process, but in the opinion of the closed claims reviewers the defense of the anesthesiologist was substantially assisted by good documentation of the consent. These included claims where the plaintiffs contested the validity of consent obtained after premedication or in the case of postoperative rescue blocks, consent obtained after general anesthesia.

One of the other ways that inadequate consent can enter into a malpractice claim is as a source of dissatisfaction that becomes one of the triggers for the claim. In at least three claims in the database, this was very explicitly the case when patients alleged that they were pressured into accepting an anesthetic that they did not want. In one notable claim the allegation was that the anesthesiologist asked a patient in active labor to sign a form attesting that she was making an anesthetic choice "against medical advice" or agree to transfer to another hospital in order to receive a general anesthetic for cesarean section rather than going along with the anesthesiologist's strongly preferred plan of a spinal. After reluctantly agreeing to the spinal, the patient had a neuraxial cardiac arrest from which she was resuscitated with some residual deficits. Not surprisingly, a claim was filed against the anesthesiologist with a ruling for a substantial payment by the defendant.

Although it is not strictly an issue with consent, a failure of communication with the surgeon was an important issue in one claim where the alleged masking of the signs and symptoms of compartment syndrome led to ischemic injury and a substantial payment by the defendant anesthesiologist. The anesthesiologist became the sole defendant without support from the surgeon when it was determined that the surgeon was not informed of the plan for a postoperative pain block and was not involved in the decision to perform the block. Whether a regional block can mask the pain of compartment syndrome and delay its diagnosis is a controversial issue, so at the very least it is important to acknowledge this concern in communications with patients and surgeons in higher risk situations [38, 39]. Considering the time pressures that arise on the day of surgery and the variability of individual responses to postoperative pain, it may be beneficial whenever possible to use a shared decision-making model that incorporates preoperatively distributed written or video decision aids for the patient which can enhance the discussion between patient and anesthesiologist, improve patient satisfaction, and reduce claims that may in part be initiated because of problems with communication around regional anesthesia [39, 40].

Conclusions

Over the three decades of its existence the closed claims database has documented a decreasing number of claims associated with neuraxial cardiac arrests, an increasing proportion of claims for LAST due to peripheral nerve blocks, and decreasing numbers of neuraxial hematoma claims. Most injuries associated with regional anesthesia claims are temporary and related to obstetrics or peripheral nerve blocks. However, block-related complications, including high neuraxial blocks, neuraxial cardiac arrest, episodes of LAST, and neuraxial hematomas, continue to result in significant patient injury and death. There was a significant delay from symptom onset to diagnosis for neuraxial hematomas, and almost all of these claims resulted in permanent neurologic injury. Anesthesiologists must be vigilant for these high-severity injuries and adequately monitor patients undergoing regional anesthesia.

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33 United States: Chronic Pain Management (American Society of Anesthesiologists' Closed Claims Project)

Albert H. Santora

Key Points

- The American Society of Anesthesiologists' Closed Claims Project's database of insurance claims resulting from the practice of chronic pain management is summarized in this chapter.
- The first study showed that most claims (76 %) relating to chronic pain management were associated with temporary or nondisabling injuries, with 64 % of claims resulting from injury that was not apparent until after discharge. Half of the claims related to spinal cord injury.
- The second study revealed that 22 % of the chronic pain management cases were associated with cervical procedures. Direct needle trauma to a nerve or the spinal cord was the most common cause of injury (31 %).
- The third study analyzed claims associated with implantable devices used to treat chronic pain.
- Of note, reviewers deemed that in a significant percentage of cases patient care was "substandard," and that appropriate informed consent was lacking in many instances.

2004: Chronic Pain Management

In 2004, Fitzgibbon et al. published the first study from the Closed Claims Project on the subject of chronic pain management [1]. "The purpose of the study was to identify and describe issues and trends in chronic pain management liability for anesthesiologists." Chronic pain management claims were compared to claims collected from surgical/obstetric cases. Data from 5475 closed claims collected between 1970 and 1999 were analyzed. Acute pain management claims were excluded from the study. A total of 5125 surgical/obstetric and 284 chronic pain management cases were identified.

Chronic pain management claims were divided into two main categories: Claims resulting from the performance of *invasive procedures* and those associated with *noninvasive* pain management treatments. *Invasive procedures* included "nerve blocks, injections, ablative procedures, implantation or removal of devices, and maintenance of devices (including catheters)" [1]. *Noninvasive* pain management activities "included primarily systemic medication management and medical opinions or consultations. Behavioral modification therapy was also included in this category." A few cases were assigned to a third category called "multiple procedures." The results of the study are summarized on Tables 33.1, 33.2, and 33.3. The authors reported that most "chronic pain management claims resulted in temporary or nondisabling injuries (76%)" [1]. The most common primary outcomes reported in closed claims relating to chronic pain management were (in order of frequency):

1. Nerve damage
2. Pneumothorax
3. Headache
4. Back pain
5. Brain damage
6. Death

Death and brain damage were significantly higher for surgical/obstetric claims than for chronic pain management claims. The **median payment** for chronic pain management claims was less than that paid for surgical/obstetric for both historical epics cited in the study:

A.H. Santora, MD (✉)
St. Mary's Hospital, Athens, GA, USA
e-mail: acsantora@bellsouth.net

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_33

Table 33.1 Procedures in chronic pain management claims (n = 284)

	Claims	
	No.	%
Invasive procedures	276	97
Injections	138	49
Epidural steroids ± associated agents	114	
Trigger point	17	
Facet	4	
Other	3	
Blocks	78	27
Peripheral	28	
Stellate ganglion	19	
Other autonomic	9	
Neuraxial	9	
Upper/lower extremity	7	
Axial	4	
Head and neck	2	
Ablative procedures	17	6
Agent	13	
Technique	4	
Implantation or removal of devices	12	4
Implantable pump	5	
Nerve stimulator	4	
Catheter	3	
Device maintenance	20	7
Other interventions[a]	11	4
Noninvasive pain management	8	3
Medication prescription	5	
Opinion/diagnosis	2	
Cupping procedure	1	

***Source*:** Fitzgibbon et al. [1]. Reprinted from Anesthesiology. Used with permission from Lippincott Williams & Wilkins
Total does not sum to 100 % because of rounding
[a]Includes three claims involving multiple procedures associated with complications. One of these claims involved invasive plus noninvasive pain management

1970–1989

- Median payment for chronic pain management claims: **$25,500**
- Median payment for surgical/obstetric claims: **$110,000**

(*Significant difference*).

1990–1999

- Median payment for chronic pain management claims: **$60,000** (approx.)
- Median payment for surgical/obstetric claims: **$110,000** (approx.)

(*No significant difference*).

Summary of the 2004 Chronic Pain Management Analysis [1]

- No pediatric patients were in the chronic pain management group.
- Chronic pain management claims increased from 2 % in the 1970s and 1980s to 10 % of all claims collected in the 1990s.
- The most common complications associated with *invasive procedures* were nerve injury and pneumothorax. Pneumothorax was the most common complication for trigger point injections.
- Most chronic pain management claims resulted in temporary or nondisabling injuries (76 %).
- Sixty-four percent of the chronic pain management claims resulted from injuries that were not apparent until after discharge from the treatment facility.
- "Blocks and injections together accounted for 78 % of claims related to *invasive* pain management" [1].
- "Epidural steroid injections (+/ − associated agents) accounted for 83 % of injections and 40 % of all chronic pain management claims" [1].
- "Peripheral blocks and autonomic blocks each accounted for 36 % (total 72 %) of the 78 block claims" [1].
- During the 1990s, the size of payments for chronic pain management claims and surgical/obstetric claims was not significantly different.

Analysis of More Severe Outcomes from the 2004 Study

1. Half of the 63 nerve injury claims involved the spinal cord.
   (a) Fourteen were associated with epidural steroid injection (six resulting in paraplegia, one in quadriplegia)
   (b) Five were after blocks (two with paraplegia)
   (c) Three were after ablative procedures (one with paraplegia)
   (d) One after cervical facet injection
   (e) Two after implantation or removal of devices (one with paraplegia, one with quadriplegia)
   (f) Four after device maintenance (four with paraplegia)
   (g) Three after other invasive procedures (two with paraplegia)
2. "Of the 18 claims for paraplegia or quadriplegia, 4 were associated with epidural abscess, 8 with chemical injury in which the anesthetic or neurolytic agent was injected into the spinal cord, and 4 with hematoma. Two of the claims for hematoma involved administration of epidural steroids in patients who had received anticoagulants" [1].

Table 33.2 Primary outcome for invasive pain management claims

					Injections (n = 138)											
	All invasive procedures (n = 276)		Blocks (n = 78)		Epidural steroid + agents (n = 114)		Trigger facet other (n = 24)		Ablative (n = 17)		Implant/removal (n = 12)		Maintenance (n = 20)		Other/multiple (n = 11)	
Outcome	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Nerve injury	63	23	14	18	28	25	2	8	8	47	2	17	4	20	5	45
Pneumothorax	59	21	40	51	0	0	18	75	1	6	0	0	0	0	0	0
Infection	35	13	2	3	24	21	0	0	0	0	3	25	4	20	2	18
Death/brain damage	26	9	4	5	9	8	0	0	1	6	0	0	9	45	3	27
Headache	21	8	1	1	20	18	0	0	0	0	0	0	0	0	0	0
Increased pain/no relief	21	8	7	9	10	9	0	0	0	0	2	17	1	5	1	9
Retained catheter	9	3	1	1	4	4	1	4	0	0	3	25	0	0	0	0
None	7	3	1	1	4	4	0	0	1	6	1	8	0	0	0	0
Other	42	15	8	10	18	16	3	13	6	35	1	8	4	20	2	18

***Source*:** Fitzgibbon et al. [1]. Reprinted from Anesthesiology. Used with permission from Lippincott Williams & Wilkins

Epidural injection of steroids (±local anesthetic and opioids) and injections, including trigger point, facet, and others, are listed separately, with percentage shown for each separate category. Otherwise, the percentage of claims implies the percentage in each invasive procedure group. Totals sum to more than 100 % because of multiple complications in some claims

Table 33.3 Payment, standard of care, and prevention: chronic pain management versus other claims

	Chronic pain (n = 284)		Surgical/obstetric (n = 5125)		
	No.	%	No.	%	*P*
Payment made to plaintiff	142	53	2777	59	NS
No payment	126	47	1891	41	NS
Standard care	155	65	2501	56	≤0.01
Substandard care	84	35	1934	44	≤0.01
Injury became apparent in anesthesia facility	71	36	2166	83	≤0.01
Injury became apparent after discharge	127	64	443	17	≤0.01
Complication preventable by better preanesthetic evaluation	15	7	395	9	NS
Not preventable by better preanesthetic evaluation	213	93	4080	91	NS
Complication preventable by better postanesthetic care	26	12	431	11	NS
Not preventable by better postanesthetic care	195	88	3592	89	NS
Appropriate informed consent documented	141	66	2404	72	NS
Appropriate informed consent not documented	74	34	959	29	NS

***Source*:** Fitzgibbon et al. [1]. Reprinted from Anesthesiology. Used with permission from Lippincott Williams & Wilkins
Claims in which items could not be assessed were excluded from analysis on an item-by-item basis. ***P*** values were calculated by *Z* test
NS not statistically significant

3. Thirty-five claims involving infection were reported. Infection was most often associated with epidural steroid injection. Many of the infections reported were serious:
   (a) Meningitis: 34 %
   (b) Epidural abscess: 20 %
   (c) Osteomyelitis: 9 %
4. Nine of 26 claims resulting from death or brain damage involved an epidural steroid injection. Interestingly, only epidural steroid injections that contained local anesthetics with or without an opioid resulted in death or brain death.
5. Use of a "test dose" was not standard practice.
6. "Three severe outcomes were the result of a delayed respiratory depression from epidural morphine administered along with the [epidural] steroid" [1].

Conclusions from the 2004 Study

Fitzgibbon et al. [1] offered suggestions for safer practice based on the findings of their study:

1. A test dose should be used when administering a regional block.
2. The volume of solutions injected into the epidural space [for pain blocks] should not exceed that of a typical "test dose" used to confirm placement of an epidural catheter.
3. The addition of local anesthetics and opioids to an epidural steroid injection was associated with more severe outcomes (death and brain damage). One should question whether or not the adjunctive drugs are really necessary.
4. "It is important to establish a monitoring system for pneumothorax and to instruct patients as to the symptoms and signs of a pneumothorax after intercostal nerve blocks, stellate ganglion blocks, trigger point injections, and brachial plexus blocks" [1].

2011: Injury and Liability Associated with Cervical Procedures for Chronic Pain

In 2011, Rathmell et al. analyzed Closed Claims Project data involving cervical procedures administered for chronic pain [2]. The claims under study were collected from January 1, 2005 through December 31, 2008. For the specified epoch, 1627 total claims were collected in the Project's database. Of those, 294 claims involved chronic pain management cases, and 64 were related to cervical procedures. Those 64 claims represented 22 % of the chronic pain cases and 4 % of the total cases collected. The claims associated with cervical procedures were compared to those associated with other chronic pain interventions. Table 33.4 documents patient and case characteristics. Of note, the patients with claims involving cervical procedures tended to be healthier women when compared to other chronic pain-related claimants. The primary diagnosis of claimants was cervical radicular pain (50 %), neck pain of musculoskeletal origin (28 %), complex

Table 33.4 Patient and case characteristics

Characteristics	Cervical procedures ($n = 64$)	Other pain claims ($n = 230$)	P value
Age, year*	49 ± 13	46 ± 14	0.773
Female sex	47 (73)	130 (57)	0.011
ASA physical status 1–2	54 (89)	151 (66)	< 0.001
Year of event			
1991–1999	11(17)	64 (28)	0.0063
2000–2006	52 (83)	166(72)	
Substandard care	30 (52)	107(52)	0.558
Payment made	30(51)	99 (43)	0.183
Payment amount, $†			
Median	388,600	242,850	0.146
Range	642–2,681,720	5500–2,967,000	

Source: Rathmell et al. [2]. Reprinted from Anesthesiology. Used with permission of Lippincott Williams & Wilkins.
* Data are given as mean +/- SD. (cross) Payment amounts adjusted to 2007 dollars using the Consumer Price Index. Claims with no payments were excluded.

regional pain syndrome (CRPS) (11 %), and spinal stenosis (5 %). Seven claims arose from stellate ganglion blocks administered to CRPS patients with upper arm pain.

Eighty percent of the events were directly related to the procedure performed. Direct needle trauma to a nerve or the spinal cord was the most common cause of injury (31 %). The authors noted that particulate steroid injections were associated with the overwhelming majority of cases resulting in spinal cord infarction or stroke. The authors reported that in one *failure to diagnose* claim the patient's pain was later discovered to be the result of lung cancer. With respect to spinal cord injuries, of 38 patients, 33 (87 %) suffered permanent disabling injuries while 1 died. Table 33.5 lists characteristics of spinal cord injury claims. Table 33.6 lists comparisons between claims that resulted from spinal cord injury and those that did not.

The authors noted that sedation or general anesthesia was used in 67 % of cervical procedures associated with spinal cord injuries but in only 19 % of cervical procedures not associated with spinal cord injuries [2]. Furthermore, they reported:

"… in a subset of patients ($n = 54$) in whom the level of responsiveness could be determined, 25 % with spinal cord injuries were judged nonresponsive during the procedure compared with 5 % without spinal cord injuries."

The debate within the literature regarding the use of moderate sedation or general anesthesia while performing invasive procedures is ongoing (see Chap. 34). The authors did site the cautionary recommendations of the ASRA Practice Advisory concerning the use of general anesthesia or heavy sedation in blocks performed on adult patients [3]. The authors stated that their analysis "…shed little light on the role for radiographic guidance in the safety of cervical interventional pain treatment" [2].

Conclusions from the 2011 study are the following:

1. Injuries associated with cervical procedures administered for chronic pain are often severe and permanent.

Table 33.5 Characteristics of spinal cord injury

Characteristics	Value
Severity of injury	
No injury or emotional only*	1 (3)
Temporary injuries†	3 (8)
Permanent disabling injuries	33 (87)
Death	1 (3)
Cause of injury	
Procedure related	36 (95)
Needle trauma	20 (53)
Cord infarction after intra-arterial injection	6 (16)
Hematoma caused by cord compression	3 (8)
Dural puncture	2 (5)
High block/total spinal	1 (3)
Other procedure related	3 (8)
Undetermined	1 (3)
Patient condition	1 (3)
Patient expectations not met	1 (3)
Permanent injury manifestations	
Quadriplegia/quadriparesis	9 (27)
Paraplegia/paraparesis	6 (18)
Hemiplegia/hemiparesis	3 (9)
Other injuries‡	15 (45)

Data are given as number (percentage) of 38 claims
Source: Rathmell et al. [2]. Reprinted from Anesthesiology. Used with permission from Lippincott Williams and Wilkins.
* Spinal cord injury was the result of the patient's deteriorating condition (cross). Three claims in which paresthesia and/or pain occurred that resolved within weeks (double-cross). Twelve involved ininjury to one limb: 10 at a new site (not the presenting site) and 2 at a preexisting site of pain.

2. Injuries to the spinal cord were most commonly related to direct needle trauma.
3. The use of particulate steroids may lead to more serious injury after cervical epidural injection.
4. The use of heavy sedation and general anesthesia during the administration of cervical procedures was associated with a higher rate of injury.

Table 33.6 Characteristics of cervical procedure-related claims: comparison of claimants sustaining spinal cord injury versus no spinal cord injury

Characteristics	Spinal cord injury ($N = 38$)	No spinal cord injury ($N = 26$)	P value
Types of blocks or injections ($n = 58$)			0.004
Epidural	31 (91)	12 (50)	
Facet	1 (3)	1 (4)	
Stellate ganglion	1 (3)	6 (25)	
Trigger point	1 (3)	5 (21)	
Epidural type/route ($n = 43$)			0.074
Interlaminar	20 (65)	7 (58)	
Transforaminal	10 (32)	2 (17)	
Unknown	1 (3)	3 (25)	
General anesthesia or sedation used ($n = 58$)			0.001
Neither	12 (33)	18 (82)	
Sedation only	23 (64)	3 (14)	
General anesthesia	1 (3)	1 (5)	
Patient responsive during procedure ($n = 54$)*			0.049
Yes	24 (75)	21 (95)	
No	8 (25)	1 (5)	
Radiographic guidance used ($n = 45$)			0.031
Yes	22 (76)	7 (44)	
No	7 (24)	9 (56)	
Contrast used ($n = 33$)			0.027
Yes	12 (57)	2 (17)	
No	9 (43)	10 (83)	
Radiographic guidance would have prevented injury ($n = 40$)†			0.053
Yes	10 (45)	3 (17)	
No	12 (55)	15 (83)	

Source: Rathmell et al. [2]. Reprinted from Anesthesiology. Used with permission from Lippincott Williams and Wilkins
* kappa Score = 0.520. (cross) Judged by an on-site reviewer.

5. The evaluation of patients with chronic pain should be thorough and consideration should be given to other coexisting conditions such as cancer.

Finally, the study supports the practice of obtaining informed consent which specifically states that the proposed therapy may not alleviate the painful condition and that the intervention may have significant risks, even when all standards of care are observed.

2016: Injury and Liability Associated with Implantable Devices for Chronic Pain

Fitzgibbon et al. [4] analyzed claims that were associated with the use of implantable devices used to treat chronic pain. Of 10,545 claims in the database, 148 were identified that were associated with implantable devices. The two most common devices identified in the study were implantable drug delivery systems (IDDS) and spinal cord stimulators (SCS). The claims were for injuries that occurred between 1990 and 2013.

The claims were divided into two categories: *Surgical Device Procedures* and *Maintenance*-related claims. Surgical device procedures included implantation, replacement, and removal of hardware. Maintenance claims were associated with issues such as medication administration and delay in diagnosing signs and symptoms associated with device-related injury.

Findings (148 Claims in Database of 10,545)

- Claims associated with IDDS: 64 %
- Claims associated with SCS: 29 %
- Claims associated with Surgical Device Procedures: 72 %
- Claims associated with Maintenance: 28 %
- Brain death or severe permanent injury: Maintenance (56 % of patients)
- Brain death or severe permanent injury: Surgical Device Procedures (26 %)
- Care Judged as "Less than appropriate" IDDS: 78 %
- Care Judged as "Less than appropriate" SCS: 43 %
- Payments Made IDDS: 63 %

- Payments Made SCS: 33 %
- Median Payment IDDS: $149,650
- Median Payment SCS: $334,526

Types of Injuries Related to Implantable Devices

The list of injuries associated with the 148 claims analyzed in the study includes the following:

- Death
- Severe permanent nerve, spinal cord, or brain damage
- Temporary minor injuries

Severe injury or death occurred in a high percentage of patients.

Damaging Events

The list of damaging events includes the following:

1. Maintenance-Related Claims
   (a) Programming errors
   (b) Pocket-fill and side port-fill problems
   (c) Wrong drug administered

2. Surgical Device Procedure-Related Claims
   (a) Delayed recognition of granuloma formation
   (b) Needle trauma to spinal cord or cauda equina
   (c) Epidermal hematoma
   (d) Infections
   (e) Retained sponges, leads, and other parts such as catheter fragments
   (f) CSF leaks
   (g) Device placed in the wrong place
   (h) Inadequate pain relief

Recommendations

- Two people should check prescriptions, dispensing, programming, and refill procedures.
- Patients and their families should be informed of changes made to the device or to the medical prescription.
- Patients and their families should be educated as to symptoms associated with device-related injuries and advised to report symptoms promptly.
- Meticulous attention must be paid when filling the device reservoir to avoid depositing medications in the patient's subcutaneous tissue.
- "Standard infection control measures, aseptic surgical techniques, and appropriate monitoring of wound healing with appropriate training for management of infectious complications are essential" [4].
- Multi-plane imaging may decrease complications associate with device and catheter placement.

Conclusion

The three publications that were reviewed in this chapter are the only Closed Claims Project studies dealing with chronic pain management. While the number of closed claims associated with chronic pain management is a small proportion of the total claims that have been collected, the severe outcomes reported in these claims serve notice to practitioners of chronic pain management. Closing comments include the following:

- In a significant percentage of cases, reviewers judged that care of the patient had been "substandard."
- Appropriate informed consent was lacking in many cases.
- The use of heavy sedation and general anesthesia during the performance of cervical procedures was associated with a higher rate and degree of injury.
- The use of particulate steroids in cervical epidural injections may predispose to more severe vascular injection-related injuries.
- Thorough evaluation of the patient before intervention should seek all potential preexisting conditions that can cause pain, for example, cancer.
- A test dose should be administered when performing a block.
- The volume of medication administered in a block should be minimized.
- Even "superficial" blocks, such as trigger point injections, pose risk.
- Informed consent should be as comprehensive as practicable. Follow-up protocols should be used. The patient and caretakers should be informed as to the risk of falls, local anesthetic toxicity, duration and extent of blocks, device function, and how to self-diagnose and react to a potential pneumothorax.
- One should consider whether narcotics and local anesthetics really are essential adjuncts to epidural steroid injections.
- Only physicians who have appropriate training in the placement of implantable devices and who have extensive expertise in the maintenance of these devices should use them in their chronic pain practices.
- Meticulous standards must be observed when implanting, maintaining, refilling, and removing implantable devices.
- The patients who have implantable devices and their caretakers must be educated as to the symptoms associated with device malfunction or device-related injury and report their symptoms immediately to the physician responsible for their chronic pain care.

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Part VII

Medical Legal Aspects

Medical Legal Aspects of Regional Anesthesia: Physician Perspective

34

Albert H. Santora

Key Points

- A legal relationship exists when a patient voluntarily and with informed or, under special circumstances, implied consent, seeks the care of a physician who accepts the responsibility to render such care.
- It is suggested that anesthesiologists familiarize themselves with basic legal tenets and terms relating to liability and malpractice in the event that a claim is brought against them. Familiarity with the legal process before being sued is also recommended.
- Many professional guidelines, standards, and statements exist, including those published by the American Society of Anesthesiologists, which address all aspects of anesthesia practice.
- Use of other items, such as pre-procedural checklists and time outs, are recommended to help achieve optimum safety when administering regional anesthesia.

The purpose of this chapter is:

1) To present an introduction to basic medicolegal terminology and precepts
2) To cite professional guidelines and statements related to the practice of regional anesthesia
3) To introduce the reader to the American Society of Anesthesiologists' Closed Claims Project and to extol its contribution to defining and understanding medicolegal issues impacting the practice of anesthesia in the United States
4) To comment on medicolegal topics of special interest to practitioners of regional anesthesia

A.H. Santora, MD (✉)
St. Mary's Hospital, Athens, GA, USA
e-mail: acsantora@bellsouth.net

Introduction: The Physician–Patient Relationship

Ethical Foundation

The physician–patient relationship is a legal contract. Its ethical foundation was grounded by classical physicians such as Hippocrates (c. 460–370). In *Epidemics, book 1, section 11, his* advice to physicians was:

> **"As to diseases, make a habit of two things—to help, or at least to do no harm"** [1].

In Latin, his "*Primum non nocere*" admonition is cited twice in the "Physicans' Oath."

> **"… I will use treatment to help the sick according to my ability and judgment, but never with a view to injury and wrongdoing."**

> **"… In whatsoever houses I enter, I will enter to help the sick, and I will abstain from all intentional wrongdoing and harm…"** [2].

Unfortunately, some patients experience harm while under the care of a physician. "Malpractice" jurisprudence deals with this aspect of medicine.

The Legal Definition of the Physician–Patient Relationship

A legal relationship is established when a patient voluntarily seeks the care of a physician who accepts the responsibility to render such care. The patient (or his legal surrogate), after fulfilling the requirements of understanding and accepting the terms specified in an informed consent disclosure, voluntarily agrees to enter into a physician–patient relationship. If the patient is unable to consent, for example, if he is unconscious, an emergency exception may be applied under the theory of implied con-

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_34

sent. This "reasonable person" standard is based on the supposition that if the patient were conscious and reasonable he would want to receive medical care.

The physician–patient relationship has a beginning point and point of termination. Termination of the relationship is usually agreed upon by mutual consent of the physician and the patient. Under certain circumstances, the relationship can be terminated unilaterally. If terminated by the physician, the patient must be given notice and time to find another doctor. The duties of the physician include:

- Adhering to accepted "standards of care"
- Practicing in a "reasonable and prudent" manner
- Obtaining informed consent from the patient before performing certain medical procedures
- Maintaining medical records
- Examining the patient
- Using consultants and referring physicians when appropriate.

Informed Consent

The American Society of Anesthesiologists' (ASA) *Manual on Professional Liability 2010* covers many topics of medicolegal concern including that of the Informed Consent [3]. Over many years, the concept of Informed Consent has evolved to its present definition that varies in different states. The "professional practice standard" and the "reasonable person standard" (or a combination of both) is utilized in different states to define the scope of information that is disclosed to the patient in the informed consent process. The process is founded on the:

> **… principle of the right of self-determination. This principle recognizes that patients are autonomous, that is, they are independent agents with the capacity to make decisions regarding their well being without coercion from others** [3].

The physician should confirm that the patient is a reasonable person who has the "competence" and "capacity" to make an informed decision [3]. The informed consent can be valid whether it is verbal, implied, or written. Obviously, a written consent is preferred should the necessity arise to defend one's relationship with a patient. The informed consent should include the following:

- A description of the care planned for the patient
- Risks versus benefits (short and long term)
- Alternative care options
- Whether the physician or another team member will be involved in the care of the patient
- Discussion of the physician's professional recommendations
- Documentation that the patient is satisfied with the quality and amount of information disclosed
- Written documentation in the patient's record that informed consent has been obtained.

The ASA Manual sites risks that should be discussed with the patient when a regional anesthetic technique is part of the patient's plan of care [3]. These include:

- Numbness
- "Spinal headache"
- Backache
- Failure of the technique
- Bleeding
- Infection
- Nerve damage
- Persistent weakness or numbness
- Seizures
- Coma
- Death
- Awareness/recall
- Hearing impairment
- Visual disturbances
- Urinary retention

The American Society of Anesthesiologists' *Syllabus on Ethics*, published in 1999 devoted an entire section to the informed consent issue [4]. A pertinent quotation from this publication follows:

The most common theory of suit relating to informed consent is negligence. Negligence means that the anesthesiologist did not provide sufficient disclosure to permit a patient to make an informed decision.

Finally, when obtaining informed consent speak to the patient on a layperson's level. Describe medical terminology in terms that the patient understands. Always confirm in writing that the patient understands all of the information that has been discussed.

Professional Standards, Guidelines, and Statements

The American Society of Anesthesiologists (ASA) has published many standards, guidelines, and statements that address the Society's position on every aspect of anesthesia practice. All of these can be read on its web site (www.asahq.org) under the "For Members" tab. One need not be a member of the society to access this information. Guidelines and statements do not carry the weight of law; the ASA recognizes that circumstances arise when its guidelines may not be observed. If a physician deviates from accepted standards and guidelines, he should explain his decision to do so in the

patient's record. However, the physician's treatment should still conform to the accepted standards of care as a general proposition.

Physicians who practice regional anesthesia should read and understand all of the standards, guidelines, and statements of his particular professional society. With regard to anesthesiologists, the ASA has published many statements, including the following:

1. *Guidelines for the Ethical Practice of Anesthesiology* [5]
2. *Statement on Regional Anesthesia* [6]
3. *Statement on Standard Practice for Avoidance of Medication Errors in Neuraxial Anesthesia* [7]
4. *Guidelines for Neuraxial Anesthesia in Obstetrics* [8]
5. *Statement on Anesthetic Care During Interventional Pain Procedures for Adults* [9]
6. *Statement on Privileging for Chronic Pain Management* [10]

In conclusion, the guidelines of the ASA establish standards that promote the safe practice of anesthesia, and they should be followed whenever possible.

Risk Management and Quality Assurance

The purpose of risk management and quality assurance programs is to decrease the likelihood of causing preventable injury to patients and to assure that the level of care rendered meets or exceeds customary standards. The ASA published a number of Quality Management Templates over the years. Furthermore, in 2008 the ASA chartered the Anesthesia Quality Institute (AQI) the purpose of which is to establish a national registry of anesthesia cases and outcomes. Analysis of data leads to the updating of practice parameters utilizing an evidence-based strategy. The ASA web site, www.asahq.org provides information concerning the society's stance on risk management and quality assurance.

Physicians who incorporate risk management and quality assurance programs into their practices will at least improve compliance with institutional, legal, societal, and professional obligations. The impact of a malpractice lawsuit may very well be moderated if appropriate risk management and quality assurance programs have been in effect before an untoward event happens. In theory, these programs should help physicians adopt policies, practice habits, and protocols to make anesthesia delivery safer for the patient.

Malpractice: Basic Legal Considerations

The ASA *Manual on Professional Liability (2010)* deals with many medicolegal issues [3]. It is an excellent primer for the physician who desires an introduction to topics of legal concern.

Basic Tenets

Although a physician may be involved with the criminal legal system, the vast majority of medical malpractice litigation deals with civil concerns that are dealt with by tort laws. Medical malpractice may include battery and abandonment. Most of the time, however, negligence on the part of the physician is claimed by the plaintiff. To prove medical malpractice, a plaintiff must establish that the following exist:

- *Duty*: That the physician owed him a duty.
- *Breach of duty*: That the physician failed to fulfill his duty.
- *Causation*: That a reasonably close causal relation existed between the physician's acts and the resultant injury ("Proximate Cause" in some jurisdictions, "Factual Cause" in others).
- *Damages*: That actual damages resulted because of the acts of the physician.

Certain legal terms turn up in many articles on the subject of medical malpractice. The definitions of these terms are quoted from Black's Law Dictionary, 8th Edition, 2004 [11].

- *Tort*: A civil wrong, other than breach of contract, for which a remedy may be obtained, usually in the form of damages; a breach of duty that the law imposes on persons who stand in a particular relation to one another.
- *Duty*: A legal obligation that is owed or due to another and that needs to be satisfied; an obligation for which somebody else has a corresponding right.
- *Malpractice*: An incidence of negligence or incompetence on the part of a professional. To succeed in a malpractice claim, a plaintiff must also prove proximate cause and damages. Medical malpractice: A doctor's failure to exercise the degree of care and skill that a physician or surgeon of the same medical specialty would use under similar circumstances.
- *Negligence*: The failure to exercise the standard of care that a reasonably prudent person would have exercised in a similar situation.
- *Standard of care*: In the law of negligence, the degree of care that a reasonable person should exercise.
- *Damages*: Money claimed by, or ordered to be paid to, a person as compensation for loss or injury. Damages may be actual, discretionary (for pain and suffering), or exemplary (punitive) in nature.
- *Proximate cause*: A cause that is legally sufficient to result in liability; an act or omission that is considered in law to result in a consequence so that liability can be imposed on the actor.

The most common allegation of a medical malpractice complaint is that the plaintiff was injured by a physician who

acted negligently; that the physician's practice deviated from accepted standards of care causing injury to the patient. Compensation for the injury has a monetary value in the form of damages. The size of the award is set by the jury and can vary from jurisdiction to jurisdiction.

What to Do If Sued

One of the most enduring and thoughtful theses on this subject was written by John H. Tinker, MD and William W. Hesson, JD [12]. Their disquisition should be read in its entirety. A few of their more pertinent quotations, observations, and suggestions are presented herewith:

1. It is important to understand, at the onset of this chapter, that anyone can sue anyone for anything.
2. In other words, after we [physicians] create expectations of excellence, when something goes awry, it is natural for the patient to assume that something has been done wrong—somebody was negligent, either by omission or commission.
3. It is a basic tenet that it is extremely unlikely, if not impossible, to perform procedures with a zero complication rate.
4. The message here is to expect litigation from poor results or complications, whether expected or unexpected, whether the patient was informed or not.
5. When a physician gets sued, he or she must not allow any recriminations that might occur to affect care of present or future patients.
6. Throughout the whole process, though many physicians have become quite cynical, it must be remembered that underneath the inevitable mountain of paper, the oscillation of emotions, the sometimes misleading testimony, and numerous other problems there is a patient. That patient or family *still deserves our attention and care even if they have brought suit against us.* (Legal issues often make this last assertion impractical if not impossible.)

Tinker and Hesson prudently address many other topics such as the trial process, the attorney–client relationship, expert witness testimony, and how to prepare for a deposition and an appearance in the courtroom. They advise the physician-defendant on how to act as well as how to react. To summarize their suggestions, physicians faced with a lawsuit should:

- Act professionally, honestly, and cooperatively with their attorney
- Not take the allegations of the suit personally
- Not let the suit ruin their lives and careers
- Allow their attorney to do his/her job
- Do everything possible to discover the facts
- Not forget that the patient–plaintiff *may* actually feel that he has been wronged and that he is entitled to learn the truth

The Expert Witness

Expert witnesses are used by attorneys to render opinions as to whether or not standards of care have been breached. If breached, did the physician's act or omission cause an injury to the patient? Qualifications of an expert witness vary from state to state. For example, must the expert have been in active practice when the event under consideration occurred? Must the expert be board certified in the same specialty as the defendant? How much money does the expert make for his testimony? Does the expert have any conflicts of interest with either party in the suit?

The ASA published guidelines concerning expert witness testimony [13]. Interestingly, an ASA member may file a complaint with the Society's Judicial Council if he deems that sworn expert testimony rendered in a legal proceeding is in violation of the Society's Guidelines [14]. The complaint can be filed only after all judicial proceedings have been finalized. If the Judicial Council determines that an expert witness's testimony is in violation of guidelines, the Council will "…submit a resolution for sanction of the member to the Board of Directors" [14]. The Board will review the case and then vote on a resolution for sanction. Sanctions include censure, suspension, or expulsion from the society. For an honorable expert witness, a sanction from the Board of the ASA would constitute a significant reprimand. For the less than honorable witness, such a sanction would be inconsequential. The society has set reasonable guidelines that its members should observe if they accept the responsibility and pecuniary rewards of acting as an expert witness.

American Society of Anesthesiologists' Closed Claims Project

The ASA Closed Claims Project serves as a model for any other specialty or entity that contemplates collecting, analyzing, and reporting data accrued by examining closed insurance claims. The Project has been collecting data since the 1980s [15]. Detailed and standardized analyses of more than 10,000 "closed" anesthesia related malpractice lawsuits have been conducted. ("Closed" is defined as settled). Data are obtained voluntarily from insurance carriers who cover approximately 50 % of American anesthesiologists.

The limitations of the Project have been cited elsewhere. These include the lack of a denominator so actual incidences of various outcomes cannot be determined, reliance on voluntary cooperation offered by the insurance

industry, and concerns over biases relating to changing patterns of practice, poor inter-rater reliability, the study's retrospective design, and outcome severity. Nevertheless, the Project's investigators have uncovered patterns and trends that "…discern how the process of care contributes to the genesis of adverse outcomes" [16]. Some of the objectives of the Project have been to define the damaging events and adverse outcomes that are associated with the delivery of anesthesia care, to hypothesize the mechanism of the events, to ascertain whether current standards of patient monitoring could have prevented some of the events, to report financial settlement patterns, and to evaluate the appropriateness of care rendered. Much more information is presented in the Project's many publications that can be accessed on its web site: (*ASA Closed Claims Project*).

Review of the Project's publications is a starting point for those interested in medicolegal matters relating to the practice of anesthesia in the United States. Many of the findings are dealt with in depth in other chapters of this book.

Additional Topics for Consideration Regarding the Practice of Regional Anesthesia

Performing Regional Blocks on Anesthetized Patients

The performance of regional blocks on anesthetized or heavily sedated patients is a practice that generates much debate. Those who recommend performing blocks on patients who are awake or lightly sedated (verbally responsive) maintain that the patient can tell the physician if he experiences pain during needle/catheter placement or during the injection of the anesthetic. Also, an awake or lightly sedated patient may be able to tell the physician if he is experiencing early signs of a toxic reaction caused by the local anesthetic or if he is developing a more profound or extended block than planned. An abnormal response may clue the physician to verify proper needle or catheter placement. *The ASRA Practice Advisory on Neurologic Complication in Regional Anesthesia and Pain Medicine* [17] advised against the routine placement blocks in anesthetized adult patients. Many authors support this recommendation [18–24], while others do not [25]. The *Advisory* stated that the practice would be more appropriate with respect to anesthetized pediatric patients after due consideration had been given to risks versus benefits in each case. Many authors support this contention [26–30]. In an editorial commenting on a review by Meyer et al. reporting four cases of long-term or permanent neurologic complications associated with epidural analgesia [31]. Berde and Greco warn practitioners that severe outcomes do result from the practice of regional anesthesia on children [32]. Whether or not a patient is anesthetized at the time of the block may alter the mechanism of injury. This debate requires research.

Awareness and Regional Anesthesia

The psychological sequelae of unexpected awareness or recall experienced during a procedure performed under sedation or regional anesthesia with sedation can be significant. Kent et al. analyzed 27 cases of unexpected explicit recall that had been reported to the ASA Anesthesia Awareness Registry [33]. The patients in the study reported experiencing unexpected auditory/tactile sensations, paralysis, pain, and distress during their procedures. The psychological sequelae, some of which were reported to be persistent, included anxiety, flashbacks, dreams/nightmares, depression, and chronic fear. A small percentage of patients reported that these sequelae had led to a negative impact on their jobs, friendships, and family relationships. Post Traumatic Stress Disorder had been diagnosed in 15 % of the patients. With respect to medicolegal issues, another study reported that the lack of informed consent had been a major factor leading to claimants' allegation of malpractice [34]. Also, lack of emotional support, interest in, or concern for the patient reportedly led to legal complaints.

In concluding consideration of the topic of awareness, it is important for the practitioner of regional anesthesia to make sure that the patient has a realistic understanding of the types of sensations, whether auditory or tactile, to expect during his procedure. The patient must understand that even if a block is supplemented with sedation it is *probable* that he will feel and hear things in the operating room or procedure suite. Beware that a patient may have been told by his or her surgeon, obstetrical, or preoperative nurse that *"**… the anesthesiologist will pop in an epidural and you won't feel a thing.**"* Take time to listen to a patient's concerns and expectations. Be sure that the medical record documents preoperative discussions concerning events that may lead to awareness and recall. Assure the patient that his comfort and safety are integral parts of the anesthetic plan.

Can Regional Anesthesia Worsen Medicolegal Risk?

A provocative article by Wedel is entitled Can Regional Anesthesia Worsen Outcome? Medicolegal Risk [35]. In certain cases, perhaps it might. The ASA's Closed Claims Project has documented that most nerve injury complaints have involved general anesthesia. In a majority of cases, the etiology of the injury could not be identified. This reality has created "breach of duty" and "causation" problems for the plaintiff. However, when a nerve injury occurs after administration of a regional block, the plaintiff's attorney may

invoke the doctrine of *res ipsa loquitur*: "the thing speaks for itself." If the theory is accepted, the burden of proof shifts to the defendant to show that he did not cause the injury. This may prove difficult. After all, the defendant stuck a needle into the patient! Wedel wrote "*Whether an increased medicolegal risk is associated with regional as compared with general anesthesia is unclear. Analyses of closed claim data are simultaneously reassuring and concerning*." Despite Wedel's warning, regional anesthesia may have advantages over general anesthesia in certain circumstances. Regional blocks may be used to supplement general anesthesia and to provide extended periods of pain relief postoperatively. The physician's choice of anesthetic technique is based on medical principles and practices, not on legal hypotheticals.

Checklists

The utility of checklists is a well-established safety measure in many industries. For example, a pilot would not start his plane's engine if the preflight checklist were not completed. In medicine, the use of checklists before performing a procedure has been advocated even though randomized trials have not established their effectiveness, cost, and utility [36, 37]. Evidence-based research has been conducted that supports the effectiveness of a pre-surgical checklist though implementation issues, cost, flexibility to change, and actual benefits of checklist use still need investigation [38].

The potential for harm arising from using a checklist is low. One should consider whether or not using a checklist before performing a procedure should be another layer of safety offered to the patient. Table 34.1 lists the items that should be confirmed if this is the case. The checklist should be designed to be utilitarian and easy to complete.

Table 34.1 Pre-procedure checklist

1.	Patient identity confirmed
2.	Time out complete
3.	Informed consent complete
4.	Allergies noted
5.	Patient medications, history and physical examination reviewed
6.	Pertinent laboratory data reviewed (e.g., coagulation studies and platelet count)
7.	A functioning I.V. has been established before the procedure
8.	Resuscitation drugs and equipment on hand
9.	Sterile technique protocol observed
10.	Hand wash, mask, gloves used
11.	All questions answered before the procedure begins
12.	Other pertinent information depending on type of block used, for example, fetal heart rate before and after performing an epidural for a laboring patient
13.	Signature, date, and time the checklist is completed

Avoiding Wrong-Site Blocks

Both the American Society of Anesthesiologists and American Society of Regional Anesthesia and Pain Medicine recognize that wrong-site blocks continue to be a cause for concern. Both professional organizations acknowledge efforts by entities such as the Joint Commission with its "Universal Protocol™" and the World Health Organization and its pre-surgical checklist that serve as guides to promote safer medical practice. Anesthesia professionals offer valuable input to regulatory agencies to make future checklists more effective and relevant.

The incidence of wrong-site blocks is not known. The use of protocols and checklists has not eliminated the problem. With respect to chronic pain management, Cohen et al., reported an incidence of 0.027 % in analyzing quality assurance data from ten institutions over 2 years [39]. This study included 48,941 collective procedures. The authors noted that the lack of observing a "universal protocol" was common to most of the cases of wrong-site block. Lack of communication, not marking the operative site, too few and variable ancillary personnel, a large number of cases and rapid turnover, multiple providers involved with the case, and bilateral pathology seemed to increase the risk of wrong-site intervention. Interestingly, many times the patients realized that the intervention was being performed at the wrong site but said nothing! Table 34.2 lists the authors' suggestions for practitioners of chronic pain management. Concerning the performance of blocks in general, Mulroy et al., published a regional block pre-procedural checklist (Table 34.3) [40]. To these suggestions, this author suggests that the practitioner take into account Operator Fatigue. Devising and using a well-conceived checklist hopefully will insure the administration of proper-site regional anesthesia.

Table 34.2 Steps to consider for preventing wrong-site errors [39]

1.	Full implementation of [the] "Universal Protocol™"
2.	Implementation of [the] "Teams STEPPS™" approach or similar system emphasizing teamwork and communication (Agency for Healthcare Research and Quality; www.ahrq.gov)
3.	Make reporting mandatory
4.	Minimize personnel turnover during cases
5.	Designate clear-cut responsibilities rather than overlapping duties
6.	Avoid bilateral preparation and drape for unilateral procedures
7.	Perform time out in the procedure room and confirm with awake patient before sedation is administered
8.	Whenever possible, have relevant imaging studies available in the room
9.	Standardize "left-right" fluoroscopy orientation and always confirm spinal level by counting from above and below
10.	Take "extra" precautions in patients with unusual anatomy, bilateral pathology, and when patients with the same name or procedure are scheduled together

Table 34.3 Regional block pre-procedural checklist

1. Patient is identified, two criteria
2. Allergies and anticoagulation status are reviewed
3. Surgical procedure/consent is confirmed
4. Block plan is confirmed, site is marked
5. Necessary equipment is present, drugs/solutions are labeled
6. Resuscitation equipment is immediately available: airway devices, suction, vasoactive drugs, lipid emulsion
7. Appropriate ASA monitors are applied: intravenous access, sedation, and supplemental oxygen are provided, if indicated
8. Aseptic technique is used: hand cleansing is performed; mask and sterile gloves are used
9. "Time out" is performed before needle insertion for each new block site if the position is changed or separated in time or performed by another team

Mulroy et al.: [From Erratum Statement] [41]

Table 34.4 Criteria required in the time out process

1. That the process is standardized
2. That all members of the procedure team are present at the time the process is initiated and none leaves during conduction of the time out
3. That a designated member of the team starts and records the time out
4. That the time out is conducted immediately before starting the invasive procedure (block)
5. That all members of the procedure team actively communicate during the time out
6. If a patient has more than one procedure and the person performing subsequent procedures is different another time out must be performed
7. Documentation of the time out is entered in the medical record

The Time Out

The Joint Commission (JC) requires documentation that a time out has been performed before a procedure is undertaken on a patient. This includes a time out for regional anesthesia interventions. The time out is only part of the Joint Commission's Universal Protocol™. All sections of the Protocol should be observed. The specific requirements of the Universal Protocol™ can be accessed (www.jointcommission.org). The professional staff at the facility where the procedure is performed determines the amount and type of time out documentation that is recorded in the medical record. The criteria required in the time out process are found in Table 34.4. The information collected in the time out includes, but is not limited to the items listed in Table 34.5.

Special care must be taken to verify the procedure site if the block is unilateral or if the patient is moved after initial examination. Perform the time out **immediately** before the procedure begins, and the patient is in position for the block.

Table 34.5 Information confirmed by the time out process

1. Correct patient identity
2. Correct site verified
3. Is patient marked correctly? (*See "Mark the Procedure site" on the Universal Protocol™*)
4. Can the mark be seen during performance of the procedure?
5. Procedure to be performed
6. Identify members of the procedure team who were present during the time out. All members participate in the time out
7. Date, time, and sign the time out document and enter it into the medical record

Pre-procedure Verification Process

The Universal Protocol™ specifies steps to be followed to conduct acceptable pre-procedure verification of the patient's identity and the procedure. The ***critical step*** in this process is to identify the patient and to place an identification bracelet on his wrist or leg if the patient is a baby. Two [2] licensed health care providers should verify that this step has been conducted properly.

Prevention of Falls and Other Block-Related Adverse Events

Many patients are discharged home after receiving a nerve block as part of their postoperative pain management regimen. Common blocks are those of the brachial plexus, femoral nerve, popliteal fossa, and other peripheral nerves. Placement of a catheter and utilization of a pump will extend the duration of the block. Most of these patients have a motor component to their blocks. As long as the block is present, the patient is at risk of falling especially if the block is of the lower extremity. The sensory component of the block may prevent the patient from feeling pressure, pain, or malpositioning that can cause tissue or nerve damage. In addition, the block may prevent the patient from feeling the pain associated with cast pressure or too tight a dressing. Finally, the patient might experience catheter-related problems.

To help prevent injury to patients who are discharged with an active block, the patient and his caretaker must be educated as to any special care required. Both the patient and his caretaker must be willing to take on added responsibilities to assure that the block does not contribute to postoperative complications. After the patient and his caretaker understand their responsibilities, they should sign an agreement stating that they understand the instructions, that they have no questions, and that they accept the added responsibility associated with the block.

Table 34.6 Instructions and information given to the home caregiver and the patient who is discharged with an active regional block

1.	The name of the block
2.	Sensations that the patient will feel while the block is in effect
3.	Instructions for proper use of the catheter and pump
4.	Instructions on removing the catheter
5.	Signs and symptoms of local anesthetic toxicity
6.	Instructions on how to prevent falls
7.	Instructions on how to protect a blocked limb
8.	Instructions on when to begin oral pain medications
9.	Instructions on how the patient can contact the person responsible for managing the block
10.	Instructions to follow if the patient or caregiver has any problems or questions or if the patient manifests any sign to toxicity, bleeding, pain, or problems with the catheter or pump

The education process should include written material and instructions delivered by medical personnel who are trained to discuss all aspects of caring for the postoperative block. Each facility should design forms specific to its needs. Some of the things that need to be discussed, in writing, and verbally with the patient and caretaker are listed in Table 34.6. It is important that the patient and caregiver understand all instructions and that their understanding is documented in the medical record.

Recommendations

The following recommendations are made concerning ways to avoid a lawsuit, to practice safer anesthesia, and to better understand the medicolegal system. A few final comments are offered to those who have been subject to suit.

Ways to Avoid a Lawsuit

- Carry adequate malpractice insurance
- Be honest
- Act professionally at all times
- Keep meticulous records
- Practice only within the standards of care
- Adopt risk management and quality assurance protocols
- Understand your duties to the patient: The Physician–patient relationship
- Obtain proper informed consent
- Never coerce a patient into accepting a care plan

Practice Safe Medicine

- Know the guidelines and statements of your specialty.
- Take time to examine the patient and document preexisting conditions.
- Know the patient's history and medication regimen.
- Examine all laboratory data preoperatively (e.g., coagulations tests).
- Practice only those techniques in which you are fully trained and proficient.

Get to Know the Medicolegal System

- Stay current with medicolegal articles in the literature such as The ASA Closed Claims Project publications.
- Establish a relationship with a malpractice attorney and start to review cases. Attorneys are always looking for physicians to review records, to offer judgments, and sometimes to testify at trial.
- If one decides to become an Expert Witness, always follow the guidelines of your specialty. Anesthesiologist should observe all of the ASA ***Guidelines for Expert Witness Qualifications and Testimony*** [13].

What to Do If Sued

- Expect to get sued at some point in your career. Be prepared to deal with it.
- Understand that as a general proposition, the physician will not have the right to choose his attorney. His insurance company will assign an attorney.
- Because of the manner in which legal pleadings are typically drafted, a complaint on its face may allege potential exposure to liability in excess of applicable insurance coverage limits resulting in an "excess letter" from the insurer to the insured. The letter will advise the insured of his right to retain a personal counsel, which will be at the insured's expense. Excess exposure is not a prerequisite to the retention of a personal attorney.
- As a defendant, try not to let the rigors of a lawsuit affect your care of patients.
- A lawsuit is a matter of money. If you acted properly do not take it personally.
- Remember that if you are sued there actually might exist a patient or family member who feels that the patient has been wronged. All parties are entitled to seek the truth of the matter.
- Listen to the advice of your lawyer. You may not understand the rules of the legal process. Good insurance companies retain competent lawyers to serve their insured physicians.
- You will survive and learn from the ordeal. Do not let the added stress affect your patient care responsibilities.

Conclusion

In this chapter, the author has attempted to present basic medicolegal considerations specific to the practice of regional anesthesia. The significance of professional guidelines and practice statements was discussed. The important work of the ASA Closed Claims Project was highlighted. Special topics with medicolegal implications were presented for the practitioner of regional anesthesia to consider. Finally, many recommendations were offered for one to consider if sued. Being sued is inevitable in a long medical career. One will minimize the risk if he is proficient, organized, cautious, vigilant, and practices within the standards of care. One should become familiar with the risk management and quality assurance programs in place where one practices. Maintain malpractice insurance with a high quality company. Finally, the physician should establish a genuinely empathetic relationship with his patients and their families.

Acknowledgment The author thanks H. Joseph Byron, Esq. for reviewing this chapter and offering expert editorial advice concerning legal issues.

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Medical Legal Aspects of Regional Anesthesia: Legal Perspective

35

Bridgette Toy-Cronin and Kelly Byrne

Key Points

- Understanding of regional anesthesia malpractice claims from a lawyer's perspective is helpful in appreciating the legal process involved, including requirements for record-keeping, documentation of consent, and cases of practicing outside of guidelines.
- Legal systems and definitions of malpractice vary around the world; however, for most jurisdictions, a successful claim requires that patient be able to establish that the anesthesiologist owed them a duty of care and that this duty was breached, resulting in injury.
- Important legal issues can arise from lack of documentation of procedures, incomplete records, absence of or incomplete patient consent, issues with handover of care, and failure to adhere to recommended guidelines and practice standards.

Introduction: Lawyer's Perspective on Common Issues in Regional Anesthesia Malpractice Claims

Lawyers and doctors have been trained in very different intellectual traditions. When a lawyer is instructed to defend a doctor from a malpractice claim, this is a stressful time for the doctor and these different intellectual approaches can cause frustration and confusion. This chapter therefore aims to orient regional anesthetists to the lawyer's perspective on defending claims that might arise from their practice.

The challenge of writing a chapter on medicolegal issues for an international textbook is that there are important differences in legal systems of different countries. These differences can make generalization difficult, and, if the wrong information is given, even harmful. This chapter is therefore necessarily a broad brush, introducing readers to the lawyer's perspective on defending claims that an aspect of a regional anesthetic has given rise to liability. What that liability is, varies between countries. In New Zealand, where we practice, there is a national no-fault insurance scheme that bars claims for personal injury for anything short of "outrageous" conduct. Patients can however complain to a tribunal that makes findings about whether a doctor has breached a patient's rights. At the other end of the spectrum is the United States, where patients can bring civil legal claims against doctors for personal injury, and frequently do. The civil law countries of continental Europe have markedly different legal systems to that of the common law countries (the United Kingdom, Canada, Australia, United States and New Zealand). All these countries have some form legal liability for medical malpractice whether founded in tort (a civil wrong) or contract law. The form of liability can go by different names, e.g. "malpractice" in the US and "negligence" in the UK, and we have used the term "medical malpractice" here for consistency.

Regional anesthesia is a high risk area of practice. In a UK analysis, 44 % of the medicolegal claims were related to regional anesthesia (including spinal and epidural anesthesia) [1], and claims related to regional anesthesia had the largest combined dollar value of claims paid, (although the mean payment per claim was significantly less than the mean payment related to respiratory events or events related to central venous line cannulation). Unsurprisingly, previous

B. Toy-Cronin
Faculty of Law, University of Otago, Dunedin, New Zealand
e-mail: btoycronin@gmail.com

K. Byrne, MBChB, FANZCA (✉)
Department of Anaesthesia, Waikato Hospital,
Pembroke Street, Hamilton, New Zealand
e-mail: kpa.byrne@gmail.com

B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2_35

studies have shown that fear of ligation or medicolegal concerns are in the top three worries that practitioners have in regard to their practice [2].

In most jurisdictions, the basic elements that a patient has to establish to make a successful claim for malpractice are that:

1. You, the anesthetist, owed the patient a duty of care
2. You breached that duty (whether by an act or omission)
3. The patient suffered an injury as a result of your breach

Whether a practitioner has been negligent seems to have little bearing on the likelihood of being sued or even whether there is a pay out to the claimant [3, 4]. A study published in the New England journal of medicine concluded that "the severity of the patient's disability, not the occurrence of an adverse event or an adverse event due to malpractice, was predictive of payment to the plaintiff" [4]. Patients and the public at large, often equate a negative outcome with malpractice. Practitioners, therefore, need to be aware of how they can give themselves the best opportunity to a successful defence.

Case 1

Ali has been practicing anesthesia at public hospital in Australia for 25 years. He performs a general anesthetic on a 65-year-old patient who presented for a left total knee joint replacement. Six weeks following the surgery at orthopaedic follow-up clinic, the patient complained of ongoing quadriceps weakness and altered sensation. Examination revealed significant weakness and paresthesia in the distribution of the femoral nerve. The surgeon suggested to the patient that it may be the result of the femoral nerve block undertaken at the time of the surgery. The patient has no recollection of a femoral nerve block being discussed during the anesthetic consent. Ali has no record of a written anesthetic consent although maintains the patient did consent to the femoral nerve block after a discussion of the risks and benefits. There is a note on the anesthetic chart indicating that femoral nerve block was undertaken. The note contains the drug dose but no other information.

The patient makes a claim against Ali alleging malpractice.

This chapter uses three hypothetical scenarios as a starting point to discuss the lawyer's perspective on avoiding or defending allegations of medical malpractice. Before we get started however, a legal disclaimer: these scenarios are purely fictional, and any relationship to real events is coincidental.

Scope of Consent

Most, if not all, jurisdictions would consider separate anesthetic consent essential. This has been a significant change in practice over the past decade, and there are several persuasive arguments in the literature for this practice that we will not revisit here [5, 6]. A cornerstone of the consent process is providing the different options for anesthesia and analgesia and coming to a shared decision with the patient. A crucial part of this process is discussing the benefits and possible complications of each of the anesthetic options.

Precisely what you need to discuss with a patient to create valid consent varies between countries. Your insurer is likely to provide up-to-date information about the scope of consent required in your country. The majority of complaints for regional anesthesia practice arise from nerve injury and failure of planned blocks, so it is a sensible defensive strategy to always discuss these risks with a patient, regardless of whether you are required to discuss them under your consent law.

In Australia, where Ali is practicing, and in some other common law countries, the standard involves asking, "What would a reasonable patient in this patient's position want to know about the risks and benefits of this anesthetic?" This standard was developed in the Australian High Court case *Rogers v Whittaker* where enucleation of one eye led to sympathetic ophthalmia and blindness in the remaining eye of the patient. The patient had asked about risks and made the doctor aware that she was concerned about damage to her "good" eye. The doctor considered the risk of sympathetic ophthalmia, which was considered 1 in 14,000, was too remote to warn the patient and produced evidence from other specialists that supported his practice in not discussing this risk.

The Court found that the failure to warn was negligent and that a doctor must discuss "all material risks" inherent in the treatment. A risk is "material" if a reasonable patient in that particular patient's situation would be likely to attach significance to it, or if the doctor "is or should reasonably be aware that the particular patient, if warned of the risk, would be likely to attach significance to it". While it is of course not possible to guess what a patient might consider important, the Court thought that the patient's questions about risks and concern about avoiding harm to her "good" eye were sufficient to alert the doctor that sympathetic ophthalmia was a "material risk."

The underlying policy of this consent process, and the many similar consent laws around the world, is that the doctor and patient engage in a discussion and that the doctor listens to the particular patient's concerns, and thinks about their individual situation. This allows the doctor to provide relevant information so the patient can make an informed choice. Consider, for example, a patient coming to clinic to discuss

anesthetic options for release of a Dupuytrens contracture. If the patient asks about recovery times and mentions wanting to be able to practice for an audition to the Julliard School for violin, then you should make very careful notes about your consent discussion for a brachial plexus block and the alternatives discussed. Similarly, a patient saying they must get away from clinic quickly because they are singing in an amateur production, should alert you to the need to carefully consider and document the potential risks to the voice from intubation. In this case, Ali says he did warn the patient of the risks of a femoral nerve block and the patient consented. The question is then how to prove this consent.

Documenting Consent

Litigation commonly centers on what was discussed in the consent process. What risks were identified to the patient and what was the patient's response? Verbal and written consent are both valid forms of consent. From a lawyer's perspective, written consent is preferable. Written consent provides an independently verifiable record of what was discussed. Verbal consent is much harder to prove, relying on the credibility of witnesses who tell the decision-maker what they say happened.

Ali has no written record of the consent. His oral version of events is evidence, but it is not as persuasive as a written record. A claim has been made against him, and he therefore has a personal interest in painting his practice in the best light. Much more persuasive evidence would be a detailed contemporaneous note of what Ali discussed and the patient's agreement to the femoral nerve block. If you can produce a record of consent that details the risks and benefits discussed, and it is signed by the patient, your lawyer will be happy and will probably make reassuring noises.

Case 2

Lia is a consultant anesthetist working part-time in a private hospital. She meets a 76-year-old diabetic patient for an open anterior resection for bowel cancer on the day of surgery. She takes a history and examines the patient, and consents them for a general anesthetic and an epidural for postoperative analgesia, documenting that nerve injury is one of the potential risks of the epidural.

The operation takes place on a Tuesday morning. Preoperatively, Lia sites an epidural and then performs a general anesthetic for the procedure. She starts the epidural infusion in theater, and it is continued into the postoperative period. Initially, in recovery, the motor block in the patient's legs is 2/5, and this resolves to 0–1/5 by Wednesday morning. By Wednesday evening, the patient complains of increasing weakness in her legs. Lia says she was unaware of these symptoms until she received a phone call from the ward staff on Thursday morning, asking her to review the patient. In the nursing notes, there is a note of the increasing leg weakness but no clear indication of whether this information was communicated to any medical staff. Lia reviews the patient at 9 am on Thursday morning and orders the epidural infusion be discontinued. She makes a brief note of the order. Lia says she also called the orthopaedic surgeon to urgently review the patient. There is no record of that request. An orthopaedic surgeon reviews the patient at 3 pm that afternoon. An MRI scan shows epidural hematoma and spinal stenosis. The orthopaedic surgeon performs a laminectomy later that evening. The patient recovers some leg function but requires ongoing assistance with walking and is unable to undertake cooking or cleaning activities. The patient files a claim against Lia alleging malpractice for nerve injury.

Calling Your Insurer

Doctors pay many thousands of dollars (or euros) in malpractice insurance. The insurer will want control of the claim and how it is defended. When you become aware of a potential claim, call your insurer and notify them. You may be obliged by the terms of your policy to do this, and in any event it is a good idea. Your insurer is used to dealing with claims in your country, and will therefore be best placed to put you in touch with someone to advise you on how to proceed. In some countries and with some claims, doctors will be told to apologize to the patient. In other countries or with other claims, an apology is considered legal suicide. In most countries, apologies are not considered an admission of liability and can sometimes head off legal action. It is important to get advice on your particular situation, in your particular country, as soon as possible.

Defending a Complication for Which the Patient Has Been Consented

Lia consented the patient for nerve injury, a complication that unfortunately occurred. However, consenting a patient for a complication, that then occurs, is not a guarantee that a claim will not arise. When a patient has an adverse outcome, they

may feel that they should be given redress and there is often something in the chain of events that, when examined retrospectively, looks like it may fall below the standard of care owed at law. This may be enough to justify filing a claim. The patient may be supported by expert witnesses who are also influenced by the severity of the adverse outcome and who share the patient's sense that there should be some remedy. ("No-fault" compensation schemes are attractive for this reason, as patients can be compensated without having to search for someone on which to pin liability.)

Where a complication arises that the patient has been made aware of in the consent process, a written record of that consent will assist in defending the claim. Written, contemporaneous records of the time of actions and events will also be crucial in defending the claim, provided there has not been negligent practice. The difficulty in Lia's case is that while the consent records are good, the records thereafter have gaps. If the patient alleges the delay in diagnosis led to her injury, the question is then which medical practitioner(s) owed the patient the duty of care.

Case 3

Lars, who is 57 years old, is an anesthetist in a busy orthopaedic hospital. A 45-year-old man presents for rotator cuff surgery. Lars consents him for a general anesthetic and an interscalene block and documents the consent. Lars anesthetizes and intubates the patient and then performs the interscalene block under ultrasound guidance. One week after the surgery the patient complains of neuropathic pain in the arm that has had surgery. Despite early referral to the pain clinic, the patient develops complex regional pain syndrome in that arm. Nerve conduction studies identify a nerve injury at the site of the interscalene block. The man consults a lawyer, and sues Lars for malpractice. The claim alleges Lars has breached his duty of care, citing the American Society of Regional Anesthesia (ASRA) guidelines that suggest that interscalene blocks should not be performed in anesthetized patients [8]. *Lars has never been sued before and is devastated. He is angry and shocked and is considering taking early retirement.*

Handover of Care

Lia's position is that the nursing staff did not tell her that the patient was complaining of increasing leg weakness until Thursday morning. Lia says she then acted promptly and requested an urgent consultation from orthopaedics. Lia's defence suggests liability for the nursing staff (for failing to inform her promptly) and/or the orthopaedic surgeon (for failing to urgently review the patient).

In this type of scenario, Lia will need to instruct an independent lawyer, a lawyer who is not also representing the nursing staff or the orthopaedic surgeon. The success of Lia's defence, and her strategy for either defending or settling the claim, will depend in large part on what can be proved regarding the handover. It is for this reason that it is a good idea to document clearly the information that was communicated to the other relevant specialists and the urgency at which review of the patient was required. Likewise, when receiving a referral, it is important to document in the notes what your understanding of the situation is, and what information had been given to you by the referring physician.

Records

Lia made only a brief note of her consultation on Thursday. What should she do? What she should not do is alter the original notes to "improve" them. While this is often tempting, it is an error. If anyone realizes that the notes have been altered after the fact, Lia's credibility and professionalism will immediately, and probably irreparably, be called into question. For the same reason, if there are notes that she thinks will count against her, she should not destroy them. Altering or destroying records can give rise to criminal or civil liability, quite apart from malpractice [7]. Lia can document handover of care as an addendum to the notes, as long as she clearly labels it with the current day's date so that it is clear when it was made. So, for example, if she heard on Friday morning that the laminectomy was probably only partially successful, she could make an addendum then. Once a claim is made though, she should not make any addendums.

Lia can provide further information to her lawyer to assist her lawyer in advising her. When she does talk to her lawyer, she should be candid with the lawyer. An important part of the lawyer's job is to advise about the likelihood of successfully defending the claim, and what strategy to take. If Lia only gives her lawyer information that shows Lia in the best possible light, or worse, incorrect information, the lawyer will not be able to perform these key roles. In all likelihood, less favourable facts will come light further down the track. That could affect Lia's credibility and make the case harder to defend. It is therefore important to give your lawyer all the relevant information so your lawyer can give you accurate advice.

The Legal Weight of Guidelines

Guidelines are evidence that can be used in a legal case to prove whether the care the doctor provided was in breach of their duty. If the doctor's practice was outside the guidelines,

then the claimant can use them to argue that the care provided fell below the standard expected at law. The guidelines are used in this way as evidence of what a responsible body of medical practitioners considers a reasonable standard of care and therefore an independent marker of safe practice.

Practicing outside the guidelines will not however necessarily be sufficient for a claimant to prove a breach of duty. There may be a number of grounds on which the anesthetist can argue that the guidelines should not be followed, or at least should not have been followed in that particular case.

An example of a claim founded on practice outside the guidelines appeared in a 2012 editorial in the British Journal of Anaesthesia [9]. In that case, the patient suffered a very rare complication of a central line insertion (a fistula between the internal jugular and the vertebral artery), resulting from an inadvertent arterial puncture during insertion of a central line without ultrasound guidance. She was left with a small visual field defect after the repair of the fistula. Two years before the incident, the National Institute of Clinical Excellence (NICE) guidelines had recommended that all central lines be placed under ultrasound guidance. The patient, citing failure to follow the NICE guideline, sued for malpractice, arguing the complication may have been avoided if the guidelines had been followed.

The anesthetist's counsel argued that the approach chosen "was a recognised technique, the one he was most familiar with and therefore the technique that would be expected to minimise the risk of harm to the patient" [9] and that a significant number of other anesthetists were practicing that way. The defence also referred to the fact that implementing guidelines within 3 months of publication (as is recommended for NICE guidelines) is not always possible in reality. The claimant withdrew the case. We do not know why but we can speculate that, having heard the evidence that supported deviation from the guidelines, the claimant was not confident of success. The case illustrates that deviation from a guideline can be defended by justifying an alternative technique and the practical difficulty of implementing the guideline.

Another means of justifying deviation from the guideline is to directly discredit the guideline. This would involve calling expert evidence that the guidelines are out of date or not supported by "… the rigorous methodology that would justify the authority they profess to hold, be this in terms of their influence on clinical practice, or their use in establishing legal standards" [9]. Additionally, if in a group practice, evidence of discussion about this topic, and a group decision to practice outside the guidelines and reasons for doing that would be evidence that may help persuade a decision-maker that a reasonable standard of care had been provided. The more well recognized the guidelines are, the more difficult this will be to do. Lars's practice deviated from the ASRA guidelines so this line of argument may be difficult, depending on where he is practicing.

Lars could bring evidence to persuade the decision-maker that in the case of this particular patient or in this particular hospital, it was reasonable to deviate from the guidelines. For example, Lars made a record of the consent. That record may be helpful in defending his practice if it records that he documented the possibility of complications and the benefits of undertaking the procedure this way, particularly if he noted this was outside the guidelines but had good reason for doing so. For example, "Discussed the increased risk of nerve damage when the block was done under general anesthetic. The patient wants a block but would prefer it be done under general anesthetic, and understands the increased risk involved." Alternatively, an anesthetist might be able to bring evidence that the hospital he was practicing in did not provide the equipment or training to enable her or him to follow the guideline.

As is apparent from this discussion, it will depend on the guidelines and on the evidence that you can bring to prove your practice outside them was still a reasonable standard of care. Documentation of a considered decision is very helpful. Where possible however, it is safer to practice within some well-recognized guidelines in the area, e.g., ASRA for regional anesthesia. Rather than having to provide evidence as to why you practiced outside the guidelines, you can instead use the guidelines as evidence that your care met the standard expected at law.

The Emotional Toll of a Claim

The stress and anger that Lars experienced after being served with a claim for malpractice is a common experience. In the United States, negative emotional reaction to being sued has even been named: Medical Malpractice Stress Syndrome (MMSS) [10, 11].

Lawyers are fond of telling their clients to try and be objective and retain some emotional distance from their case. While emotional detachment is often considered a key attribute of being a professional, and likely something you strive for in practice, it is probably unattainable when you are at the subject of the claim. Discussions with your lawyer will help to educate you about the legal process, the evidence that is required, and your prospects of a successful defence. This in itself can help reduce stress, as it increases a sense of control and reduces panic. However, simply putting aside the emotional response or striving to be detached is unlikely to be successful and may be harmful. The literature on MMSS has some useful practical suggestions for managing stress and seeking support, including surrounding yourself with trusted advisers, maintaining other interests (such as sport and hobbies) and taking an active role in your defence.

Conclusion

A claim of malpractice is just that, a claim. Even if you practice without breaching your duty of care towards your patients, you are not immune from a claim being made against you. Several things can help protect you from a claim:

1. Familiarize yourself with the law in your country about what constitutes valid consent. Your insurer will probably publish this information.
2. Engage with patients during consent and listen carefully to what they say.
3. Warn the patient of the risks of nerve injury and, particularly in obstetric anesthesia, incomplete blocks. These are the most common sources of claims.
4. Be courteous and respectful. Patients are less likely to make claims if they have been treated with dignity.

If you are the subject of a claim, then your lawyer will be interested in evidence. Lawyers need to be able to present evidence that counters the claimant's version of events. For example, evidence of consent, evidence of thoughtful deviation from guidelines, evidence of handover of care to another practitioner. It is for this reason that doctors are frequently admonished to keep careful records. They are evidence that can clear up misunderstandings and end a claim. Therefore,

1. Keep thorough records.

If you are notified of a claim, then keep these points in mind:

1. Do not alter records.
2. Call your insurer.
3. Choose a lawyer (this may have to be done in consultation with your insurer):
   (a) Make sure the lawyer has expertise in the area.
   (b) If there is a co-accused (such as the hospital or another practitioner), consider whether you need a separate lawyer, e.g., if your defence is that the other practitioner was at fault, not you, you need a separate lawyer.
4. Be honest with your lawyer and provide him or her with accurate information, even if it does not show you in the best light.
5. Seek support from your family, friends, and colleagues.

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B.T. Finucane, B.C.H. Tsui (eds.), *Complications of Regional Anesthesia*, DOI 10.1007/978-3-319-49386-2