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ROBERT N.N. HOLTZMAN, MD
Assistant Clinical Professor of Neurological Surgery, College of Physicians and Surgeons of Columbia University, The New York Neurological Institute, New York, NY 10032. Associate Neurosurgeon, Lenox Hill Hospital, New York, NY 10021, USA

BENNETT M. STEIN, MD
Byron Stookey Professor of Neurological Surgery, College of Physicians and Surgeons of Columbia University; Chairman of the Department of Neurological Surgery, The New York Neurological Institute, New York, NY 10032, USA

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This volume is dedicated to
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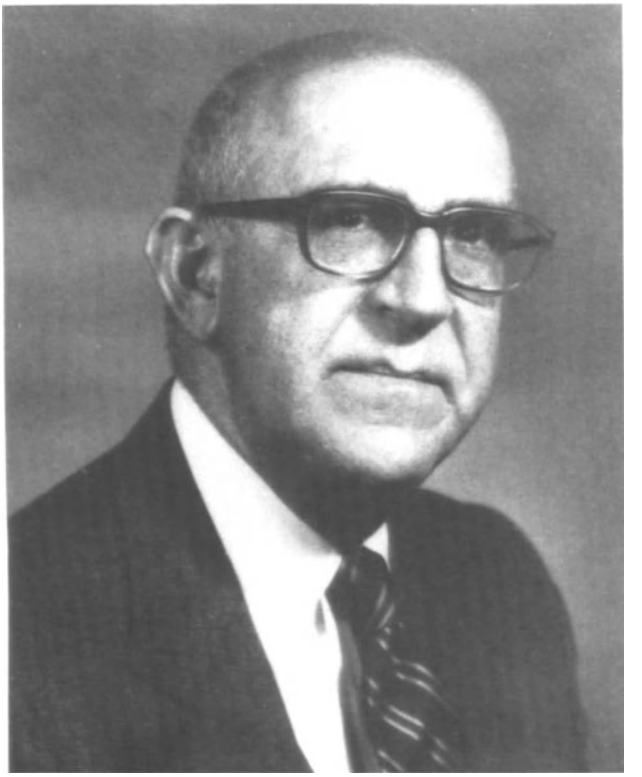

Guest of Honor: Juan M. Taveras, M.D., Professor of Radiology, Harvard Medical School; Former Chief of Neuroradiology, New York Neurological Institute, Columbia-Presbyterian Medical Center.

Mrs. Edna Winston

This woman endured great suffering during her life because of medical problems that today could have been diagnosed more easily and the years of suffering alleviated. She managed to raise a family of two sons with much love, attention, and adoration. My mother was a woman of exquisite aesthetics and a vibrancy of humor bordering on satire. She bore her suffering nobly. It is to her memory and the atmosphere she created in this house and home that this volume of the Stonwin Medical Conference is dedicated.

Ronald H. Winston
Harry Winston Research Foundation, Inc.

Foreword

This book is composed of individual chapters based on talks given at the Seventh Annual Stonwin Medical Conference. The subject, endovascular interventional neuroradiology, was proposed by Professor A.N. Konovalov, Chairman of the N.N. Burdenko Neurosurgical Institute during an informal dinner at his home in Moscow. Dr. Bennett M. Stein, Chairman of the Department of Neurosurgery of the New York Neurological Institute, suggested the names of prospective guests, in particular Professor Juan M. Taveras, who subsequently agreed to preside as our guest of honor. The participants included a hematologist and vascular physiologist, neuroradiologists, neurologists, and neurosurgeons from a number of countries including Canada, France, the People's Republic of China, the former Soviet Union, and the United States of America. They represented that small group of individuals who are actively pursuing the problems of aneurysmal and vascular malformation evolution and rupture with the intention of managing these lesions endovascularly. Their efforts were scrutinized and contrasted with present-day optimum neurosurgical therapies.

The Stonwin Estate, purchased by Harry Winston in 1940 in exchange for a precious gemstone, provided the idyllic setting for the three-day meeting that convened on those grounds. The exchange of ideas was accompanied by great enthusiasm and brought to the forefront the technological and physiological problems that must be faced and overcome in the development of this new specialty.

We acknowledge with deep gratitude the efforts of Mr. Ronald H. Winston in the creation and furthering of these conferences and those of his wife Mrs. Heidi Winston. Particularly valuable were Mrs. Winston's sense of organization, her concern for the participants and their wives, and her assistance with the editing of the publications.

Henry B. Roberts Jr.
Publishing and Editorial Consultant
Stonwin Medical Conference

Preface

In 1974 F.A. Serbinenko of the Burdenko Neurosurgical Institute published his work on balloon catheterization of major cerebral vessels in the *Journal of Neurosurgery*. It officially established endovascular interventional neuroradiology as both a therapeutic adjunct to existing surgical procedures and an independent means of treating vascular lesions of the cerebral circulation.

At about the same time, superselective angiography was emerging as a natural outgrowth of cerebral angiography. The development and availability of coaxial microcatheters was a major factor contributing to this technological advance. Initially, a variety of materials, including muscle, Silastic spheres, and glues, were utilized to bring about the occlusion of carotid-cavernous fistulas, aneurysms, and arteriovenous malformations. Detachable balloons and platinum coils later supplanted these early techniques. In this setting, lesions arising from tertiary branch vessels could now be reached with minimal morbidity, and outcomes approximating those derived from surgical excision and clipping could be attained.

Herein are detailed descriptions of these endovascular achievements, contrasting the results with present-day surgical technology. Experts from North America, Europe, the People's Republic of China, and the former Soviet Union contributed detailed accounts of their work in both the text and the discussions. The field of endovascular interventional neuroradiology is presently undergoing the flux of development characteristic of a new specialty, and changes are taking place continuously as technological advances and successes permit deeper, atraumatic endovascular access.

This volume begins with an analysis of the blood's coagulation mechanisms and the physiology of the circulation as it relates to thrombosis. Basic concepts presented include a discussion of the platelet and fibrin systems as they are implicated in the formation and lysis of a thrombus. Also discussed are the possibilities for reepithelialization without platelet aggregation and endovascular/endosaccular thrombosis followed by recanalization after clot formation. The applicability of such processes was considered in terms of aneurysmal occlusion. Similarly, the role fluid mechanical factors play in the focal deposition of platelets resulting in thrombosis and the formation of aneurysms in human circulation using isolated segments of arteries and veins

is discussed in terms of streamlines, fluid velocities, and wall shear stresses by analyzing the motion of particles and red blood cells on 16 mm cinefilm.

Descriptions of specialized technologies designed to bring about changes in the vascular bed that may be curative for life-threatening occlusive and embolic problems follow: Detailed information is provided on (1) the evaluation of arteriovenous malformations (AVMs) by the transcranial Doppler technique, comparing pre- and postembolization and postsurgical changes; (2) the "smartlaser," which can be guided endovascularly to vaporize atherosclerotic plaques, thereby achieving recanalization of blocked arteries in the coronary and carotid systems; and (3) intravascular placement of Hilal platinum coils for successful management of AVMs, giant aneurysms, and fistulas.

The risks of endovascular surgery over a 10-year period at New York University Hospital, with the use of present-day techniques—including the newest generation of variable-stiffness microcatheters assisted by deflecting microguide wires, small balloons, current-generation acrylics, and digital subtraction angiography (DSA)—have led to improved results as noted by Alex Berenstein, with mortality less than 1.0% and severe morbidity less than 2.3%. John Pile-Spellman has, through a team approach at the Massachusetts General Hospital, confirmed these conclusions and demonstrated that these techniques may be of value for treating vasospasm and arteriosclerotic occlusions of cerebral blood vessels.

The endovascular experience at various institutions is presented: This includes the superior orbital vein approach of Gerard Debrun for traumatic and other carotid cavernous fistulas and dural AVMs at The Johns Hopkins Hospital stands in contrast to arterial balloon catheter occlusion of those lesions, which was performed successfully in 98.4% of 630 patients by Fedor Serbinenko and coworkers at the N.N. Burdenko Neurosurgical Institute. Similarly, the latter institute's experience with aneurysms, AVMs, and other vascular lesions treated by endovascular neurosurgery since 1964 is discussed by A.N. Konovalov. Chung-cheng Wang of the Beijing Neurosurgical Institute offers his experience in intravascular embolization, and Alan Fox of the University of Western Ontario discusses his experience and offers a proposal for a scale of neurological outcome following endovascular intervention.

The specific management of aneurysms from a surgical standpoint is presented by Robert Solomon, who stresses the need for collaboration between endovascular neuroradiologists and neurosurgeons to develop the criteria for endovascular approaches and to develop strict indications for both surgical and endovascular approaches. Victor Scheglov presents the endovascular experience of 725 cases during the past 14 years at the Neurosurgical Institute of Kiev, where all aneurysms are now being managed by the endovascular technique, regardless of their location. Grant Hieshima presents the transluminal angioplasty technique for intracranial arterial vasospasm that he used in 27 vessels in 13 patients (all but one vessel remaining in its dilated state). In addition, 250 aneurysms were managed by intravascular balloon

procedures. Jacques Moret, from the Rothschild Institute, presents his experience with three modalities for endosacular aneurysmal occlusion: "Packing," "valving," and "clipping" of 100 small aneurysms using detachable balloons inflated with polymerizing substances.

The surgical occlusion of AVMs involving the posterior fossa and the corpus callosum is presented by Y.M. Filatov, S.S. Eliava, and their colleagues from the N.N. Burdenko Neurosurgical Institute. Technical advances in the therapy of AVMs in the brain are presented by F. Viñuela et al. from the UCLA School of Medicine. Spinal AVMs and spinal dural AVMs are discussed by Alex Berenstein, including their history, evolution, and response to embolization techniques. Lastly, proposals for developing a cooperative study on AVMs and for standardized training in interventional neuroradiology are described.

This volume comprises the work to date on endovascular approaches to the cerebral circulation. It stresses the value and efficacy of these approaches, which must be subjected to ongoing review to ensure the development and viability of this new specialty.

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Mrs. Susan Weiler, transcriber of the manuscript
Mrs. Ruth Winston, coordinator of the travel arrangements
Professor Leonid A. Yudin, M.D., Ph.D., Deputy Rector, Sechenov Medical Academy, Moscow, Russia

Contents

Contributors

The Seventh Annual Stonwin Medical Conference

Co-Directors and Editors

BENNETT M. STEIN, M.D. Byron Stookey Professor of Neurological Surgery, College of Physicians and Surgeons of Columbia University; Chairman of the Department of Neurosurgery, The New York Neurological Institute, New York, New York 10032, USA

ROBERT N.N. HOLTZMAN, M.D. Assistant Clinical Professor of Neurological Surgery, College of Physicians and Surgeons of Columbia University, The New York Neurological Institute, New York, NY 10032; Associate Neurosurgeon, Lenox Hill Medical Center, New York, New York 10021, USA

Guest of Honor

JUAN M. TAVERAS, M.D. Professor of Radiology, Harvard Medical School; Radiologist, Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts, 02114, USA

Contributors

S.L. BARNWELL, M.D., Ph.D. University of California at San Francisco Medical Center, Departments of Radiology and Neurological Surgery, Interventional Neuroradiology Section, San Francisco, California 94143, USA

JULIE BELL Interventional Therapeutics Corporation, South San Francisco, California 94144, USA

ALEX BERENSTEIN, M.D. Professor of Radiology, New York University Medical Center, New York, New York 10016, USA

DEWITTE T. CROSS, M.D. Assistant Professor of Radiology, Columbia University; Assistant Attending Radiologist, New York Neurological Institute, New York, NY 10032, USA

GERARD M. DEBRUN, M.D. Professor of Radiology, Director of Interventional Neuroradiology, Johns Hopkins Medical Institutions, Baltimore, Maryland 21205, USA

J. DION, M.D. Department of Radiology, University of Virginia Health Sciences Center, Charlottesville, VA 22908, USA

BILL DORMANDY Interventional Therapeutics Corporation, South San Francisco, California, USA

CHRISTOPHER F. DOWD, M.D. University of California at San Francisco Medical Center, Departments of Radiology and Neurological Surgery, Interventional Neurovascular Radiology Section, San Francisco, California 94143, USA

G. DUCKWILER, M.D. University of California at Los Angeles Medical Center, Department of Radiology, Los Angeles, CA 90024 USA

SHALVA S. ELIAVA, M.D. Candidate of Medical Sciences, N.N. Burdenko Neurosurgical Institute AMS, Moscow, Russia

YURI M. FILATOV, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

ALLAN J. FOX, M.D. Professor, Department of Diagnostic Radiology & Clinical Neurological Science, University Hospital, University of Western Ontario, London, Ontario, N6A 5A5, Canada

HARRY L. GOLDSMITH, Ph.D. Professor, Department of Medicine, McGill University; Montreal General Hospital, Montreal, Quebec, H3G 1A4, Canada

VAN V. HALBACH, M.D. University of California at San Francisco Medical Center, Departments of Radiology and Neurological Surgery, Interventional Neurovascular Radiology Section, San Francisco, California 94143, USA

GRANT B. HIESHIMA, M.D. Professor of Radiology and Neurological Surgery, University of California San Francisco, San Francisco, California, 94143 USA

RANDALL T. HIGASHIDA, M.D. University of California at San Francisco Medical Center, Departments of Radiology and Neurological Surgery, Interventional Neurovascular Radiology Section, San Francisco, California, 94143, USA

SADEK K. HILAL, M.D., Ph.D. Professor of Radiology, Director of Neuroradiology, Columbia-Presbyterian Medical Center, New York, New York 10032, USA

TAKESHI KARINO, M.D. Professor, Department of Medicine, McGill University; Montreal General Hospital, Montreal, Quebec HG3 1A4, Canada

A.N. KONOVALOV, M.D. Professor and Director, N.N. Burdenko Neurosurgical Institute AMS, Moscow, Russia

I. KOVAL, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

NORMAN E. LEEDS, M.D. Professor of Radiology, Mt. Sinai School of Medicine; Director of Radiology, Beth Israel Medical Center, New York, New York 10003, USA

V. LASAREV, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

P. LYLYK, M.D. ENERI, Sanchez de Bustamante, 2184 PB, 1425 Buenos Aires, Argentina

A. LYSATCHEV, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

J.P. MOHR, M.D. Sciarra Professor of Clinical Neurology, College of Physicians and Surgeons, New York Neurological Institute, New York, New York 10032, USA

JACQUES MORET, M.D. Department of Radiology, Rothschild Foundation of Ophthalmology (Fondation Ophthalmologique de Rothschild), Paris, France

L.I. MOSKOVICHYUTE, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

DOUGLAS MURPHY-CHUTORIAN Founder and Director, MCM Laboratories, Mountainview, California 94039, USA

PETER K. NELSON, M.D. Professor of Radiology, New York University Medical Center, New York, New York 10016, USA

D. PELZ, M.D. Clinical Neurological Sciences, University Hospital, London, Ontario, N6A 5A5, Canada

JOHN PILE-SPELLMAN, M.D. Massachusetts General Hospital, Boston, MA 02114, USA

JACOB H. RAND, M.D. Associate Professor of Medicine–Hematology, Director of Coagulation Laboratory, Mount Sinai Medical Center, New York, New York 10029, USA

O.B. SAZONOVA, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

FEDOR A. SERBINENKO, M.D. Doctor of Medical Sciences, Deputy Director of Research, N.N. Burdenko Neurosurgical Institute AMS, Moscow, Russia

VICTOR I. SCHEGLOV, M.D. Department of Radiology, Kiev Research Institute of Neurosurgery, Kiev, Russia

N.K. SEROVA, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

N. SMIRNOV, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

ROBERT A. SOLOMON, M.D. Assistant Professor of Neurological Surgery, Columbia University College of Physicians and Surgeons, Department of Neurological Surgery, The New York Neurological Institute, New York, New York 10032, USA

GARY SPIEGEL, M.D. Professor of Radiology, New York University Medical Center, New York, New York 10016, USA

T. TYSSEN, M.D. N.N. Burdenko Institute of Neurosurgery AMS, Moscow, Russia

FERNANDO V. VIÑUELA, M.D. Professor of Endovascular Therapy, University of California at Los Angeles Medical Center, Los Angeles, California, 90024 USA

CHUNG-CHENG WANG, M.D. Professor and Director, Beijing Neurosurgical Institute, Tiantan Xili, Beijing, People's Republic of China

ZHONG-XUE WU, M.D. Beijing Neurosurgical Institute, Tiantan Xili, Beijing, People's Republic of China

I. INTRODUCTION

CHAPTER 1

Historical Development and Current Trends in Surgical Neuroradiology

Juan M. Taveras

Neurosurgery is surprisingly young when you look at the historical development of surgery and neurology. Neurosurgery could not develop until there was a way to localize lesions. In 1879 MacEwen removed a meningioma; and in Rome in 1884 Durante (and later the same year Goodlee in London) removed intracranial tumors. In 1887 Victor Horsley in London was the first to remove a tumor within the spinal canal successfully. (His friend Gowers localized it for him.) By the end of 1888 fourteen operations for brain tumors had been reported, 11 of which were supratentorial with 30% mortality and three cerebellar with 100% mortality. The reason for the deaths was perhaps lack of technical skill. Aseptic techniques for surgery had already been developed, so probably the deaths were not due to infection. In fact, most of the time the surgeon could not even find the lesion.

Between 1886 and 1896 there was a veritable explosion of reports, probably provoked by these early papers. At least 500 surgeons reported operations on the brain. Enthusiasm decreased rapidly, however, probably owing to the high mortality and complication rates. Hence during the succeeding decade, 1896 to 1906, only 80 surgeons reported brain operations. In 1893 Starr listed 84 operations for brain tumor; in 32 of the 84 patients the tumor was not found.[1] A quote from Harvey Cushing, who may be considered the founder of neurological surgery, is in order. From an address entitled "The Special Field of Neurological Surgery" he gave in 1905:

> It seems clear that in order to advance surgical measures, specialization or better concentration of thoughts and energies along given lines is necessary. In talking the matter over with my surgical friends, many of them have expressed themselves emphatically against any form of operative specialization. But granting the wisdom and the necessity of general surgical training beforehand, I do not see how such particularization of work can be avoided if we wish more assuredly and progressively to advance our manipulative therapy. Are practice of hand and concentration of thought to go for nothing?

It was difficult to think about developing neurosurgery early on because, for the most part, there was no way to determine the site of the disease process. Neurosurgery began to develop rapidly after adequate methods for localizing the lesions were developed. For the first 30 years, these measures

all used the radiographic approach, and most still are familiar. Expertise in interpreting these images developed slowly among radiologists. Results of the special diagnostic procedures—pneumoencephalography, myelography, angiography—were intrepreted mostly by the neurosurgeons. The need to have trained neuroradiologists in hospitals where neurosurgery is practiced was not recognized until some trained individuals began to be available at some institutions. Until then, neurosurgery departments were satisfied with their performance and interpretation of neurodiagnostic procedures. I believe that *needs are created by the availability of services—not the other way around.* That is, similar to many other needs created as a result of technical developments, we now find ourselves considering what must be done to provide the services that utilize intravascular techniques for treatment of certain vascular disorders involving the brain and spinal cord, as well as the orbits and other structures of the head and neck.

Starting around 1960, one of the most baffling problems in which we were all involved during the early days of angiography was the arteriovenous malformation (AVM). Some of these lesions were huge, and surgeons sometimes were able to operate. In most cases, though, they would say, "There is nothing I can do about this," and we gave radiation therapy. I treated a number of such cases with irradiation and thought that a few were reduced at follow-up some years later when we repeated the angiogram. For the most part, however, the radiation therapy was insufficient to produce results. Such poor results stimulated some to develop methods by which the size of the AVM could be diminished. Particular credit should go to Luessenhop from Georgetown University for having been the first to publish a paper on this subject[2] and presenting his material at various meetings.

Charles Dotter, at New York Hospital–Cornell Medical Center, had an elderly patient who had been scheduled to have a leg amputation because of atherosclerosis, which had already caused gangrene of several of her toes. Although at that time (early 1960s) vascular surgery was not well developed, Dotter obtained an angiogram and realized that perhaps there was an alternative to amputation. He placed a coaxial catheter into the femoral artery and dilated the stenosed artery. Within a couple of months, the whole foot had healed.[3] This case opened the field of interventional work in the vascular system for atherosclerosis. It is now used commonly in various parts of the body, although it has found little use in brain vessels. It is not clear if it will to used for that purpose in the future or if we can improve on the results of carotid surgery done today.

Development of this field was slow after Luessenhop and Spencer's report in 1960.[2] Aside from two case reports on embolization of AVMs of the spinal cord by Newton and Adams and by Doppman et al. in 1968, there were few reports in the literature.[4,5]

The next report was presented at the International Neuroradiology Symposium in Gothenburg, Sweden by Sadek Hilal. He, with other surgeons at the Neurological Institute, gave two reports,[6,7] one of them on therapeutic

embolization of vascular malformations of the external carotid circulation and the other on magnetically guided devices for vascular exploration. Another important paper was presented by Wholey et al. [8] from Pittsburgh regarding a percutaneous balloon catheter technique for the treatment of intracranial aneurysms. I always remember Sadek Hilal's humor in presenting the material. He took the Rolls Royce sign, the two R's, and suggested Remedial Radiology as a name for the new specialty.

The surgical neuroradiology field did not begin to develop seriously until a Russian neurosurgeon, Serbinenko, published an important paper in 1974.[9] He probably had had earlier publications in Russia journals, but the publication the world saw was the one in the *Journal of Neurosurgery* in 1974: Balloon Catheterization and Occlusion of Major Cerebral Vessels. Not long thereafter, Debrun began his own development of balloons with latex, efforts that have continued to this day.[10] The Debrun balloons and catheters are used by many specialists and he is one of the true pioneers in the Western world in the area of interventional neuroradiology.

There are a number of other developments. Kerber et al.,[11] for example, developed ways to release catheters when they are guided by flow. Undoubtedly, a number of investigators have developed their own methods, working with glues, catheters, and balloons.

Perhaps one of the most important current developments is that of Victor Scheglov. He discusses herein the utilization of special detachable balloons to occlude aneurysms.

Philosophically, surgical neuroradiology is obviously a field that includes both radiology and surgery. I use the general terms radiology and surgery because the procedures are used interventionally in organ systems other than the brain as well. For the nervous system, of course, the terms would be neurological surgery and neuroradiology. Neuroradiologists and the neurosurgeons must work together so these new technological developments develop in an appropriate manner.

Training

To say that the background and training of individuals who perform these procedures are important is to make an understatement. I believe that neuroradiologists should be carrying out these procedures. What then should be their training? What about neurosurgeons who wish to engage in this field? (Dr. Leeds addresses that question in a later chapter.) It is essential that specialized training for these individuals not bypass the main specialties. In other words, I believe that an interventional neuroradiology candidate should *not* undergo a year each of training in general radiology, neurology, neuroradiology, and neurosurgery—ending up with a niche somewhere between two specialties but not being a specialist in any. I would like such physicians to be rigorously trained in general radiology, so they are familiar

with the whole field, go on to training in neuroradiology, and finally be exposed to the necessary neurosurgical background and interventional procedural training. With this schooling he or she is eligible for certification by the American Board of Radiology (and the American Board of Neuroradiology, if it ever is created).

The same requirements would (or should) apply for neurosurgeons who wish to enter the field. Whatever minimum training would be required for learning interventional neuroradiology by neurosurgeons, when finished the candidates should qualify for neurosurgical boards.

As to how long the training should be for neurological surgeons and for neuroradiologists who are to engage in interventional work is something that must be worked out and decided on by groups and committees. I personally believe that for neuroradiology, which is the area I know, individuals should have the four preliminary years of radiology training, followed by one year of general neuroradiology, and then two more years, one of them devoted to interventional procedures and the other to neurosurgery. Hence the training would last seven or eight years depending on the institution from which the individual comes. At some institutions, a full year can be saved if there is a longitudinal program.

Is this program too long? I think not: In clinical medicine we learn from the patients we diagnose and treat. It is not an experimental situation. Time is necessary to accumulate experience. The program I propose is a long one, but that amount of training is necessary to achieve the best results. These individuals move into private practice with added skills over and above those of the usual neuroradiologist or neurosurgeon.

Terminology

Some physicians who perform these procedures call themselves "embolizers," which I think is a pejorative term. The other term, used by Lasjaunias and Berenstein, is "surgical neuroangiography." I am dead set against that term as well because neuroangiography *means* angiography, that is, a recording of images. Moreover, the term implies that only the vascular system would ever be involved, which is not necessarily the case. The phrase "interventional neuroradiology" is suitable because surgical intervention is a well known term. However, this terminology may incur payment problems by third party payers. For that reason we need to think about other terms. I propose "surgical neuroradiology." What the future holds is necessarily unclear, but it is fairly certain that once a group that specializes in manipulative therapy is created, it is to be expected that the activities of that group will eventually extend beyond what we now know. For example, stereotaxic brain biopsies and the question of percutaneous disc extractions fall outside the purview of the vascular system. Hence a term implying that the field is strictly vascular is unsuitable.

Conclusion

Four major points can be made. (1) There is a need for specially interested and trained individuals in the field of interventional or surgical neuroradiology. The field is now recognized, and we must pay attention to what must be done to develop adequate services within our institutions. (2) At the same time, in the centers where there is sufficient concentration of patient material and trained personnel, we must develop and support training programs designed to provide the best possible background and experience for those who will then go to other centers to cover these needs. (3) In order to acquire the added skills the training period must be lengthened. (4) The candidates should fully qualify for specialty boards.

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II. BASIC CONCEPTS

A. HEMOSTATIC MECHANISMS AND CIRCULATORY FLOW PATTERNS

CHAPTER 2

Activation of Hemostatic Mechanisms in Interventional Radiology

Jacob H. Rand

The introduction of catheters, coils, and other devices into the vasculature of the central nervous system (CNS) must result in triggering multiple hemostatic events due to (1) injury to the vascular wall and (2) the reaction of blood to the presence of a foreign body. It would therefore be helpful to to review some of the responses that occur in order to develop a clearer picture of the hematological consequences of neuroradiological interventional procedures.

The vascular endothelium is normally nonthrombogenic. Injury to blood vessels results in activation of the hemostatic system. When this activation occurs appropriately (e.g., in response to traumatic rupture) we refer to it as the formation of a hemostatic plug. When the activation occurs inappropriately as a consequence of a disease process or as the result of mechanical therapeutic intervention within the vasculature, it is referred to as thrombus formation. Analogous to the immunological system, this system can be considered to have two major components: one cellular and the other humoral. The cellular component consists of the platelet system, and the humoral component consists of the coagulation factor cascades, which ultimately result in the formation of fibrin. How these pathways are orchestrated and which one predominates in any specific situation depend to a large extent on rheological considerations, a subject that Goldsmith and Karino review in Chapter 3, and on the type of injury sustained. For example, removal of the superficial endothelial cell layer exposes material that is highly platelet-reactive under high shear rate conditions. Trauma that exposes the deeper adventitial portion of the blood vessel may expose the flowing blood to material such as tissue factor, which would be a potent contributor to the formation of a fibrin clot.

Overview of Blood Vessel Structure

A brief review of the structure of the blood vessel is helpful for understanding platelet function. The surface of the blood vessel that interfaces with the bloodstream consists of a layer of endothelial cells. Underneath this layer is the subendothelial zone, which is exposed when the endothelium is

stripped away by injurious processes or during the course of angioplasty procedures. The subendothelium contains basement membrane constituents, including laminin and types IV, V and VI collagen, as well as several adhesive glycoproteins including von Willebrand factor (vWF)[2,3] thrombospondin,[4,5] and fibronectin.[6]

Deeper in the blood vessel wall, underneath the internal elastic lamina, is the vascular media, which contains smooth muscle cells surrounded by an extracellular matrix containing type III collagen[7–9] and fibronectin. The deepest adventitial portion of the vessel has an extracellular matrix that is rich in type I collagen. The fibroblast-like cells in this zone contain immunologically identifiable tissue factor.

Platelet Activation

Platelets are derived from megakaryocytes, which in turn are derived from multipotential hematopoietic stem cells. It has been estimated that each megakaryocyte produces approximately 7,000 to 10,000 platelets. Platelets have a complex ultrastructure that includes the presence of a variety of specialized granules. The "dense granules" contain a storage pool of adenosine diphosphate (ADP), that is distinct from the metabolic pool of ADP, along with serotonin and calcium. The α-granules contain a number of coagulation factors, including factor I (fibrinogen), factor V, factor XIII, and von Willebrand factor, β-thromboglobulin, and platelet factor 4 along with platelet-derived growth factor (PDGF), which is chemotactic and mitogenic for smooth muscle cells.

Although we usually consider the platelet system to be distinct from the fibrin system, the two are actually intertwined. First, as mentioned above, the platelet granules contain a number of coagulation factors. Also, the surface membrane of the platelet has receptors for coagulation factors and can be considered a platform for the formation of fibrin.[10,11] Another example involves the protein fibrinogen, which serves as both the precursor of fibrin and a cofactor for the process of platelet aggregation. Still another example of the link between the two systems involves the coagulation enzyme thrombin (factor IIa), which cleaves fibrinogen to form fibrin and is a potent platelet-aggregating agent. Thus whenever one system is triggered, it is not to the exclusion of the other. The "white thrombi," which are composed predominantly of platelets, also must contain some fibrinogen and fibrin; "red thrombi," which are largely fibrin with enmeshed erythrocytes, also contain platelets that participate in the process of clot retraction.

In its resting state the platelet maintains its shape as a a disk that rapidly becomes a spiny sphere upon stimulation in suspension. The platelet surface cytoplasmic membrane, viewed by electron microscopy, is surrounded by a fuzzy coat, the glycocalyx; the latter consists of transmembranous glycoproteins, which serve as receptors for adhesive glycoproteins and collagen.

Interestingly, when platelets are stimulated sufficiently to release their granular substituents, their contents are not released directly outward but, rather, are forced inward toward the center of the platelet, where the granules merge with the open canalicular system.[12] The released material then diffuses outward through the open canalicular system, which is in direct continuity with the external surface. Following release, the degranulated platelet is referred to as a "spent platelet."

How do platelets become activated? The platelet surface has receptors for agonists. Agonists that stimulate platelet activation include ADP, epinephrine, collagen, thrombin, and serotonin. When stimulated, several redundant activation pathways are activated. One involves the prostaglandin synthetic pathway. Here membrane phospholipids are converted by phospholipase A_2 to arachidonic acid, which in turn is converted by cyclooxygenase to intermediate prostaglandins. These substances in turn are converted to thromboxane A_2, a highly potent platelet-aggregating agent.[13] Interestingly, vascular endothelial cells can utilize platelet-derived endoperoxides to synthesize prostacyclin, the powerful inhibitor of platelet function.[14] Within the platelets, cyclic AMP levels are reduced during activation as a result of an increase in phosphodiesterase. In addition, there is activation of the diacylglycerol pathway.[15]

With respect to blood vessel injury, platelets appear to react in a two-step fashion consisting of adhesion followed by aggregation. Upon disruption of the vascular endothelium, blood platelets rapidly come into contact with the exposed surface, attach to it, and then undergo a spreading reaction on the subendothelium. This response is referred to as platelet adhesion. The platelets then release their granular contents in two directions: downward into the blood vessel and outward into the lumen of the blood vessel. The materials released into the blood vessel wall provoke the migration and proliferation of medial smooth muscle cells, which ultimately form the neointimal plaque. The granular contents released into the lumen result in a vasoconstrictive effect and in the recruitment of additional platelets, which stick to the adherent initial monolayer of platelets and form a platelet aggregate, or platelet microthrombus. These two processes—adhesion and aggregation—involve different sets of platelet receptors and different sets of adhesive glycoproteins.

Tschopp et al.[16] made a major contribution to the understanding of platelet adhesion. They showed that when blood from patients with von Willebrand factor (vWF) deficiency is perfused over deendothelialized blood vessels there is a marked decrease in the number of platelets that adhere to the surface compared to platelets from normal individuals. When vWF is added to the system, the platelets adhere normally, indicating that there is not an intrinsic platelet defect in this disorder but, rather, that the diminished adhesion is the result of vWF deficiency.

The vWF appears to mediate the binding of platelets to exposed vascular subendothelium: Both subendothelium and platelets have binding sites for

vWF. With respect to subendothelium, our group has previously shown that vWF is present there,[2,3] and that the deposition of vWF depends on endothelial cells.[17] Regarding the specific binding site within the subendothelium, we have implicated a collagen-like protein in this process.[18,19]

With respect to the platelets, the major binding site for vWF is the glycoprotein Ib complex. In Bernard-Soulier syndrome, there is an inherited deficiency of this glycoprotein complex that results in defective ristocetin-induced binding of vWF[20] as well as defective adhesion to deendothelialized blood vessels.[21] Thus the vWF axis involves platelets having a receptor for an intermediary glycoprotein, vWF, which in turn binds to extracellular matrix.

An analogous disorder is seen in the case of thrombasthenia, an inherited platelet function abnormality originally described by Glanzmann[22] as a bleeding disorder manifested by defective clot retraction. Here there is either a decrease or an abnormality of the glycoprotein IIb/IIIa complex (GP IIb/IIIa) which serves as the binding site for fibrinogen and several other adhesive glycoproteins.[23] Thus similar to the vWF axis, there is a platelet glycoprotein receptor that recognizes adhesive glycoproteins.

It should be pointed out that the GP IIb/IIIa complex recognizes several other adhesive glycoproteins (e.g., vWF, fibronectin, thrombospondin, vitronectin[24] in addition to fibrinogen. However, given the high plasma concentration of fibrinogen, compared to the other adhesive glycoproteins, it is likely to be the major physiological ligand for this receptor complex. Interestingly, in isolated systems where platelets have been removed from plasma and washed, vWF is also capable of binding to GP IIb/IIIa and of mediating platelet aggregation. It is unlikely to be of physiological consequence, however. The platelet glycoproteins can be identified by two-dimensional electrophoresis utilizing rabbit anti-human platelets and by polyacrylamide gel electrophoresis.[23]

It is important to mention that this system is not unique to platelets, and that the family of glycoprotein IIb/IIIa-like receptors has been named the "integrins." For example, analogous to the platelet disorder thrombasthenia is the white blood cell disorder known as leukocyte adhesion deficiency. Patients with this disorder have a tendency to develop bacterial infections owing to an impairment in the ability of their leukocytes to adhere normally. These leukocytes lack the equivalent of GP IIb/IIIa. These patients have normal platelet function, which is consistent with the defect being genetic and completely distinct from thrombasthenia.

The family of GP IIb/IIIa-like receptors, the integrins, are homologous and generally consist of two major components designated the α- and β-chains. These transmembranous proteins require calcium to maintain their conformation and their ability to bind to their ligands.

Ligand proteins bind to the platelet integrin receptors. vWF,[25] discussed earlier as the ligand for GP Ib, is a multimeric glycoprotein synthesized in endothelium and in megakaryocytes. Approximately 15% of the vWF in blood is present within platelets. The material, synthesized by endothelium,

is released in a bipolar manner: underneath into the extracellular matrix, and apically into the bloodstream. vWF has been localized on the platelet surface following platelet activation.[26]

Most fibrinogen is synthesized in the liver, with perhaps a small amount synthesized in megakaryocytes. Fibronectin is a major adhesive glycoprotein synthesized in endothelium, liver, monocytes, megakaryocytes, and fibroblasts. The plasma form of fibronectin is also called cold-insoluble globulin. Thrombospondin is synthesized in endothelium, from where it is secreted into the extracellular matrix of the subendothelium, and in megakaryocytes, where it is packaged into the platelets, α-granules. Although vitronectin (serum spreading factor) binds to the GP IIb/IIIa complex, and is used to get a second integrin vitronectin receptor, its role in hemostasis is not yet clear.

With one exception, all of the ligands for the GP IIb/IIIa receptor share a structural feature, the 3-amino acid sequence arginine-glycine-aspartic acid. This sequence was identified by the pioneering work of Ruoslahti and Pirschbacher[27] on fragments of the fibronectin molecule. They made progressively smaller fragments of the fibronectin molecule and found that this sequence was critical for blocking fibronectin binding to the integrin receptor. Even the substitution of alanine for glycine or of glutamic acid for aspartic acid results in the loss of this peptide's activity.

In the case of vWF, there are thus two recognition sites for platelet glycoprotein receptors: an arginine-glycine-aspartic acid region and a GP Ib recognition site. Fibrinogen, interestingly, has a total of four recognition sites for GP IIb/IIIa, two of which are arginine-glycine-aspartic acid regions at the ends of the α-chains and two which consist of decapeptide sequences at the ends of the γ-chains.[28]

To summarize, the platelets' adhesive properties utilize a general strategy that is shared with other cell types. The platelets have transmembranous glycoprotein receptors that bind adhesive glycoproteins. These adhesive glycoproteins can in turn mediate the binding of platelets to extracellular matrix materials and to each other.

Fibrin Formation

There are two initiators to the formation of fibrin: contact activation and tissue factor. The initiation of the contact activation pathway was clarified in the 1950's with the investigation of a patient named John Hageman, who had a markedly prolonged activated partial thromboplastin time but no symptomatic bleeding problems.[29] This patient was deficient in a coagulation factor, now known as factor XII, which triggers the contact activation pathway by an alteration in its conformation, in the presence of anionic surfaces, which exposes its active enzymatic site. Activated factor XII(XIIa), along with two additional cofactors (high-molecular-weight kininogen and prekallikrein) activates factor XI to factor XIa. Factor XIa, in turn, activates factor IX, which together with factor VIII as a cofactor, activates factor X.

Factor Xa, together with factor V, activates prothrombin (factor II to thrombin (factor IIa); thrombin then cleaves fibrinogen to form fibrin monomers, which polymerize to form fibrin. Thrombin also activates factor XIII, which covalently cross-links adjacent fibrin subunits.

A significant problem in our understanding of the above pathway is that patients who are totally lacking factor XII, prekallikrein, or high-molecular-weight kininogen have markedly impaired coagulation by the in vitro parameters of the activated partial thromboplastin time or the whole blood clotting time and yet have no clinically discernible bleeding defect. It is thus not clear what role this pathway might play in vivo.

The other initiating pathway, the tissue factor pathway,[30] was discovered during the 1830s when DeBlaineville found that thrombi developed when he injected rabbits intravascularly with an extract of brain. The material responsible for this "thromboplastic" activity is tissue factor. The complete amino acid sequence of tissue factor is now known. It is a transmembrane protein with an intracellular tail. The extracellular domains of the molecule contain binding sites for factor VII and factor X, forming a quaternary complex that includes phospholipid, tissue factor, and the two coagulation factors. This complex results in activation of factor X to factor Xa. Factor Xa then goes on to cleave prothrombin as described above. Thus there are two pathways by which factor X can be activated: via IXa and factor VIII or via tissue factor and factor VII.

To complicate things a bit further. Factor IX is also activatable via two means: One is by factor XIa (as described above), the other is via tissue factor and factor VIIa.[31] Thus tissue factor VII has two substrates: factor X (as described above) and factor IX, which would go on to activate factor X. If the tissue factor pathway is indeed the physiological initiator of fibrin formation, this second route could explain why patients with a deficiency of factor VIII or factor IX (the classic hemophilias) bleed, even though those deficient in factor XII, high-molecular-weight kininogen, or prekallikrein do not. It still does not explain why factor XI deficient patients (hemophilia C) can have bleeding symptoms. Two mechanisms have been proposed for factor XI's role in physiologic hemostasis. One is the possibility that a pool of platelet-associated factor XI may be the relevant enzyme. The second is that factor XI may be activated by thrombin.

There are several positive feedback mechanisms that further amplify the process of fibrin formation. For example, thrombin feeds back to increase the cofactor activities of factors V and VIII. Moreover, factor Xa feeds back to activate factor VII.

Mechanisms for Inhibiting Fibrin Formation

With the amplification of fibrin formation, there must exist potent inhibitory mechanisms that limit the process so a small vascular insult does not result in total vascular occlusion. Some of these mechanisms are understood.

One important mechanism appears to be the inhibition of tissue factor activity. Thus far, two inhibitors of this material have been found. The first, and far more potent, inhibitor has been named lipoprotein-associated coagulation inhibitor (LACI)[32] or extrinsic pathway inhibitor (EPI).[33] It circulates in plasma and appears to function by binding to factor Xa complexed to tissue factor. The second, placental anticoagulant protein (PAPs),[34] or the annexin family are members of the lipocortin family of proteins, which were first isolated from placenta and are now known to be present in endothelial cells, amniotic fiuid, and plasma. They function by binding to anionic phospholipids, keeping the phospholipids from being available to serve as a cofactor for the coagulation reactions. Interestingly, we have shown that the anticoagulant function of this protein is inhibited by antiphospholipid antibodies—antibodies that have been clinically associated with hypercoagulability and thrombosis.[35]

In addition, activated coagulation enzymes are inactivated by antithrombin III. Antithrombin III, a member of the serpin family of protease inhibitors, binds to the active serine site of the coagulation enzymes. Antithrombin III activity is markedly enhanced in the presence of heparin.[36] This may be physiologic relevance in that heparin sulfate proteoglycans and similar material on the endothelium may serve as binding sites which amplify inhibitor.

The thrombomodulin system[37] serves as still another inhibitor of the coagulation system. Thrombomodulin is an endothelial surface protein that binds thrombin and changes its specificities. Thrombin bound to thrombomodulin loses its procoagulant functions (i.e., its ability to cleave fibrinogen and to activate platelets and factors V, VIII, and XIII) and becomes specific for a new substrate, protein C, a vitamin-K-dependent anticoagulant protein. Thrombin-thrombomodulin cleaves protein C to form protein Ca. In turn, protein Ca, together with a second vitamin-K-dependent anticoagulant protein, protein S, is capable of degrading factors V and VIII and of enhancing fibrinolysis by blocking plasminogen activator inhibitor, enhancing the activation of plasminogen to plasmin, the major protein of the fibrinolytic pathway.

Finally, in addition to inhibition of tissue factor activity, the inactivation of activated coagulation factors and the modulation of thrombin activity are the mechanisms that promote the dissolution of thrombus formed via the fibrinolytic system.[38] Both plasminogen and plasminogen activator are prepackaged into fibrin clots as they form. Plasminogen has kringle regions that serve as the recognition sites for fibrin. The drug ε-aminocaproic acid inhibits the dissolution of clots by blocking these recognition sites.[39] Plasminogen is cleaved by the locally available plasminogen activator to form plasmin, which lyses the fibrin molecule at several sites. Plasmin can also cleave the fibrinogen molecule. However, significant fibrinogenolysis, which could lead to hypofibrinogenemia and bleeding, does not occur physiologically for at least two reasons. First, plasminogen activator binds preferentially to fibrin, and not to fibrinogen, making activation of plasmin a local affair

restricted primarily to the clot. Second, the circulating plasma has potent inhibitors of both plasmin and plasminogen activator that help restrict the process of fibrinogenolysis.

In conclusion, interventional procedures which introduce foreign bodies and instruments into the vasculature unleash a complex series of responses due to injury to the vascular endothelium and activation of the hemostatic and endogenous anticoagulant systems. Knowledge of how these reactions occur and the possible means of modulating them is critical in order to optimize interventional techniques.

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Discussion

Reendothelialization and Modulation of Thrombosis

Dr. S. Hilal: In surgical-radiological intervention, it is important to be able to achieve reepithelializatin without clotting. Do you see any way to do it in the face of this long list of factors and subfactors? Is there any way we can manipulate these factors to achieve the effect of endothelialization without platelet aggregation?

Dr. Rand: I suppose that it must depend on the specific type of intervention that is being used.

Dr. S. Hilal: For example, putting in prostheses, balloons, or coils. Should we soak the ballon in von Willebrand factor?

Dr. Rand: There are a number of potential interventions. For example, peptide fragments of adhesive glycoproteins, such as the RGD fragment, could be used to inhibit additional formation of platelet thrombus following a therapeutic maneuver. Also, monoclonal antibodies directed against active sites on the glycoprotein receptors or on adhesive glycoproteins must have the capability of inhibiting platelet function. An example involves work done by Dr. Barry Coller using the Folts model of coronary occlusion. The Folts model causes constriction of a coronary artery in the dog and the subsequent creation of a thrombus within this constricted artery. Coller found that you can inhibit the formation of an occlusive thrombus by preoperatively or concurrently infusing a murine antibody directed against the glycoprotein IIb/IIa complex. Following this infusion, the vessel remains patent even though the antibodies are no longer being infused. There also appears to be a "passivation" occurring on the surface.

The answer to your question in "yes." We are going to have effective methods for modulating thrombosis: and the therapeutic intervention to an extent will be similar to that of the drunk searching under the light for the key. If we were having this conference 10 years ago I would have told you that the therapeutic intervention would involve the use of aspirin or dipyridamole or of heparin coating the catheter. At the present time the therapeutic intervention involves peptides that have the ability to specifically inhibit the portion of the hemostatic process you want to inhibit, or it may involve monoclonal antibodies, which can inhibit the abilty of a receptor to recognize ligands. I have no doubt that additional advances in our understanding will progressively yield more effective methods for controlling these processes.

Dr. Bernstein: Do you need platelets to create the endothelium?

Dr. Rand: You do not need platelets to create new endothelium. For example, if you make a rabbit thrombocytopenic and then perform angioplasty of the aorta, new endothelium grows even in the presence of thrombocytopenia. It grows out laterally from branch sites. When you do an angioplasty procedure, for example, there are either branch sites you do not deendothelialize or border regions that have not been hit. Endothelium grows out from these branch sites and from the border regions.

Dr. Bernstein: You mentioned prostaglandin as one of the parts of the cascade in the platelet itself. Does it not also have a vasoactive effect?

Dr. Rand: Yes, prostaglandins are vasoactive. Thromboxane produces vasoconstriction, and prostacyclin produces vasodilatation. In fact, one of the problems with prostacyclin therapy is its hypotensive effect resulting from the vasodilation. Platelets themselves are also vasoactive in that they induce local vasoconstriction upon activation due to release of serotonin. About 99% of the serotonin in blood is present in the

platelets within the dense bodies; serotonin is released when the platelets become activated.

Dr. Holtzman: What happens when a metallic surface becomes covered with thrombus? Does the thrombus continue to propagate?

Dr. Rand: The thrombus propagates only up to a point.

Dr. Holtzman: Why, when you put in a coil do you see a clot that is much more extensive than the coil itself?

Dr. Hilal: You should not. It is amazing how mildly thrombogenic these coils are, and channels can be maintained around the coils. They are not as thrombogenic as you might think. However, if you do see clots, platinum coils may be the answer.

Dr. Stein: That's true. Platinum is absolutely inert, but if you mix copper with it thrombosis occurs. The other possibility is that the coils cause obvious major injury to the intima of the cerebral vessels, which are medium-sized arteries. That is an unavoidable part of the procedure. The coils are packed in tightly, and some of them almost perforate the artery; yet there may be rivulets of blood flowing around the coils with no thrombosis.

Dr. Rand: In my experience, the surface injury probably results in platelet deposition and aggregation. We now know where tissue factor is located in various tissues and within the blood vessels, so we know that the intima of the blood vessel has no tissue factor in it. Tissue factor in blood vessels is present almost entirely within the adventitial surface, so it is likely that as you puncture the deeper portions of the blood vessels tissue factor is being released. There is a balance, though, of pro- and anticoagulant activities with the tissue factor and platelet activity material and the anticoagulant processes (which are triggered almost as soon as the procoagulant effects appear). These activities involve the inhibition of tissue factor, activated clotting protein, and platelets—all in that microenvironment around the site of injury. Certainly, as Dr. Goldsmith is about to discuss, flow factors are important in helping to decide the concentration of the reactants at the specific site. Flow factors also help to decide which limb of the coagulation system will predominate.

Dr. Rand: A common question is how to create a biocompatible material that is resistant to clot formation. why is it that virtually every form of "inert" material ultimately induces thrombus formation? The question of why a clot forms in a particular area is clearly complex. Some important factors include the nature of the vascular injury, the charges on the surface, the chemical composition of the surface in which the blood is seen, and the blood flow factors.

Recanalization and Control of Thrombosis

Dr. Bernstein: After the clot is formed, how can you prevent recanalization? Would you empirically use ε-aminocaproic acid for a period of time to prevent it?

Dr. Rand: The way I think of a clot forming is that fibrinogen is not simply cleaved to form fibrin. Rather, the fibrin clot has packaged within it the precursor fibrinolytic components, which ultimately result in its disintegration and dissoultion under physiological circumstances. One of the things that we might be able to do is to try to keep plasminogen from being incorporated into the thrombus. We know that ε-aminocaproic acid can do that. It is likely, then, that if EACA were present during the period when you are inducing thrombus there should be a substantial decrease in the rate of clot dissolution. Clearly, experiments would have to be done to test this theory.

Dr. Bernstein: Would you have to administer it chronically?

Dr. Rand: Not necessarily. The survival of ε-aminocaproic acid in the circulation is brief. In theory, it is possible to inhibit incorporation of plasminogen into the forming thrombus. Subsequently, once the thrombus has formed with a minimum amount of plasminogen in it, the ε-aminocaproic acid is cleared rapidly. You do not have to worry about clot continuing to form while you are administering the ε-aminocaproic acid, which would be the major contraindication. A major practical problem is formation of thrombus about the catheter itself.

Dr. Bernstein: Once the occlusion is in place, you want it to stay there. The goal is to prevent lysis of the territory you have occluded. How do you accomplish it?

Dr. Rand: A potential therapeutic maneuver that has a high likelihood of working would be infusion of ε-aminocaproic acid while you are doing the maneuver and subsequent to the clot being formed; then stop the ε-aminocaproic acid. The fibrin itself consists of fibers that are forming. It is believed that plaminogen must be incorporated within these fibers for the fibrin to be cleaved efficiently. You should be aware that there are other inhibitors of fibrinolysis as well, including tranexemic acid and aprotinin.

Dr. Viñuela: What is the possibility of hemorrhage in other systems?

Dr. Rand: With respect to ε-aminocaproic acid, the major problem is the potential for too much thrombosis.

Dr. Bernstein: But it does not promote thrombosis, it prevents lysis.

Dr. Rand: There is the possibility of excessive thrombosis extending from the site of initiation. A possible protocol to be considered is the infusion of ε-aminocaproic acid for approximately 20 minutes prior to the procedure in order to administer a loading dose of 3 to 4 grams, thereby attaining a systemic dosage: it is then continued at approximately 1 gram per hour during the procedure and stopped right after the procedure. It would then be cleared rapidly. This method provides the potential of having blocked significant amount of plasminogen or plasmin from being incorporated into the fibrin clot that you have induced. Of course, it should be tried in an animal model first.

Dr. Heishima: Does heparin impair deposition of fibrin?

Dr. Rand: Yes, by its inactivation of the activated coagulation factor enzymes via antithrombin III.

Dr. Heishima: We do many of our procedures under heparin to avoid unwanted thrombosis. Is it possible to deposit the occluding material in a fully heparinized state and then, when we are prepared to have thrombosis occur, the ε-aminocaproic acid can be given?

Dr. Rand: Yes.

Dr. Bernstein: Is there an antagonist to ε-aminocaproic acid?

Dr. Rand: No, as far as I am aware you must simply wait for it to be cleared, and clearance is rapid. In order to maintain therapeutic plasma levels of ε-aminocaproic acid, it must be administered at a continuous rate of 1 gram per hour.

Dr. Bernstein: Would a clot form in the presence of ε-aminocaproic acid? Can it be dissolved with TPA? The goal is to occlude a territory, but is a normal territory becomes occluded is it be resistant to dissolution?

Dr. Rand: It would be relatively resistant to TPA because tissue plasminogen activator works by cleaving plasminogen. There is likely to be lysis of the surface of the fibers of the clot, but there would not be sufficient penetration of the interstices of the clot to would allow local plasmin to dissolve the fibrin.

Dr. Fox: Can the ε-aminocaproic acid be mixed with other substances that we might be depositing locally? Will it work if we deposit it as part of the embolus we are inducing?

Dr. Rand: ε-Aminocaproic acid is a small molecule, an amino acid, so I expect it would diffuse rapidly. It is good that you raised the point because it brings to mind additional information that we have about ε-aminocaproic acid from the neurosurgical literature involving its use during the frequently encountered aneurysmal bleeding.

We know that a lot of the drug produces good results, but too much creates problems. High doses ("industrial doses") of ε-aminocaproic acid can promote bleeding, which is understood to be due to a inhibition of platelet functions at high concentrations. Hence it is possible that the deposit of large quantities or high concentrations of this material in the local environment may produce an effect opposite to that which we had intended.

Dr. Holtzman: Is it possible to create a capsule (that is, a time-release capsule) wherein the thrombogenic material would release a small amount of ε-aminocaproic acid locally over time into the clot?

Dr. Rand: Yes. However, you would have to ensure that the concentration is not at the level at which platelet function is inhibited. Also, you might consider use of the other inhibitors of fibrinolysis: aprotinin and tranexemic acid. It is possible that they may, in fact, have properties that make them better. It is also possible that combinations of these drugs might work.

Dr. Heishima: Our understanding of recanalization is that it is more than just fibrinolysis. Do you believe that if you prevent fibrinolysis you will also interfere with recanalization?

Dr. Rand: There is a cellular component to recanalization that involves the growth of endothelial cells onto and over the clot laterally. We know that these cells are capable of producing collagenases and other proteolytic enzymes that cause dissolution. When we inhibit fibrinolysis, we are going a long way toward keeping the clot intact. We know from experience with the therapeutic use of fibrinolytic agents—streptokinase, urokinase, tissue plasminogen activator—that when a clot has formed the susceptibility of that clot to fibrinolysis depends on how quickly we begin to dissolve the clot.

Dr. Heishima: Do you therefore recommend giving heparin and ε-aminocaproic acid concomitantly?

Dr. Rand: I do not recommend their active *clinical* use at this point—prior to an experimental trial. Rather, I would recommend a *trial* of fibrinolysis inhibitors, I think that ε-aminocaproic acid has pharmacological properties that offer advantages regarding the inhibition of clot dissolution without promoting further clot propagation.

CHAPTER 3

Flow Patterns and the Localization of Vascular Disease in the Circulation

Harry L. Goldsmith and Takeshi Karino

Fluid mechanical factors play an important role in the localization of sites of atherosclerosis, the focal deposition of platelets resulting in thrombosis, and the formation of aneurysms in the human circulation. The sites are confined mainly to regions of geometrical irregularity where vessels branch, curve, and change diameter and where blood is subjected to sudden changes in velocity, direction, or both. In such regions, flow is disturbed and separation of streamlines from the wall with formation of eddies are likely to occur. We describe here the flow patterns and fluid mechanical stresses at these sites and consider their possible involvement in the genesis of the above-mentioned vascular diseases. However, to understand the mechanics of flow in branching, expanding, and curved vessels, it is first necessary to deal with some basic fluid dynamic concepts. It is particularly necessary, as there is a common misunderstanding among physicians and surgeons that the formation of eddies at sites of disturbed flow represents turbulent flow. As explained below, this is usually not the case. As is the custom in many textbooks of medical physiology, we begin our lesson in fundamental hydrodynamics by defining the steady laminar flow of a liquid through a circular cylindrical tube, known as Poiseuille flow.

Basic Fluid Mechanical Principles

Laminar, Viscous Flow Through a Tube

Consider the case, illustrated in Figure 3.1, of a liquid made to flow steadily through a cylindrical tube with rigid walls, of radius R, at a volume flow rate Q milliliters per second in the axial Z direction. A basic tenet of fluid dynamics is that the elements of the liquid at the wall are at rest: the no slip condition. As one proceeds from the wall toward the axis, adjacent cylindrical layers or laminae of fluid slide over each other, like the cylinders of a telescope being pulled out, at progressively increasing velocity, reaching a maximum at the tube axis. In any diametrical plane, such as the one shown in Figure 3.1 (MM′), the distribution of velocity in the axial direction (velocity profile) at a given flow rate depends on the radial distance r from the tube

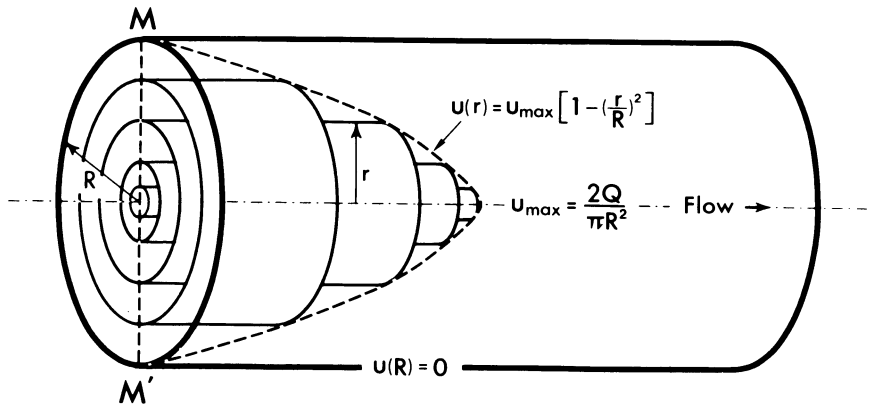


Figure 3.1. Poiseuille flow of a viscous fluid through a circular tube of radius R. The motion is pictured as the telescopic sliding of adjacent cylindrical fluid layers over each other. The layer at the wall is at rest, and the velocity u(r) in a direction parallel to the walls increases parabolically to a maximum at the axis, as shown by the dashed line, which gives the velocity profile in the diametrical or median plane, MM', of the tube. It is in this plane that movements of model particles and cells in Figure 3.2 is shown. (Reprinted with permission of Karino and Goldsmith.[1])

axis and the tube radius, and it is parabolic, given by:

$$u(r) = \frac{2Q}{\pi R^4}(R^2 - r^2) \tag{1}$$

where u(r) is the fluid velocity at a given radial position (r). The velocity gradient, or shear rate (G), in Poiseuille flow is also a function of the radial distance, decreasing from a maximum at the tube wall to zero at the tube axis (Figs. 3.2 and 3.3):

$$G(r) = -\frac{du}{dr} = -\frac{4Q}{\pi R^4}r \tag{2}$$

with a value at the wall given by:

$$G(R) = \frac{4Q}{\pi R^3} = \frac{2u(0)}{R} \tag{3}$$

u(0) being the centerline fluid velocity ($=2\bar{U}$), the mean velocity in Poiseuille flow.

The Poiseuille, parabolic velocity profile is achieved in the tube at a distance large enough from its entrance that the frictional effect of the wall is manifested across the entire diameter. This distance, known as the entrance length, is usually expressed as the number of tube diameters necessary to establish nonradial flow in the tube. Work, in the form of a pressure (P), must be applied to initiate and maintain fluid flow. This work overcomes the

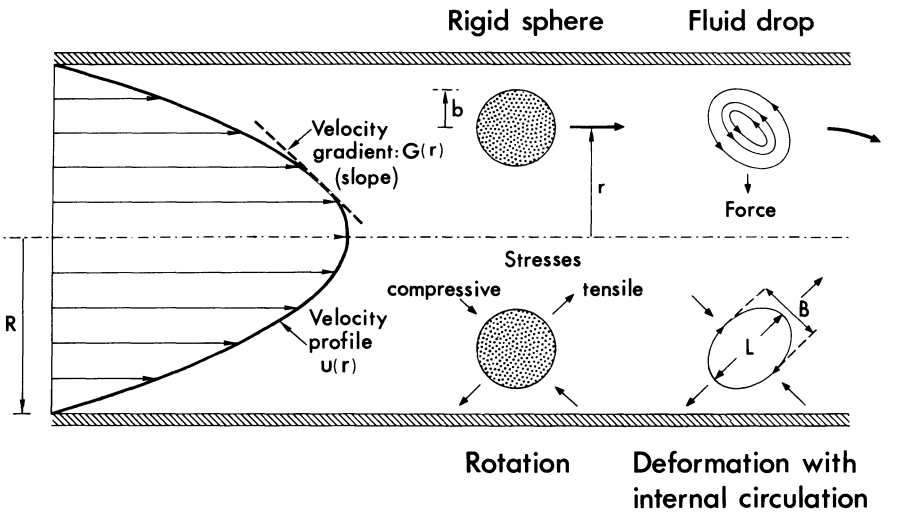


Figure 3.2. Effect of fluid mechanical stresses on suspended particles in a liquid undergoing Poiseuille flow. Shown are the parabolic velocity profile and the linearly varying velocity gradient in the median plane (cf. Fig. 3.1). A rigid sphere rotates with uniform angular velocity; a deformable liquid drop is distorted into an ellipsoid of length L and breadth B by the external fluid stresses, and it orients itself at a constant angle to the direction of flow. Unlike the rigid sphere, the drop migrates away from the tube wall. (Reprinted with permission of Goldsmith.[2])

frictional resistance to flow due to intermolecular forces in the liquid resisting shear. When the velocity profile is fully established and each fluid element moves at a constant velocity (there being no velocity components in the radial direction), there is a balance between two forces. The *normal* component of the fluid stress (i.e., the force per unit area acting in a direction perpendicular to that of the flow), given by the gradient in the Z direction of the pressure applied to make the liquid flow $\Delta P/\Delta z$, is opposed by a *tangential* force per unit area due to wall friction retarding movement of the liquid, represented by the wall shear stress, $\tau(R)$. The force balance is expressed by the equation:

$$-\frac{\Delta P}{\Delta z} \cdot \pi R^2 = 2\pi R\tau(R)$$

whence

$$-\frac{\Delta P}{\Delta z} = \frac{2\tau(R)}{R} \tag{4}$$

The fluid shear stress $\tau(r)$ is defined as the tangential force per unit area exerted in the direction of flow on a layer of fluid at a radial distance (r) by

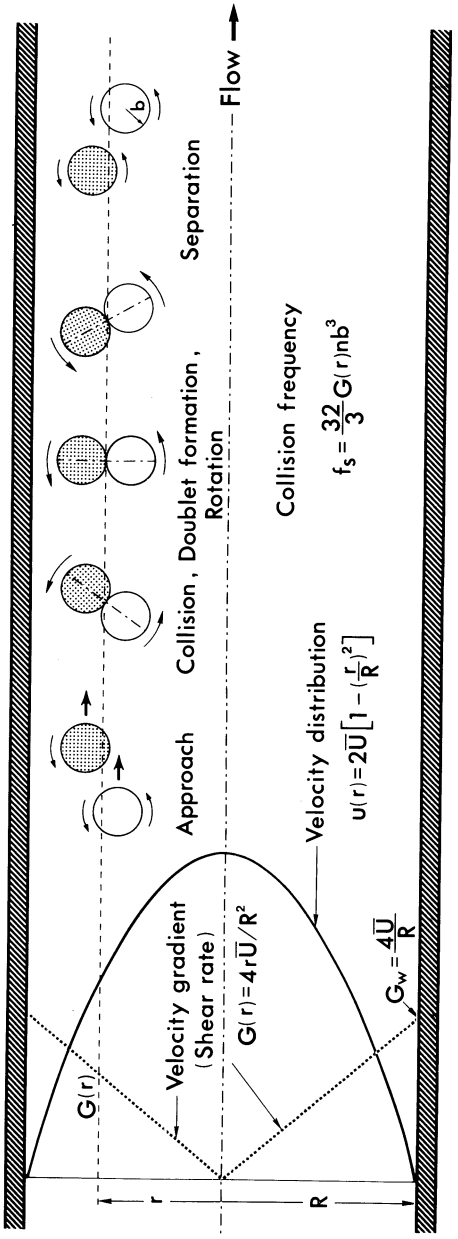


Figure 3.3. Two-body collision between equal-sized rigid spheres in Poiseuille flow. The figure shows a tracing from photomicrographs of the approach, formation, and rotation of a transient doublet as well as separation of spheres. The dashed line represents the midpoint of the line joining the sphere centers at a radial distance r from the tube axis. As can be seen, the radial positions of the spheres are displaced during the collision. Such displacements increase markedly with increasing particle concentration, as three, four, and multibody collisions become more frequent. (Reprinted with permission of Karino and Goldsmith.[1])

fluid at a radial distance (r + dr). In the case of a liquid obeying Newton's second law, the shear stress is directly proportional to the shear rate, the constant of proportionality being the viscosity (η), or the coefficient of internal friction:

$$\tau(r) = \eta G(r) \tag{5}$$

Thus the viscosity is the force per unit area (units: g/cm-s^2 or kg/m-s^2) required to maintain unit gradient in velocity (units: 1/s); its units are g/cm-s (the Poise) or kg/m-s (the Pascal second in SIU). Plasma is a newtonian liquid with a viscosity of about 0.011 Poise or 1.1 mPa s at 37°C, about 60% more viscous than water.

Returning to Eq. 4 and substituting for $\tau(r)$ from Eq. 5, we obtain

$$-\frac{\Delta P}{\Delta z} = \frac{2\eta G(R)}{R} \tag{6}$$

then substituting for G(R) from Eq. 3 finally yields

$$\frac{\Delta P}{\Delta z} = \frac{8\eta Q}{\pi R^4} \tag{7}$$

the well known Poiseuille-Hagen equation. This classical expression implies that, for a given fluid and volume flow rate, the work done to overcome internal friction, so-called viscous work, increases 16-fold every time the tube radius is halved. Similarly, the wall shear rate (Eq. 3) and the wall shear stress (Eq. 5) increase eightfold as the tube radius is halved.

Effect of Suspending Particles

Rotation and Deformation

When a particle is immersed in a liquid undergoing Poiseuille flow, it experiences stresses at its surface, there being no slip at the particle-fluid boundary. If the particle is rigid, the stresses cause it to rotate while it is carried by the flow along the tube. Thus, as shown in Figure 3.2, a sphere located at a fixed radial distance (r) rotates with uniform angular velocity, given by half the value of the shear rate at that location. A disk rotates with periodically varying angular velocity, being a maximum when oriented across the flow and a minimum when aligned with the flow.[3] By contrast, if the particle is deformable, the external fluid stresses cause it to be distorted from its original shape. As shown in Figure 3.2, an emulsion droplet is deformed from a sphere into an ellipsoid, which is oriented at a constant angle to the direction of flow. The fluid stresses are transmitted across the droplet interface, and fluid at the surface and in the interior circulates about the particle center.

At hematocrits of less than 1%, single human red blood cells (RBCs) in plasma can be shown to behave as rigid disks provided the shear stress is less than 10^{-2} N/m^2. At higher shear stresses and in media more viscous

than plasma (e.g., isotonic solution of low-molecular-weight dextran, or Ficoll), the cells exhibit fluid drop-like behavior, oriented at a constant angle to the flow with the membrane circulating around the interior.[4,5] By contrast, platelets and white blood cells (WBCs), having highly viscous interiors, remain undeformed in dilute suspensions and rotate as rigid disks and rigid spheres, respectively.

Collisions

In the absence of flow, only translational brownian motion can bring blood cells slowly into close proximity to, and collision with, each other. Far greater is the effect of the velocity gradient of shear flow in promoting collisions between blood cells. Here a simple model is provided by considering two-body collisions between equal-sized rigid spheres of radius (b) in a suspension containing n particles per cubic centimeter undergoing Poiseuille flow, as shown in Figure 3.3. The collision frequency (f_s; number of collisions suffered by a given sphere per second) at a radial distance (r), where the shear rate is G(r), is given by[6,7]

$$f_s = \frac{32}{3} G(r) n b^3 \tag{8}$$

$$= \frac{8G(r)c}{\pi} \tag{9}$$

as the volume concentration $c = 4\pi b^3 n/3$. Thus the total number of two-body collisions per second per cubic centimeter of the suspension, $F_s = fn/2$, is greater at the tube periphery where G(r) is larger and is greatly affected by the size of the particle. In dilute suspensions at the same number concentration and shear rate, the two-body collision frequency for RBCs of equivalent sphere radius b = 2.8 μm (calculated from a mean cell volume = 90 μm^3) is more than eight times greater than that of platelets whose equivalent sphere radius b = 1.2 μm (mean cell volume = 8 μm^3). Equations 8 and 9 may be applied to platelet-rich plasma, where it can be shown that for $n = 3 \times 10^5$ cells/μl (c = 0.3%) and at shear rates of 200 s^{-1} (typical of mean values in arteries of $\sim$2 mm diameter), $f_s = 1.5$ collisions/cell/s and $F_s = 2.2 \times 10^5$ two-body collisions/s/μl. However, the simple equations no longer apply to RBCs at hematocrits over 10%, as there are now multibody collisions, which result in larger, continuous radial fluctuations of cell paths.

Formation of Aggregates

In the presence of interaction forces between cells, such collisions can lead to the formation of aggregates, as can readily be demonstrated with normal RBCs in plasma flowing through a circular tube at mean shear rates of less than 50 s^{-1}. Collisions between cells result in the formation of rouleaux, which because of their deformation in the flow migrate to the axis where they

Table 3.1. Physiological parameters in the human arterial tree

Vessel	Diameter (mm)	Mean linear velocity ($\bar{U}$, mm s^{-1})			Mean Reynolds number (Re_t)	Wall shear rate[a] (G_w, s^{-1})		
		Min.	Max.	Mean		Min.	Max.	Mean
Ascending aorta[b]	23.0–43.5	—	—	245–876	3210–6075	—	—	45–305
Femoral artery[c]	5.0	−350	1175	188	283	−560	1885	302
Common carotid[c]	5.9	99	388	187	332	134	526	253
Carotid sinus[d]	5.2	85	325	156	244	130	500	240
External carotid[d]	3.8	83	327	157	180	175	687	331
Small arteries	0.3	—	—	50	2.3	—	—	1335
Arterioles	0.025	—	—	5	0.038	—	—	1600
Capillaries[e]	0.012	0.39	1.74	0.84	1.5×10^{-3} to 6.6×10^{-3}	260	1290	560

[a] Assuming Poiseuille flow.

[b] Mean systolic values from MacDonald[10]

[c] Values obtained in vivo by Anliker et al.[11]

[d] Values calculated assuming 65% flow into the internal carotid. Measured wall shear rates from ex vivo studies[12] in steady flow at $Re_t = 592$ show that at the outer wall of the sinus there is a recirculating flow with G_w varying from -135 to $+530$ s^{-1}. At the inner wall $G_w > 2000$ s^{-1}. At the inner wall of the external carotid $G_w > 1000$ s^{-1}.

[e] Values from Bollinger et al.[13] from red blood cell (RBC) velocities in human nailfold capillaries of large diameter. Calculations of wall shear rate would correspond to that in plasma flow. In "bolus flow" of a train of RBCs, much higher wall shear rates would exist in the plasma layer surrounding the RBCs.

combine into larger stable aggregates in the low shear region. The kinetics of platelet aggregation in Poiseuille flow has been studied by activation of platelets in plasma with ADP. It was shown that the rate of aggregation increases with the mean tube shear rate, $\overline{G} < 40\ s^{-1}$.[8,9] In the absence of RBCs at a 1 μM ADP concentration, microaggregates first form near the tube wall; as they grow in size through collisions with other singlets and aggregates during flow along the tube, they migrate toward the axis because their rotation is physically impeded by the wall. They eventually form a large, stable, loosely bound aggregate at the tube center.[9]

Further work covering the physiological range of shear rate ($20 < \overline{G} < 2000\ s^{-1}$) (Table 3.1) has shown that in platelet-rich plasma (PRP) the rate and extent of aggregation first increases with increasing mean tube shear rate and then decreases again.[14] In terms of aggregate volume fraction, higher shear rates clearly inhibit the formation of large particles. The successive formation of aggregates of increasing size with time is also evident. At 0.2 μM ADP, the kinetics indicate that both a weak and a strong platelet–platelet bond is involved in aggregation at physiological shear rates. The rate and extent of aggregation is significantly greater at 1 μM ADP than at 0.2 μM ADP; aggregate size is still limited at high shear rates.

The rate of platelet aggregation in whole blood is as much as nine times greater than in PRP.[15] Because no platelet thromboxane A_2 or RBC lysis could be detected, it is believed that the effect of RBCs on augmenting platelet aggregation in whole blood is largely a mechanical one. However, there is some evidence of shear-induced aggregation in the control sample of whole blood in which Tyrode's solution instead of ADP is infused, pointing to the possibility that sublytic leakage of ADP from RBCs can lead to aggregation.[16,17]

Cell Crowding and Nonnewtonian Flow Behavior at Normal Hematocrit Values

At normal hematocrit values, during flow through tubes, it is the crowding of the RBCs that changes the pattern of flow most noticeably. We have studied flow at normal hematocrit by using suspensions of reconstituted biconcave ghost cells in plasma, which are transparent to transmitted light.[18] Small quantities of normal, visible RBCs, platelets, or microspheres are added to serve as tracers of the cell motions within these suspensions. Three main effects come to the fore at high concentrations.

1. The velocity profile is no longer parabolic, as in Poiseuille flow, but is blunted in the tube center where there is a region of partial plug flow in which all the cells move with the same velocity. Thus, as shown in Figure 3.4, the velocities and shear rates in the central portion of the tube are lower than those that would be obtained with Poiseuille flow at the same volume flow rate, whereas the opposite is true at the vessel periphery. This effect,

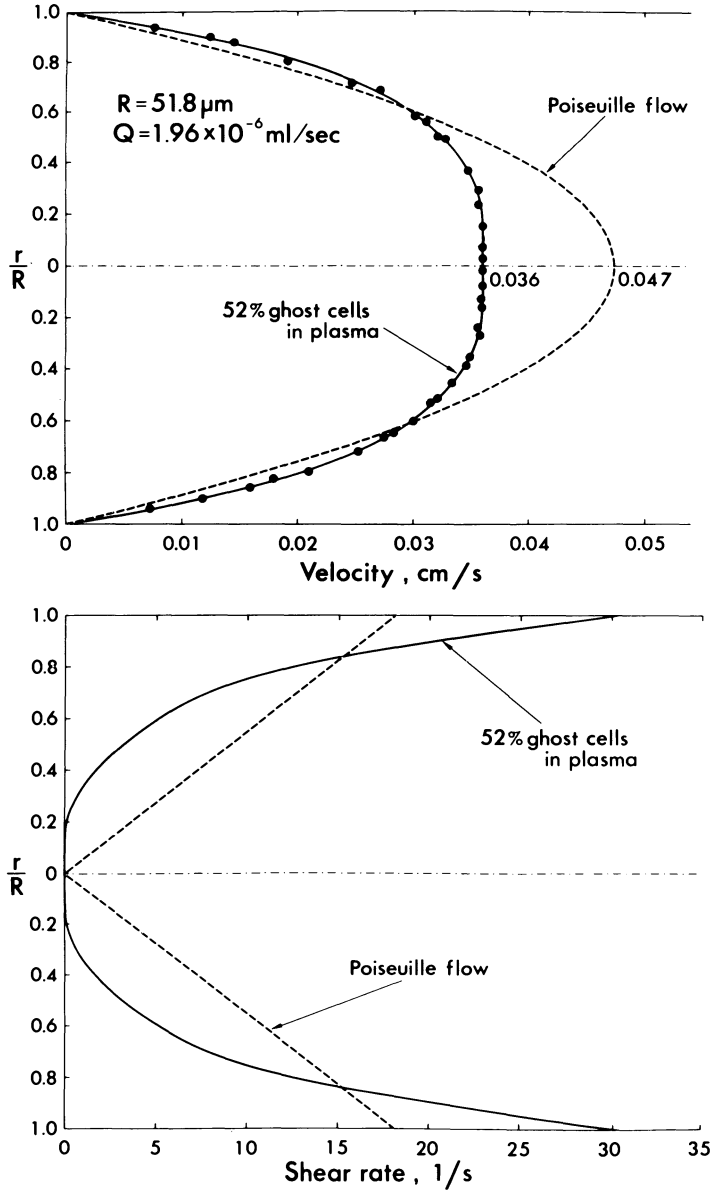


Figure 3.4. Distribution of velocity and shear rate in a 50% ghost cell suspension flowing through a 103.6 μm diameter tube, obtained from the paths of tracer red blood cells. It illustrates the deviation of the velocity profile from the parabolic one in Poiseuille flow. The velocity and shear rate distribution for Poiseuille flow were calculated assuming the blood to be a pure liquid flowing at the same volume flow rate as the ghost cell suspension. (Reprinted with permission of Karino and Goldsmith.[1])

which was earlier documented in the tube flow of suspensions of rigid spheres and disks[19] and emulsions,[20] is due to the interaction of the particles with each other and with the tube wall. In blood, the extent of partial plug flow at the vessel center is expected to be further enhanced by the formation of rouleaux of RBCs, especially at low flow rates.

2. The cell paths exhibit erratic lateral displacements. At high shear rates in tube flow, these lateral displacements exert an outward dispersive force that opposes the inward radial migration of the RBCs from the vessel wall that would occur in the absence of interactions.[21] Even if there is, on average, an RBC-depleted layer at the vessel periphery, there are still cells in collision with the vessel wall because of the multibody interactions occurring in its vicinity. Such motion has been observed and photographed in transparent concentrated suspensions of rigid spheres and disks,[19] emulsions[20,22] containing visible tracer particles, and transparent suspensions of reconstituted biconcave human ghost cells.[18,21]

3. Deformation of RBCs occurs to a degree that is not attributable to shear alone.

Inertial Effects: Reynolds Number

Thus far we have considered a flow regime in which the work required to shear the suspending liquid and to cause the suspended particles to translate, rotate, and deform is done when overcoming internal liquid friction—viscous work. More important, from the point of view of the subject of this chapter, which deals with flow in large vessels in which the velocities during the cardiac cycle are high (>10 cm s^{-1}; Table 3.1), is the work required to accelerate and decelerate the suspension, so-called inertial work. The relative importance of liquid friction and liquid inertia in a vessel is given by a dimensionless parameter known as the Reynolds number, which is the ratio of inertial to viscous forces. In tube flow, the magnitude of the inertial force is proportional to the kinetic energy per unit volume (mass $\times \bar{U}^2 \div$ volume) $= \rho \bar{U}^2$, where $\bar{U}$ is the mean velocity, and ρ is the liquid density. The magnitude of the viscous force is proportional to a shear stress $\eta \bar{U}/2R$, where $\bar{U}/2R$ is a representative shear rate. Hence the tube Reynolds number (Re_t) is:

$$Re_t = \frac{\rho \bar{U}^2}{\eta \bar{U}/2R} = \frac{2R\bar{U}\rho}{\eta} \tag{10}$$

In his classical dye-injection experiments in circular tubes with a bellmouth-shaped inlet, Reynolds discovered that the transition from steady, orderly laminar flow to turbulent flow, the latter characterized by rapid and continuous mixing of the fluid in a chaotic manner throughout the tube, occurred at approximately the same Reynolds number, about 2000. The significance of his findings is that for incompressible viscous fluids such as water and blood

if the Reynolds numbers are the same in geometrically similar vessels one can assume a dynamic similarity of flow patterns even if the vessel diameters and the fluid velocities are completely different. Thus it is more convenient to express the flow conditions in different vessels of the circulation in terms of the Reynolds number than in terms of the flow rate.

Using the above equations, valid for Poiseuille flow, representative values of Reynolds number, wall shear rate, and shear stress may be calculated for various parts of the vascular system from the known vessel diameters and volume flow rates. These values are given in Table 3.1, where it can be seen that mean linear velocities over one cycle decrease from greater than 800 to less than 1 mm s^{-1} and the mean Re_t from 6000 to less than 10^{-3} when going from the heart to the microcirculation, where viscous effects dominate the flow. The corresponding mean wall shear rates, and hence the shear stress, increase when going to the small vessels, reaching a maximum in the arterioles. It is evident, however, that wall shear rates at peak systole in some large arteries can be as high as those in small vessels.

Unsteady and Disturbed Flows in the Circulation

In general, within the circulation there is not a fully developed viscous flow with a parabolic profile. We have seen that in small vessels (Fig. 3.4) deviations from the parabolic profile are related to the effect of the crowding of RBCs on the flow. Moreover, because blood is not a homogeneous newtonian liquid, the velocity profiles are affected by flow rate and hematocrit, particularly in vessels less than 0.5 mm in diameter. In large vessels where inertial effects are important, flow is not steady but pulsatile and exhibits kinetic energy effects, as shown in Figure 3.5. The flow oscillates periodically and is somewhat out of phase with the pressure gradient.[10] Moreover, within a given vessel not all parts of the liquid move in phase with each other. Near the wall, where the shear rate, now dependent on both radial distance and time, is high and wall friction forces predominate, the liquid elements are almost in phase with the pressure gradient. In the center of the stream, however, the kinetic energy is high, and inertia of the liquid results in its lagging increasingly behind the pressure gradient and hence behind flow near the wall, as shown in Figure 3.5.

Flow is also seriously affected locally by branching and curvature, where inertial effects result in the production of secondary flows having radial components and sometimes in flow separation and eddy formation. In fact, branching occurs with such frequency that the disturbance created in the flow at one branch has not had time to dissipate before that due to another branch comes into play. That such effects may be particularly important with regard to the genesis of thrombosis and atherosclerosis has long been suspected by investigators in the biomedical as well as the physical and engineering sciences. Rapid changes in the rate and direction of fluid motion have been held responsible for bringing about alterations and injury, not

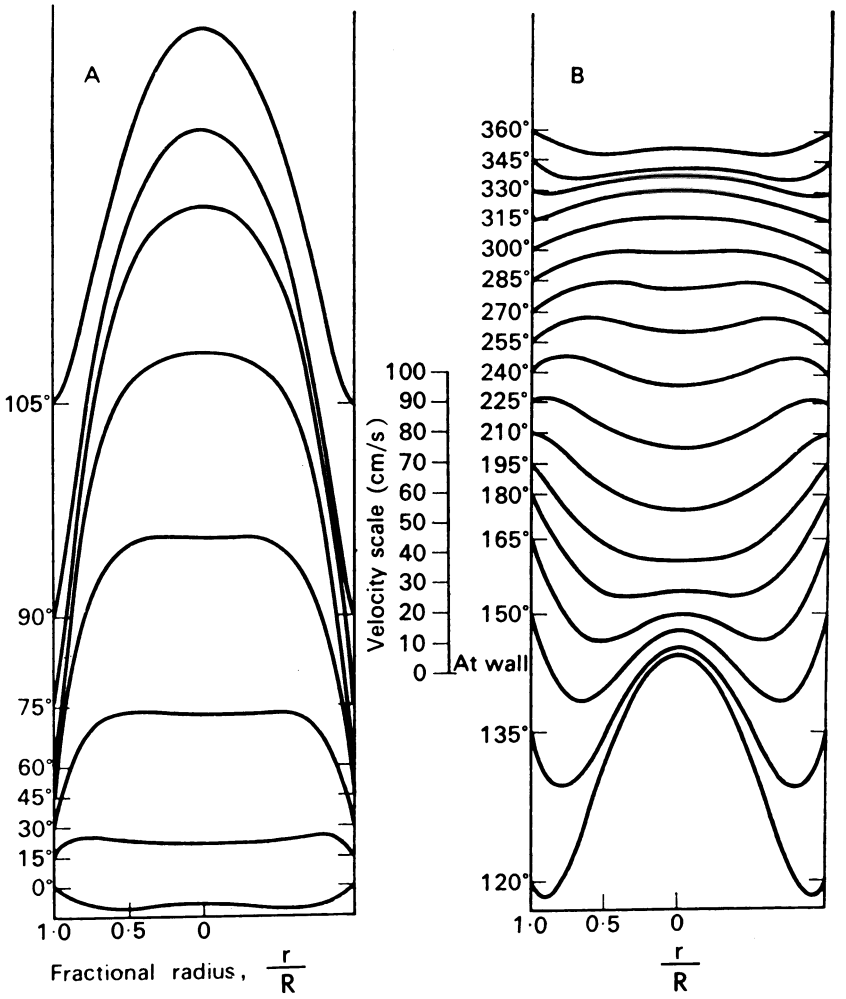


Figure 3.5. Pulsatile velocity profile in the femoral artery of a dog calculated from the measured pressure gradient, plotted at intervals $\omega t = 15°$ over one cycle ($\omega = 2\pi f$ is the angular velocity in radians per second, where f = frequency in cycles/sec; t = time). The curves were obtained by summing together the first four harmonics of the flow curves together with a parabolic velocity distribution representing the steady forward flow. The reversal of flow begins at the wall ($\omega t = 120°$ of the cycle), and flow in the center is still moving forward. As a result, the maximum reverse flow occurs at r/R between 0.3 and 0.4. (From W.W. Nichols and M.F. O'Rourke: McDonald's Blood Flow in Arteries, 3rd edition. Philadelphia, Lea & Febiger, 1990. Used with permission.)

only to endothelium[23,25] and the media[26] but also the corpuscles.[27,28] Such injury in turn could lead to the aggregation and adhesion of the cells to the injured vessel wall. Indeed, atheromatous plaques and platelet thrombi have been observed at bifurcations and stenoses.[29–31] The question here is whether disturbed patterns of flow lead to increased, localized interactions with the vessel wall. Answers to this question have been obtained from microrheological studies in our laboratory of the flow behavior of blood cells in idealized models of stenoses[32,33] and T junctions,[34,35] as well as in fixed transparent segments of natural arteries and veins.[12,36–41]

The term disturbed flow is used to distinguish the flow regimes encountered at stenoses, branches, and curved segments of vessels from laminar and turbulent flow. Laminar flow, as we saw in the example of Poiseuille flow (Fig. 3.1), is characterized by the steady, streamline motion of the fluid in layers parallel to the wall. With turbulent flow, which occurs beyond a critical value of the Reynolds number, the fluid elements exhibit irregular or random motion with respect to time and space.

In branching and nonuniform-diameter vessels in the circulation there exists an additional flow regime that is not observed in uniform-diameter straight tubes. Here there are secondary fluid motions in directions away from that of the primary flow, and often there is separation of the streamlines from the vessel wall, with the formation of a vortex or a recirculation zone between the forward flowing mainstream and the wall. To describe this flow regime, which is neither laminar nor turbulent, we have come to use the term disturbed flow.

Models of Disturbed Flow in the Circulation: Sudden Changes in Fluid Velocity

Fluid Mechanical Considerations

When blood is subjected to a change in mean velocity that is sudden and of sufficient magnitude, flow separation occurs and an eddy is formed. The way in which such flows are generated can be illustrated using the concept of the boundary layer.

In fluid mechanics, an ideal fluid is defined as one that has no internal friction or viscosity ($\eta = 0$). As a consequence it is able to flow past a solid surface and maintain a slip velocity at the interface. A real fluid has, to a greater or lesser degree (as in plasma), internal friction; and a true slip velocity is impossible. If the fluid has a low viscosity and is subjected to flow at a high velocity, i.e., the Reynolds number (Eq. 10) is large, one can picture the flow of a real fluid past a solid body as being composed of two zones. The first zone is confined to a thin layer near the solid boundary where, under the influence of viscosity, frictional forces retard the fluid motion. The velocity increases from zero at the interface to the full value in the mainstream. The

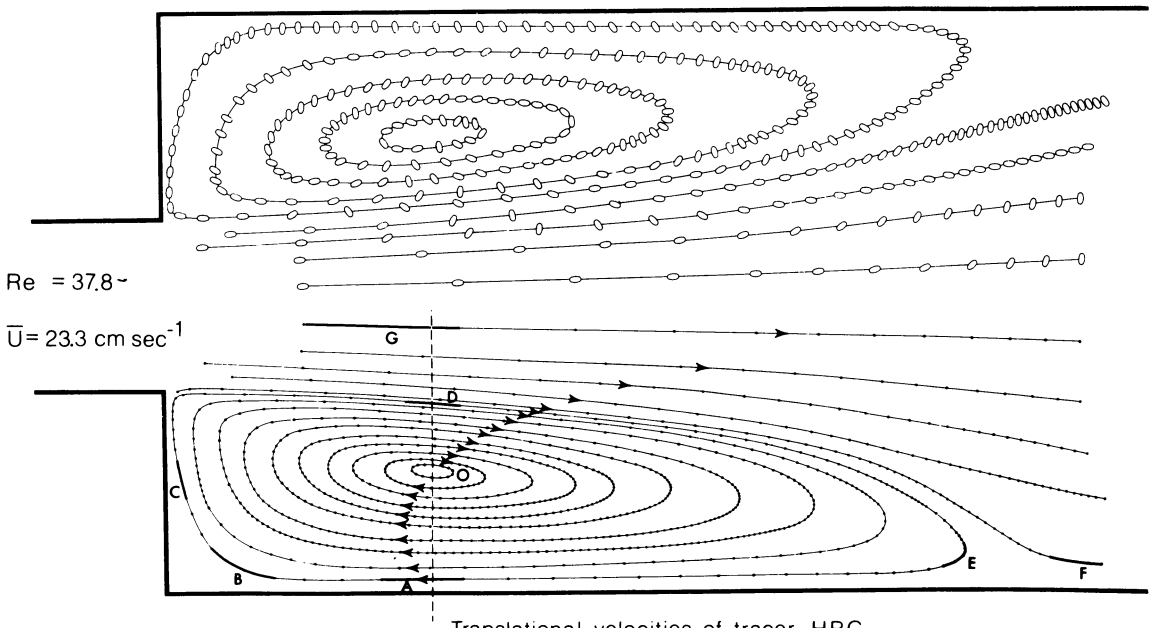


Figure 3.6. Flow separation as a liquid enters a sudden concentric expansion of vessel lumen from 150 μm to 50 μm where it is rapidly decelerated, leading to a positive adverse gradient in pressure in the direction of flow. Liquid near the wall, unable to overcome the pressure gradient, is forced to a standstill and flows backward, which leads to formation of a vortex. The mainstream is pushed away from the wall and is separated from the vortex beginning at the entrance of the expansion to the reattachment point (arrows). The region of flow separation is an annular vortex whose size increases with increasing inflow Reynolds number (Re) and the degree of expansion of the lumen. The streamlines and orientations of hardened red blood cells in the orbits of the annular vortex are shown in the lower and upper halves, respectively. As shown by the values of the translational velocities of the tracer cells, they are highly variable in the region of flow separation. (Reprinted with permission of Karino and Goldsmith [33])

mainstream is the second zone, and is regarded as an ideal frictionless fluid in which there is no velocity gradient. The first zone is known as the boundary layer, and its thickness can be calculated to be inversely proportional to the square root of a Reynolds number (Re_y) defined by $Re_y = \bar{U}y\rho/\eta$, where y is a characteristic distance perpendicular from the edge of the solid body. This approach is applicable strictly to gases and liquids of low kinematic viscosity (defined as the viscosity divided by the fluid density) flowing past streamlined bodies (e.g., and airplane wing). The analysis should not be extended to liquids subjected to laminar flow in tubes at high Reynolds numbers. The concept of the boundary layer for explaining flow separation, however, is a useful one, as the following qualitative considerations show.

Consider the sudden tubular expansion shown in Figure 3.6. A liquid flows through the tube at a constant driving pressure in the axial, Z direction; it suddenly decelerates as it enters the expansion owing to the sudden increase in cross-sectional area. Assuming the mainstream to be an ideal fluid, one can apply Bernoulli's equation relating pressure (P) to linear velocity (U) of an ideal fluid:

$$P + \rho gh + \tfrac{1}{2}\rho U^2 = \text{constant} \tag{14}$$

h being the height the liquid has traveled from a reference level. If the tube is horizontal (h is constant), differentiation of Eq. 14 with respect to flow distance Z yields:

$$\frac{dP}{dz} + \rho U \frac{dU}{dz} = 0 \tag{15}$$

This equation shows that during deceleration on entry into the expansion the gradient of flow has decreased ($dU/dz < 0$); hence the pressure gradient (dP/dz) must increase to satisfy the equation; that is, there is a positive, adverse pressure gradient attempting to drive the fluid in the reverse direction. In the "frictionless layer" (mainstream), the kinetic energy of the fluid is sufficient to overcome this pressure gradient. However, the fluid within the boundary layer, which comes under the influence of the same pressure field, consumes its much smaller kinetic energy before having moved very far. It is eventually forced to a standstill and caused to flow backward by the external pressure. Fresh fluid arrives and experiences the same retardation, and the decelerated portion of the stream rapidly increases in volume, pushing the mainstream away from the boundary: Flow separation has occurred. The fluid in the reverse flow regions coils, and a vortex is formed (Fig. 3.6). It is evident from Eq. 15 that the decrease in U as well as the rate of deceleration ($-dU/dz$) influences the size of the effect.

Model System: Blood Cells in an Annular Vortex

We undertook an extensive study of the flow behavior of human blood cells in the annular vortex formed distal to a sudden tubular expansion of a 150

μm diameter glass tube into a 500 μm diameter glass tube.[33] Such a flow geometry, illustrated in Figure 3.6 and described above, served as a model of an arterial stenosis.

Red Blood Cells

As predicted by fluid mechanical theory,[42] when dilute suspensions of erythrocytes were subjected to steady flow through the model stenosis a captive annular ring vortex was formed downstream of the expansion. Figure 3.6 shows paths and orientations of the erythrocytes in the median plane of the tube. During a single orbit, the measured particle paths and velocities, as well as the locations of the vortex center and reattachment point, were in good agreement with those predicted by the theory applicable to the fluid. Over longer periods, however, single cells and small aggregates (<20 μm in diameter) migrated outward across the closed streamlines of the vortex predicted by the theory and left the vortex after describing a series of spiral orbits of continually increasing diameter until they rejoined the mainstream. In contrast, aggregates of cells more than 30 μm in diameter remained trapped within the vortex, assuming equilibrium orbits or staying at the center. With pulsatile flow (a sinusoidal oscillatory flow superimposed in parallel with the steady flow), the observed phenomena were qualitatively similar to those described with steady flow. The vortex varied periodically in size and intensity; the axial location of the vortex center and reattachment point oscillated in phase with the upstream fluid velocity between maximum and minimum positions about a mean that corresponded to that measured in the absence of the component of oscillatory flow. At higher hematocrits (15–45%), migration of single cells persisted and resulted in lowering the hematocrit in the vortex region during both steady and pulsatile flow.[33]

The mechanism underlying the particle migration phenomenon is not a simple one; it is likely that it is partly due to the dilution effect of the cell-poor plasma taken into the vortex from the fluid layer adjacent to the vessel wall proximal to the expansion. The mechanism for trapping large aggregates in the vortex was qualitatively explained by using existing fluid mechanical theories[43] concerned with lateral particle migration near a tube wall and by the operation of a mechanical wall effect.[44]

Platelet Aggregation in the Vortex

The flow behavior and interactions of human platelets in the annular vortex were studied at 37°C using heparinized or citrated platelet-rich plasma (PRP) as well as washed platelets in Tyrode's–albumin solutions. It was demonstrated that the vortex provided favorable conditions for the spontaneous aggregation of normal human platelets through shear-induced collisions of particles while circulating in its orbits.[45] In a given suspension, the formation and growth of platelet aggregates could only be observed in a narrow range of Reynolds numbers (based on upstream linear velocity and tube diameter),

which varied from suspension to suspension. Thus in heparinized PRP, containing many sphered platelets with pseudopods and some microaggregates of two to six cells, the rate and extent of aggregation were the highest, with large elongated floating aggregates (>100 μm in length) being observed to form in less than 1 minute and within the widest range of Re_t, based on upstream velocity and diameter (between 4.5 and 17.0). In citrated PRP and washed platelet suspensions, in which no microaggregates were seen prior to flow, the degree of aggregation was much reduced. However, when platelets in these suspensions were activated with subthreshold concentrations of ADP or thrombin, the large aggregates seen in heparinized PRP were again formed. When the above suspensions were subjected to pulsatile flow in the expansion tube, there was a marked decrease in the number and size of the aggregates. Presumably, it was due to the continuously changing orbits of particles during the alternate expansion and contraction of the vortex, which shortened their residence times, and to the large variation in the shear rate in each cycle, beyond the range favorable for platelet aggregation.

The above results suggest that formation of platelet aggregates in vortices is more likely to occur in the venous circulation, where the flow is steadier and the Reynolds number lower, than in the arterial circulation.

Wall Adhesion of Platelets in the Vortex

The effects of disturbed flow on initial platelet adhesion to the vessel wall were studied using a large-scale expansion flow tube (0.92 mm diameter into 3.00 mm diameter) whose inner wall was coated with collagen fibers and suspensions of washed human platelets containing washed erythrocytes at hematocrits of 0% to 50%.[46] As illustrated in Figure 3.7, platelet adhesion was localized within the vortex and downstream on either side of the reattachment point with a local minimum at the reattachment point itself. Furthermore, platelet adhesion increased and both adhesion peaks became more pronounced as the hematocrit increased. Surprisingly though, the adhesion peak in the vortex decreased and flattened out as the Reynolds number increased. These results are inconsistent with diffusion-controlled platelet adhesion (when the rate-determining step for adhesion is the rate at which cells are brought to the vessel surface), which should show an increase in adhesion number density with increasing shear rate.[47,48] It appears that the particular flow pattern within the vortex is responsible for this localization. Thus, as illustrated in Figure 3.7A, only those cells carried by the curved streamlines to within one particle radius of the surface interact with the vessel wall and adhere to it on both sides of the reattachment point, which is also a stagnation point.[46,49] It then follows that platelet adhesion onto the vessel wall, whether it is the natural endothelium or an artificial surface, is localized wherever there is a stagnation point (or a reattachment point if it is a result of flow separation) where blood cells are carried by the flow toward the vessel wall along curved streamlines that have a pronounced radial veloc-

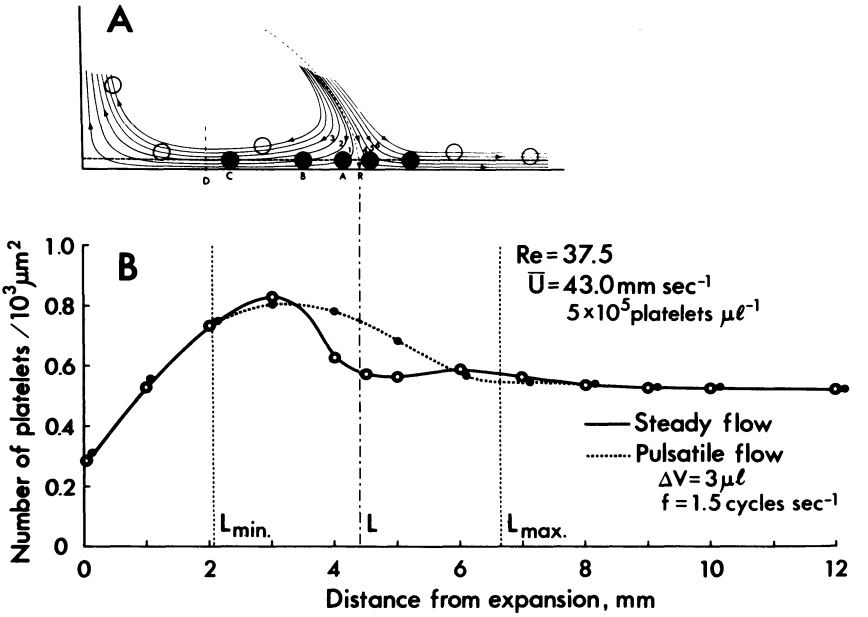


Figure 3.7. (**A**) Fluid streamlines near the tube wall downstream of the tubular expansion, showing the convective transport of particles in bulk flow to the vessel wall along the radially directed curved streamlines on either side of the reattachment point (R). The black circles represent the particles that are carried by the flow along the streamlines 1 to 6 within the critical distance for collision with the walls at points A to C in the vortex and the corresponding points downstream. Open circles represent particles that do not come close enough to collide with the wall. (**B**) Plot of the measured number density of adhering platelets obtained from an experiment carried out with a suspension of washed human platelets in Tyrodes–albumin solution containing no red blood cells. The figure shows the relation between the flow pattern and the degree of platelet adhesion in, and downstream from, the vortex during steady flow. (Reprinted with permission of Karino and Goldsmith.[46])

ity component. If this mechanism operates in the circulation, a relatively higher rate of platelet adhesion, and hence a higher risk of thrombus formation, is predictable not only in regions of disturbed flow (adhesion peaks on either side of the reattachment point), such as downstream of aortic or venous valves, mural thrombi, and stenoses, but also in all the branching arteries at the flow divider where there is a stagnation point.

In Vivo Example of Sudden Expansion of Flow: Venous Valve

As an extension of the above described studies to natural blood vessels, one of us (T.K.) developed a novel method for observing flow patterns in transparent arterial and venous segments from dogs and arterial segments

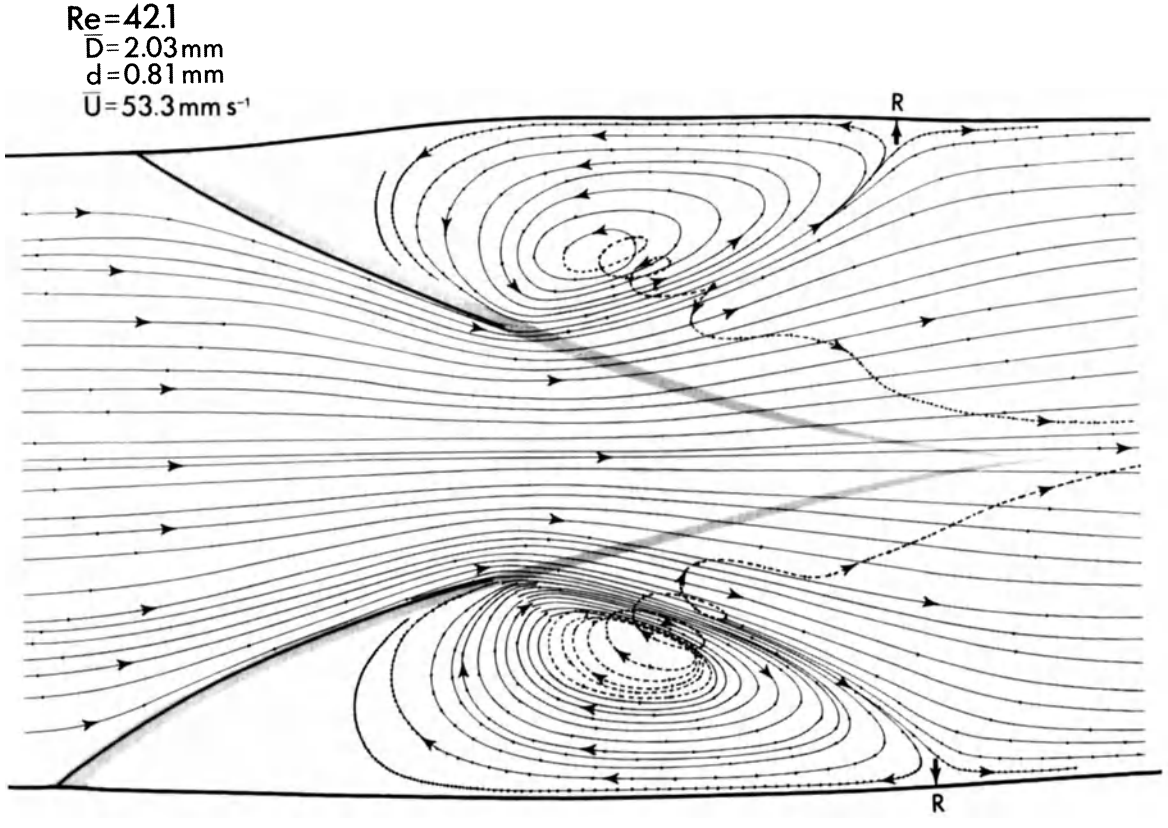


Figure 3.8. Detailed flow patterns in the common bisector plane of the valve leaflets in a 2 mm diameter dog saphenous vein containing a bileaflet valve and showing the formation of a spiral vortex in each valve pocket. In fact, they are a pair of vortices located symmetrically on both sides of the bisector plane. The solid lines are the paths of particles located in or close to, and the dashed lines are those located far away from, the bisector plane (the projection of the particle paths on the bisector plane). The arrows at R indicate the location of the reattachment point. (Reprinted from *Biorheology* 20, Karino T., Motomiya, M. Flow visualization in isolated transparent natural blood vessels, 119–127, (1983) with permission from Pergamon Press Ltd, Headington Hill Hall, Oxford OX3 OBW, UK.)

from humans postmortem.[36] The results obtained in an isolated transparent dog saphenous vein containing a bileaflet valve[37] is shown in Figure 3.8, which gives the detailed flow patterns as observed along the common median plane of the vein and valve. There is an expansion flow with flow separation occurring at the edge of the valve leaflet, which under physiological flow conditions resulted in the formation of large paired vortices located symmetrically on both sides of the bisector plane of the valve leaflets in each valve pocket. Particles continually entered the valve pockets from the mainstream, spending long periods describing a series of spiral orbits of decreasing diameter, while moving away from the bisector plane; they eventually left the vortex. With concentrated suspensions of hardened RBCs, it was found that another smaller counterrotating secondary vortex, driven by the large primary vortex, existed deep in each valve pocket (blank area of Fig. 3.8) where venous thrombi are believed to originate.[50,51] Furthermore, experiments carried out with hardened erythrocyte suspensions at 25% hematocrit showed that the erythrocyte concentration in this secondary vortex remained appreciably lower than that in the primary vortex. In such stagnant regions, fluid circulated with extremely low velocities, creating a very low shear field, which allowed erythrocytes to form aggregates. The results suggest that in some pathological states the valve-pocket vortices could act as automatic traps and generators of thrombi in a fashion similar to that demonstrated in the annular vortex formed downstream from a sudden tubular expansion.[33,45]

Models of Disturbed Flow in the Circulation: Sudden Change in Direction of Flow

Fluid Mechanical Considerations

When there is a change in the direction of flow, as at a bend or bifurcation (the latter illustrated in Figure 3.9), a fluid experiences a transverse pressure gradient across the tube forcing it to change direction. The elements of fluid with the highest kinetic energy continue to move to the outside of the bend, whereas fluid with low kinetic energy moves to the inside under the action of the pressure gradient. This action gives rise to a secondary cross flow. If the fluid enters the bend with a parabolic velocity distribution, the elements having high kinetic energy are situated in the tube center surrounded by elements with low kinetic energy at the periphery. In the bend, a secondary flow consisting of two semicircles is set up. In the case of a bifurcation (Fig. 3.9), low velocity fluid at the top and bottom of the parent tube moves across the upper and lower regions of the daughter tube to form a double helical flow near the outside wall. The high velocity fluid in the center of the parent tube moves on without being appreciably diverted. Fluid coming from the side wall of the parent tube may separate at the corner of the bifurcation, and

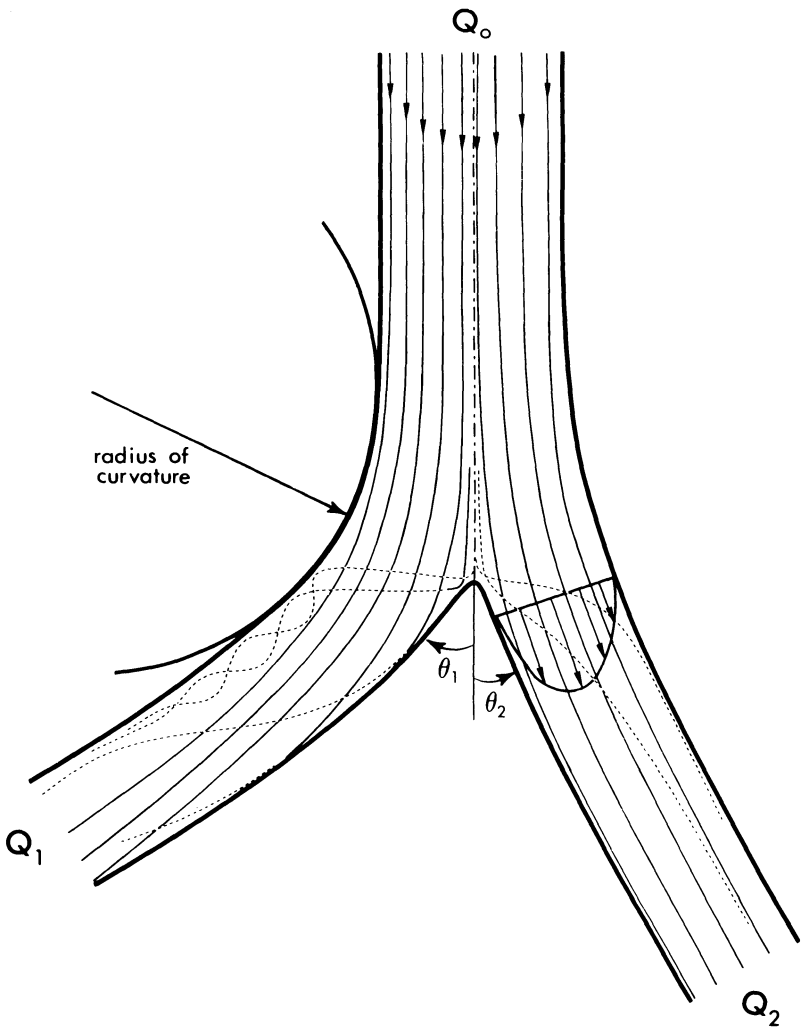


Figure 3.9. Flow through a bifurcation showing the streamlines of the mainstream in the median plane (solid lines), which move toward the inner wall of the daughter tubes, causing a secondary flow of low velocity fluid (dashed lines). The latter moves across the upper and lower regions of the entry into the daughter tube to form a double helical flow near the outside wall. The large radius of curvature of the outer walls of the bifurcation are typical of those found in the arterial circulation. The extent of secondary flow increases with increasing inflow Reynolds number, bifurcation angle, and the ratio of total cross-sectional area of daughter tubes to that of the parent tube. The velocity profile in the median plane of one of the daughter tubes is also shown. (Reprinted with permission of Goldsmith and Turitto.[52])

the streamlines from the top and bottom fill in the separated region. Figure 3.9 also shows that the velocity profile in the diametrical plane of the daughter tube is skewed toward the flow divider, which occurs because relatively high velocity fluid at the center of the parent vessel is brought into close proximity of the wall of the flow divider.

The value of the Reynolds number in the parent tube at which secondary flow patterns and flow separation are first seen depends on the geometry of the bifurcation: the bifurcation angle θ, the area ratio defined as the sum of the cross-sectional area of the daughter branches to the cross-sectional area of the parent branch, and the radii of curvature of the outer walls (Fig. 3.9).

In arterial bifurcations, θ varies from 30 degrees to 120 degrees, but the radii of curvature are large (i.e., the bends are gentle, as shown in Fig. 3.9), and this condition together with area ratios that are generally less than 1.25 (i.e., there is not a marked decrease in blood velocity) minimizes the secondary flow.

Model System: Flow Patterns at T Bifurcations

We also undertook an investigation of the flow patterns and distributions of fluid velocity and shear rate in glass models of T junctions with branching angles from 30 to 150 degrees and side-to-main-tube diameter ratios from 0.33 to 1.00, over a wide range of inflow Reynolds numbers (Re_0) and branch-to-parent-tube flow ratios (Q_1/Q_0).[34,35] Figure 3.10 shows the flow pattern obtained by photographing and analyzing the motions of 50 μm diameter latex spheres in the common median plane of a 90-degree uniform-diameter T junction when the main branch was partially occluded so that 80% of the flow left through the side branch (unlikely to occur in vivo). A large recirculation zone formed in the main tube (owing to sudden deceleration of fluid velocity as a portion of the flow is drawn off into the side tube); a small, secondary recirculation zone was formed in the side tube (owing to the sudden change in direction of the fluid, which continues to move to the outside of the 90 degree corner, toward the flow divider). Particles entering the large recirculation zone described complicated orbits; some of them rejoined the flow through the main tube, and others entered the side branch in a paired, spiral secondary flow with pronounced radial components. Some of the latter circulated through the secondary recirculation zone. When the degree of occlusion of the main tube was gradually reduced, the large recirculation zone became smaller and eventually disappeared as the flow rate ratio was reversed ($Q_1/Q_0 = 0.8$), whereas that in the side branch grew in size.

By varying the branching angle it was shown that the critical Re_0 for the formation of the main recirculation zone was lowest at 90 degrees for all Q_1/Q_0, whereas for the side recirculation zone it decreased as the branching angle increased from 45 degrees to 135 degrees. When the diameter of the side tube was decreased, the main recirculation zone, which consisted of a

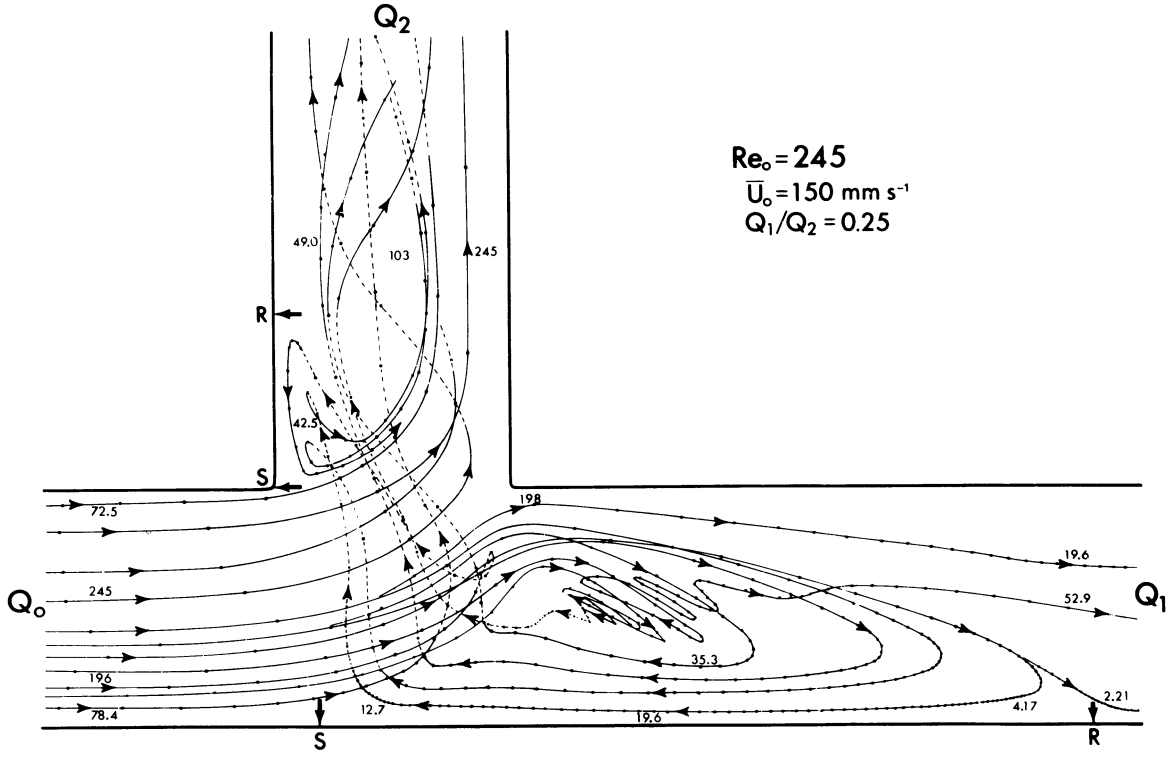


Figure 3.10. Flow patterns in the common median plane of a model 3 mm diameter glass T junction, as indicated by the paths of tracer 50 μm polystyrene spheres in aqueous glycerol. The suspension enters at the left with a mean velocity $\overline{U}_0$ (tube Reynolds number = Re_0), and 80% of the flow leaves through the side tube. The T junction, made by fitting and glueing together two pieces of glass tubing, has a low radius of curvature at the corner opposite the flow divider as well as at the flow divider, which results in a small vortex at the corner at the entry of the side tube filled with fluid from the main large vortex in the parent vessel. The points are experimental, showing particle positions at intervals of 22 ms; the numbers indicate velocities in millimeters per second. The solid lines represent particles traveling in or close to the median plane; the dashed lines represent particles closer to the tube wall. The arrows at S and R indicate the respective points where flow first separates and then reattaches to the wall. (Reprinted from *Biorheology*, 16, Karino, T., Kwong, H.H.M., Goldsmith, H.L. Particle flow behavior in models of branching vessels: I. Vortices in 90° T-junctions. 231–247, (1979) with permission from Pergamon Press Ltd, Headington Hill Hall, Oxford OX3 OBW, UK.)

pair of spiral secondary flows located symmetrically on both sides of the common median plane of the T junction, became smaller and thinner and was confined to a thin layer adjacent to the tube wall, wrapped around the mainstream.[35]

The effect of radius of curvature of the walls at the junction was studied by comparing the critical inflow Reynolds numbers (Re_0) for the formation of recirculation zones and their sizes in the square T junction (Fig. 3.10) (radii of curvature $<2\%$ of tube radius) with that in a rounded T junction (radii of curvature $\sim$ tube radius).[34] It was found that the recirculation zone in the side tube formed at a much lower Re_0 in the square junction than in the rounded junction, and that at a given Re_0 and Q_1/Q_0 a larger main recirculation zone existed in the rounded junction. It appears that the formation of the side recirculation zone is largely affected by curvature of the wall at the bend opposite to the flow divider, whereas that of the main recirculation zone is largely affected by the curvature at the flow divider.

In Vivo Example of T Bifurcations: Aortic T Junctions

As an example of a natural arterial T junction, we investigated the flow patterns in transparent segments of a dog abdominal aorta containing branches of the celiac, superior mesenteric, and right and left renal arteries.[38,39] The flow patterns illustrated in Figure 3.11 for the aortoceliac junction resemble those observed in the model T junctions, but the degree of flow disturbance, even at an inflow Reynolds number as high as 609 is much less. At the geometrical flow ratio (Q_1/Q_2 = area ratio, aorta/celiac artery) flow separation occurred at $Re_0 \sim 300$, well below the mean physiological $Re_0 \sim 700$. However, instead of a large main standing recirculation zone as in the glass models, under physiological flow conditions there was only a pair of recirculation zones, confined to a thin layer close to the wall surrounding the mainstream. There was no side recirculation zone, no doubt due to the gentle curvature of the bend opposite the flow divider. This characteristic was shared by all the aortic T junctions studied, as was the sharp curvature of the bend at the flow divider. From the results obtained in the glass model T junctions, this situation represents the optimum condition for minimizing the size of both regions of separated flow. Nevertheless, the curved streamlines of the recirculation zone and secondary flows bring blood cells toward the vessel wall in a zone around the flow divider and in the side branch on the outer wall.

As the inflow Reynolds number was increased, the recirculation zones increased in length; and then at $Re_0 \sim 1200$ there was a sudden transition from disturbed to turbulent flow. Typical flow patterns observed at an early stage of turbulent flow at the same celiac and cranial mesenteric (superior mesenteric) artery junctions as those shown in Figure 3.11 are illustrated in Figure 3.12. It is evident that the recirculation zones of Figure 3.11 have completely disappeared, and the tracer particles exhibited random motion

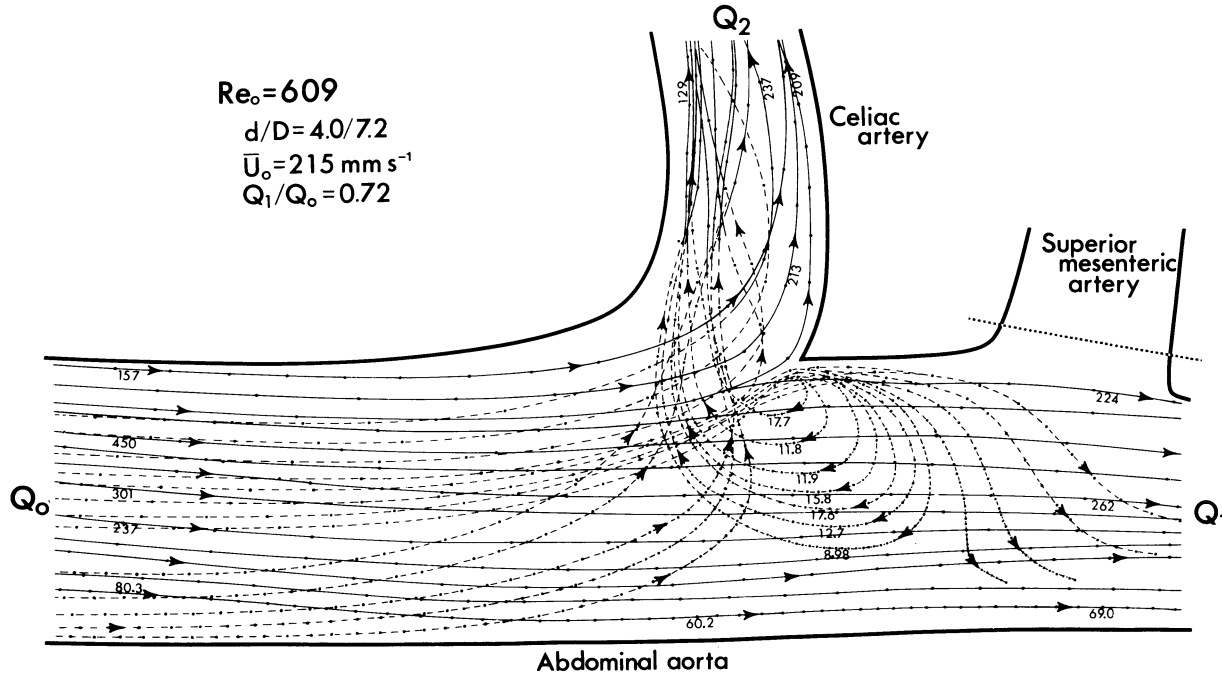


Figure 3.11. Flow patterns at the aortoceliac artery junction of an isolated transparent dog abdominal aorta obtained from the analysis of cine films of the paths of 200- to 250- μm polystyrene spheres suspended in oil. Unlike the model T junction of Figure 3.10, curvature of the wall opposite the flow divider is high, and that at the flow divider is low. This arrangement minimizes the flow disturbance and results in the formation of paired thin-layered recirculation zones on both sides of the common median plane, adjacent to the vessel wall and wrapped around the undisturbed mainstream. Numbers on the streamlines indicate polystyrene sphere velocities in millimeters per second. (Reprinted with permission of Karino et al.[38])

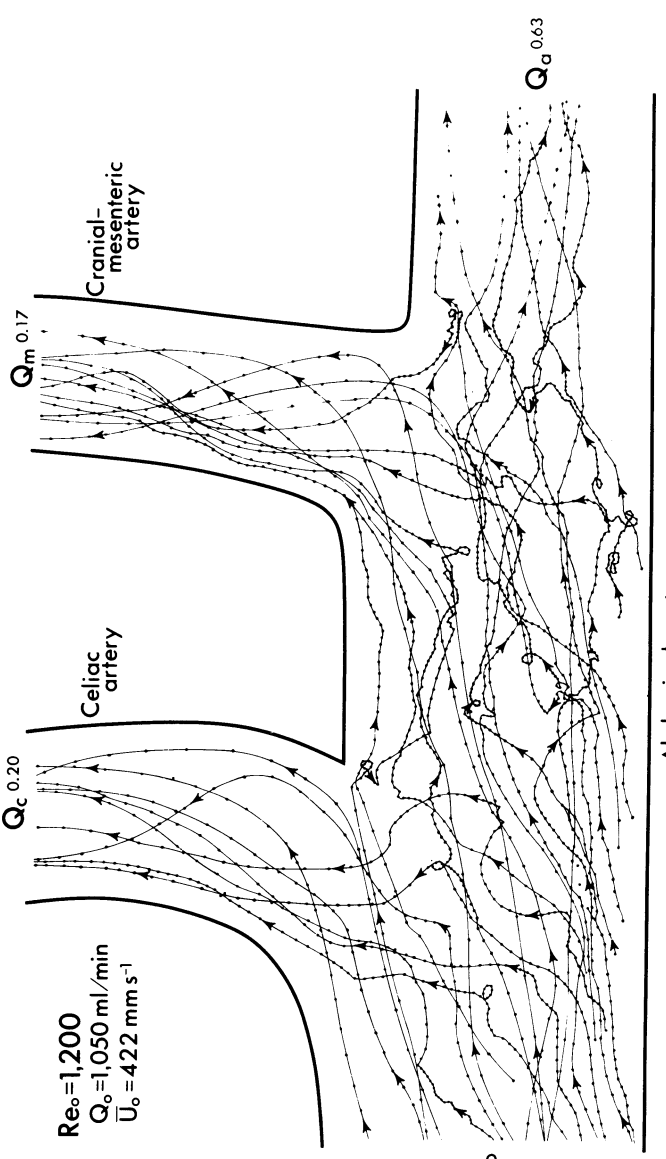


Figure 3.12. Particle flow behavior at the onset of turbulent flow. Note the random-like paths of tracer polystyrene spheres located near the artery walls (the same segment of the dog abdominal aorta as in Figure 3.11). Also note that the recirculation zones shown in Figure 3.11 have completely disappeared. (Reprinted with permission of Karino et al.[38])

and sometimes described small circles near the vessel wall. Flow in the side branches, however, remained nonturbulent.

Human Carotid Bifurcation: A Unique Y Bifurcation

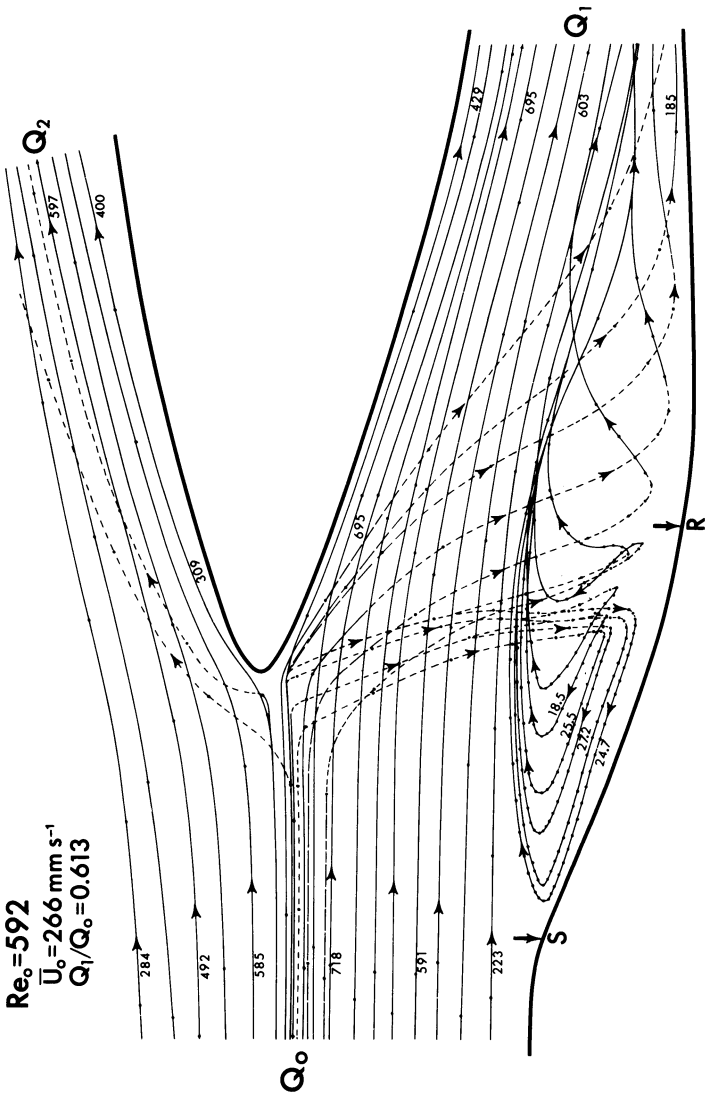
The human carotid bifurcation, unlike other Y bifurcations, exhibits a marked flow disturbance associated with a large recirculation zone located in the carotid sinus. The flow patterns were studied in detail using a transparent arterial segment prepared from a human subject postmortem.[12] It was found that a standing recirculation zone consisting of a pair of complex spiral secondary flows, located symmetrically on both sides of the common median plane of the bifurcation, formed in the carotid sinus over wide ranges of inflow Reynolds numbers (Re_0) and flow ratios (Q_1/Q_0; internal/common carotid). Figure 3.13, top part, shows the detailed flow patterns in the carotid sinus. Particles were deflected at the flow divider and traveled laterally and slowly along the wall above and below the common median plane, almost at right angles to, and encircling, the mainstream. They then changed direction, moving back along the outer wall of the internal carotid artery at the site of the sinus, describing spiral orbits in the recirculation zone before rejoining the mainstream. Downstream from the stagnation point (R), a strong counterrotating double helicoidal flow developed. The formation and the size of the recirculation zone were largely dependent on Q_1/Q_0 as well as on Re_0. The size of the recirculation zone increased from about 4 mm at $Re_0 = 300$ to a maximum of about 9 mm at $Re_0 > 800$.

Measurements of the velocity profiles (Fig. 3.13, bottom) showed that the profiles were strongly skewed toward the inner walls of the bifurcation, creating a high shear field along the vessel wall downstream from the flow divider. Owing to the presence of the paired standing recirculation zones in the carotid sinus, the wall shear rate, and hence the wall shear stress, changes sign and becomes negative at the separation point (S); it becomes positive again downstream from the stagnation point, indicated by R. Thus in the carotid sinus there is a region where the vessel wall is stretched in opposite directions by the counter-directed wall shear stresses.

The results suggest that under physiological conditions (mean $Re_0 \sim 600$; $Q_1/Q_0 \sim 0.7$[53,54]), a standing recirculation zone exists in the carotid sinus. It affects local mass transfer and interactions of blood cells with the vessel wall, which may lead to thrombosis and atherosclerosis in this region.

In Vivo Example of Curved Vessel: Aortic Arch

The aortic arch and descending aorta provide an example of markedly disturbed flow not only because of the curvature of the aorta itself but also because of flow at high mean Reynolds numbers (>1000) and the existence of major branches in the arch. We studied the flow patterns using isolated


Q1
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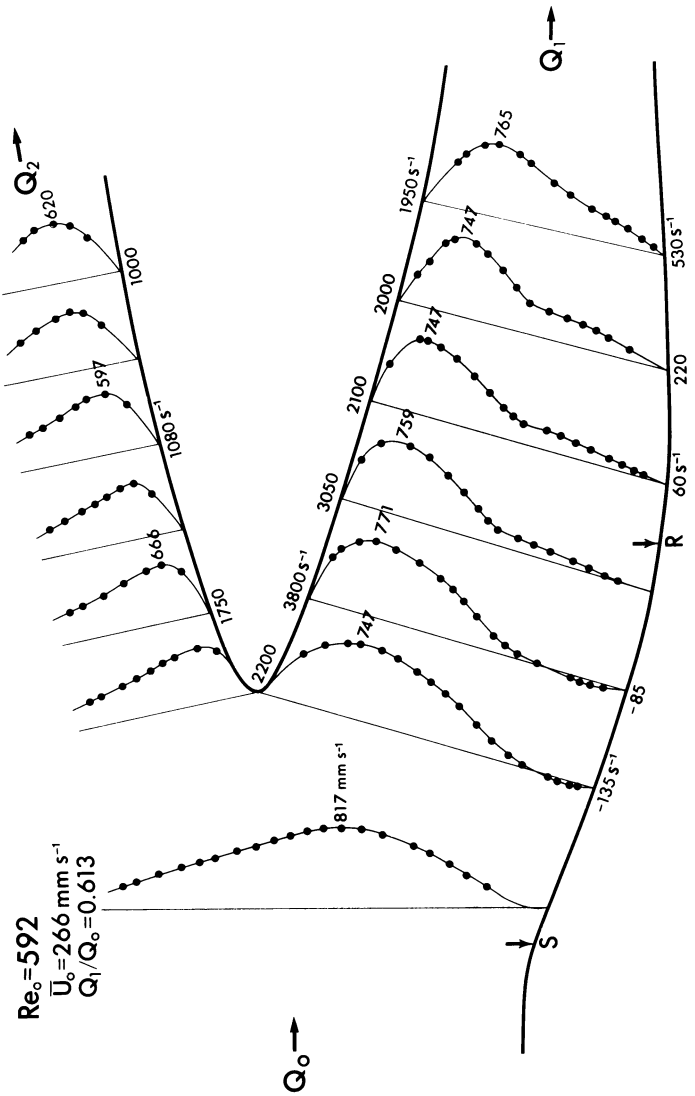

Figure 3.13. (**Top**) Detailed flow patterns in the human carotid artery bifurcation during steady flow, showing formation of a recirculation zone (paired spiral secondary flows) and a counterrotating double helicoidal flow, both located symmetrically on either side of the common median plane in the internal carotid artery. The solid lines are the paths of particles in or close to, and the dashed lines the paths that are far away from, the common median plane (the projection of the particle paths on the common median plane). The arrows at S and R denote the respective locations of the separation and stagnation points. The numbers on the streamlines (particle paths) indicate the translational velocities in millimeters per second, (**Bottom**) Distribution of fluid (tracer particle) velocity and shear rate in the common median plane of the human carotid bifurcation during steady flow. The measured maximum velocity at each cross section is given in millimeters per second. (Reprinted with permission of Motomiya and Karino.[12])

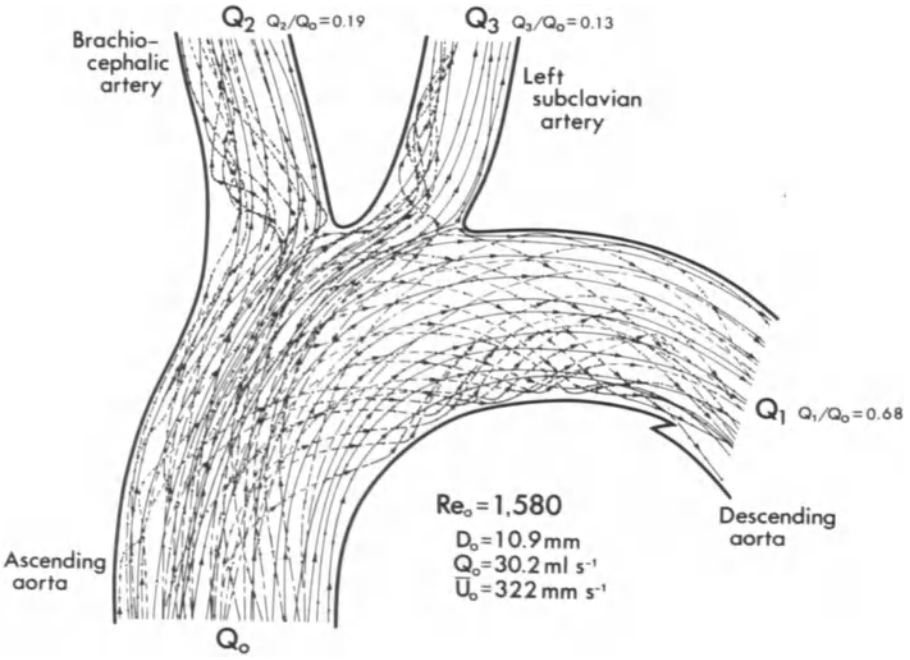

Figure 3.14. Disturbed flow as a result of curvature in a vessel segment. Shown are the detailed flow patterns in the dog aortic arch at an inflow Reynolds number (Re_0) = 1580 obtained using an isolated transparent dog arterial tree containing the whole heart, aortic arch, and descending aorta. The figure shows the fluid streamlines traced from an analysis of cine films of the paths of polystyrene particles as in Figure 3.10. It demonstrates the existence of three major flow components: a quasiparallel undisturbed flow located close to the common median plane of the ascending aorta and two daughter branches (solid lines), a single clockwise spiral helicoidal secondary flow near the ventral periphery of the aorta and branches (dashed lines), and secondary flows generated at the flow dividers of the side branches (dashed lines). (Reprinted from Fluid Control and Measurement. Sohara, Y., Karino, T. Secondary Flows in the dog aortic arch, 143–147, (1985) with persmission from Pergamon Press Ltd, Headington Hill Hall, Oxford OX3 OBW UK.)

transparent dog arterial trees containing the whole heart, aortic arch, and descending aorta.[55]

Flow studies were carried out at inflow Reynolds numbers from 500 to 2000 while varying flow rate ratios in the daughter vessels. For the aortic arch, most flow experiments were carried out with the aortic inflow distributed to the daughter vessels as follows: brachiocephalic artery 20%, left subclavian artery 15%, thoracic aorta 65%. Under these conditions formation of complex secondary flows and eddies were observed at each branching site of the aortic arch and in the aortic sinus. Figure 3.14 shows tracings of particle paths during steady flow in the aortic arch of a young dog. As shown in Figure 3.14, it was found that the flow in the aortic arch consists of three major components: quasiparallel undisturbed flow located close to the common median plane of the ascending aorta and the two daughter branches, spiral secondary flows located near the ventral periphery of the aorta and the side branches, and the mainflow to the side branches. Flow separation does occur at the inner (lower) wall of the aortic arch. However, no recirculation zone was formed downstream of the separation point. Instead, the region of separated flow was filled with the peripheral spiral secondary flows. Thus looking down the aorta, the flow in the aortic arch appeared as a single helicoidal flow revolving in a clockwise direction, rather than the two that had been anticipated. When the flow rates in the side branches were reduced from the control values, a recirculation zone was formed in each branch adjacent to the vessel wall opposite to the flow divider. Particles in the mainstream were deflected sideways at the flow divider and traveled laterally. Some entered the side branches; others traveled backward along the vessel wall, and after describing multiple spiral orbits rejoined the mainflow in the descending aorta or the side branches. In vessels having a partially opened aortic valve, it was also observed that strong eddies were formed at the entrance region of the aorta slightly downstream of the aortic sinus.

The velocity distributions in the common median plane were calculated at several locations in the aorta and the side branches. The velocity distributions in the entrance region of the aorta are blunted and skewed toward the inner (lower) wall of the arch. This situation was true for all the vessels studied. Downstream of the branching site of the subclavian artery the skewness of the distribution reversed, and the location of the maximum velocity shifted toward the outer wall of the arch.

The velocity of distribution in the diametrical plane normal to the common median plane was also calculated. The results showed that the velocity distribution was blunted also in this plane and skewed toward the dorsal side of the aorta, largely due to the fact that the axes of the side branches are located not exactly on the median plane of the aortic arch but off-center toward the dorsal wall of the aorta. In the case of older dogs, the curvatures of the bend at the apex portion of the aortic arch were much sharper than those of younger dogs, resulting in the formation of more pronounced spiral helicoidal flows in the aorta. It was also observed that behind the valve

leaflets a well defined standing vortex was formed in each aortic sinus at all the Reynolds numbers studied.

Flow Patterns and Vascular Disease

Flow Patterns in the Human Circle of Willis

Aneurysms

It is known from statistical data that most intracranial saccular aneurysms occur selectively at certain branching sites of the circle of Willis. The possible connection between blood flow patterns and the localization of these aneurysms in human intracranial cerebral arteries is presently being investigated.[56] Flow patterns and velocity distributions at the major branching sites of the circle of Willis have been studied using isolated transparent segments prepared from humans postmortem. Saccular aneurysms were found at the flow divider of three anterior communicating–anterior cerebral artery junctions having a long and relatively large diameter communicating artery, as shown in Figure 3.15. In each case the aneurysm was located around the flow divider, having a large branching angle where the fluid elements from the central core of the inflow vessel, located at the leading edge of the velocity profile, directly impinged on the vessel wall around the flow divider. Incipient aneurysms were also found at the flow divider of the middle cerebral artery bifurcation and at the branching site of the anterior choroidal artery from the internal carotid artery where flow patterns similar to those described above existed. By contrast, the approaching velocity profiles at the bifurcation of the internal carotid artery and at the basilar artery (at which sites the incidence of aneurysm formation is lower) were found to be either blunted or bipolar. In the case of the carotid bifurcation, it was due to the development of strong swirling flows in the carotid siphon. In the case of the basilar artery bifurcation, shown in Figure 3.16, it was due to insufficient entrance length for the development of a parabolic profile proximal to the bifurcation. Here the approaching velocity profile was largely dependent on the anatomical structure of the vertebral arteries. The approaching velocity profile was bipolar or blunted when the diameters of the two vertebral arteries were equal or close to each other and formed a symmetrical Y junction at the entrance of the basilar artery, whereas it was quasiparabolic when the diameters of the two vertebral arteries were different. The above findings suggested that the blunted or bipolar-shaped velocity profile observed in both bifurcations of the internal carotid artery and the basilar artery may play a protective role in aneurysm formation at these two sites.

As shown in Figure 3.16, for the case of approximately equal diameter daughter vessels the flow was considerably disturbed at the Y bifurcation, and complex secondary flows were found to exist over a wide range of Re_0 and flow ratios (Q_1/Q_2). Particles in the mainstream were deflected sideways

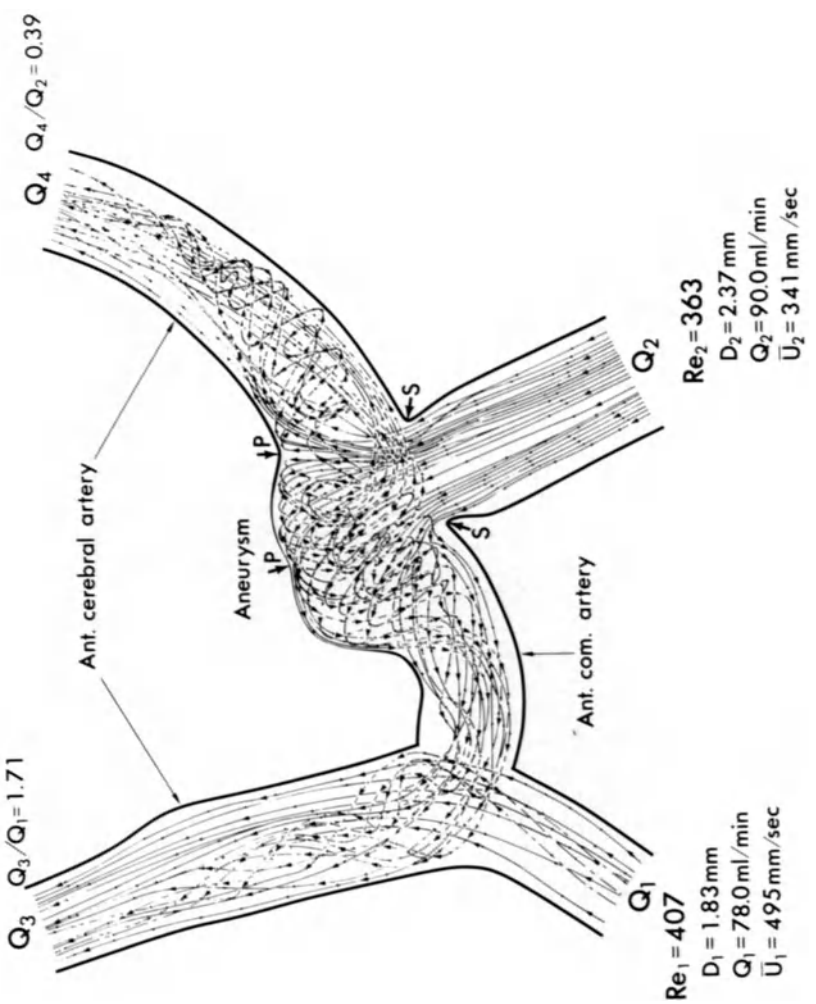

Figure 3.15. Flow patterns in an H-type anterior communicating artery junction with an aneurysm. Note the formation of spiral secondary flows in the aneurysmal sack that extend distally into both the anterior cerebral artery and the anterior communicating artery. (Reprinted with permission of Karino.[40])

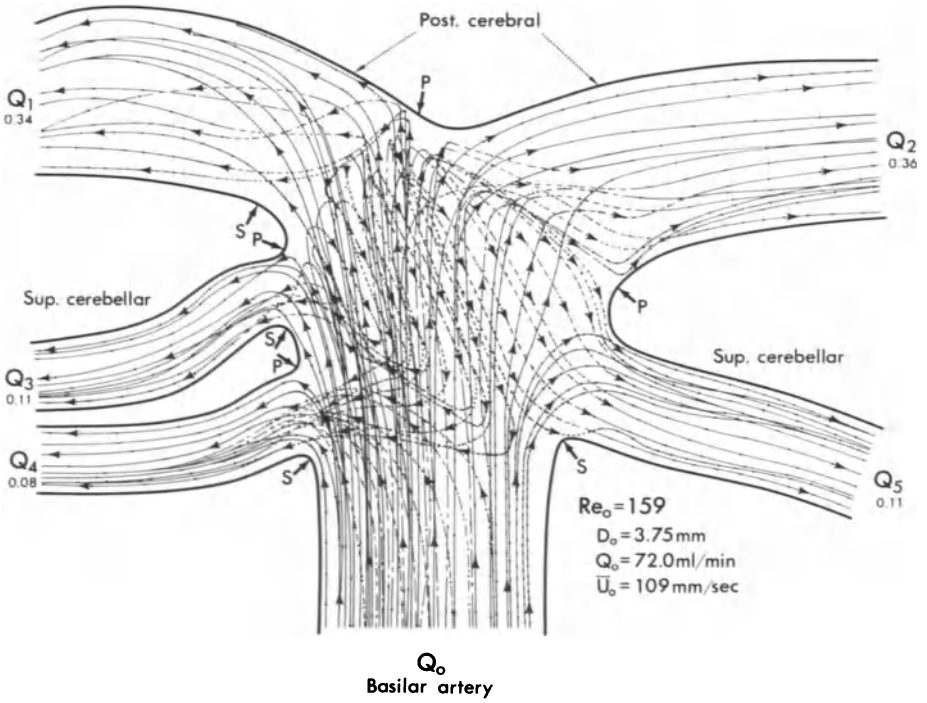

Figure 3.16. Flow patterns at the human basilar artery bifurcation showing the formation of complex secondary flows in the basilar artery proximal to the flow divider. The arrows at S and P indicate the respective locations of the separation and stagnation points. (Reprinted with permission of Karino.[40])

at the flow divider, traveled backward along the vessel wall, and entered one of the right or left superior cerebellar arteries. With increasing Re_0, the deflected particles started to describe multiple spiral orbits, creating a region of highly disturbed flow over the entire lumen of the basilar artery between the superior cerebellar arteries and the flow divider of the bifurcation.

Atherosclerotic Wall Thickening

It appears that local flow patterns are involved in the localization of atherosclerosis, as is illustrated by studies of the middle cerebral bifurcation.[40] It was found that in each of the five vessels studied atherosclerotic thickening of the vessel wall was localized around the hips of the bifurcation. When the flow patterns were studied in detail in these vessels, it was discovered that a standing recirculation zone, similar to that observed in the carotid artery bifurcation, was formed along the outer wall of one or both daughter vessels (depending on the Reynolds number in the parent vessel and the flow ratios in the two daughter vessels) at the exact locations where the atherosclerotic

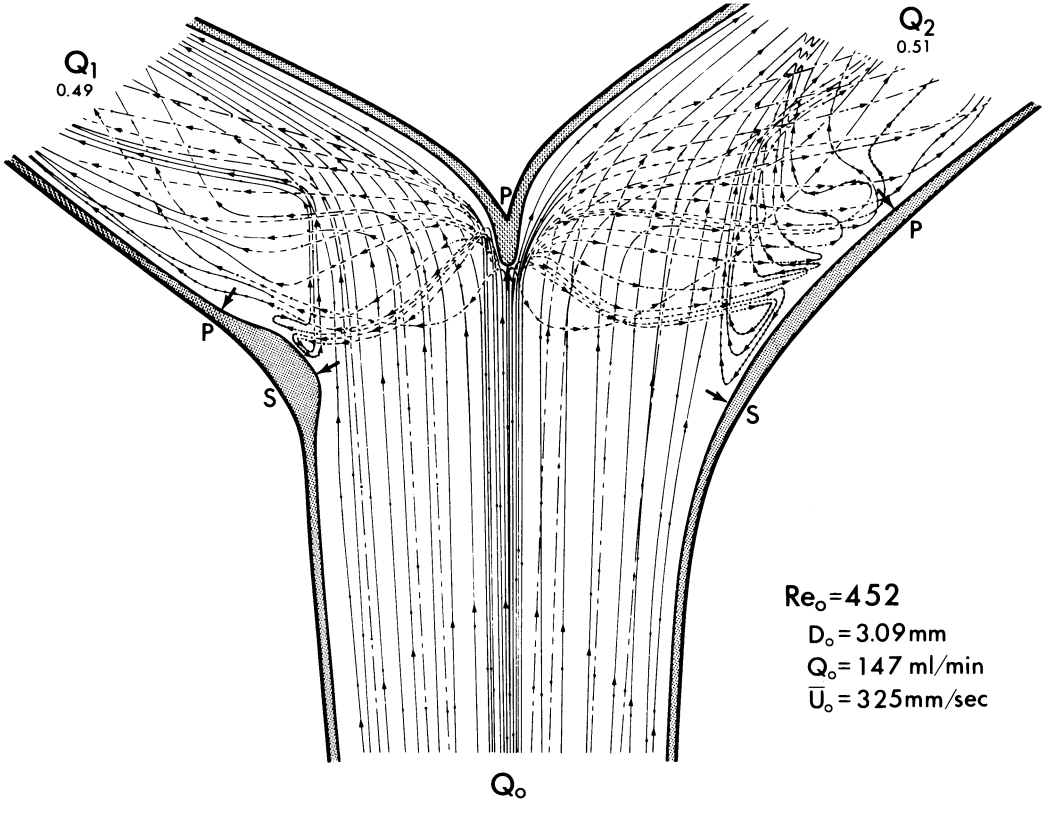

Figure 3.17. Detailed flow patterns at the middle cerebral artery bifurcation, showing the formation of secondary flows and recirculation zones along the outer walls of the bifurcation during steady flow. Note that the exact locations and the longitudinal lengths of the formed recirculation zones closely match those of the atherosclerotic wall thickening. The solid lines are the paths of particles in or close to the common median plane, and the dashed lines are the paths that are far away from the common median plane (projection of the particle paths on the common median plane). The arrows at S and P denote the respective locations of the separation and stagnation points. (Reprinted with permission of Karino.[40])

thickening of the vessel wall occurred. Furthermore, under the normal physiological range of flow rates and flow ratios tested, there was a strong correlation between the longitudinal length of the regions of disturbed flow and that of the atherosclerotic wall thickening. Figure 3.17 shows the detailed flow patterns observed in steady flow in one of the bifurcations having an almost perfectly symmetrical structure and spatial arrangement of the daughter vessels. As is evident from Figure 3.17, even when the flow in the parent vessel was distributed equally to the two daughter vessels the region of disturbed flow (formed along the outer walls of the bifurcation) was much longer in the right side branch where the region of atherosclerotic wall thickening was also longer than that in the left side branch where the wall thickening was confined to a narrow area. During pulsatile flow the complex spiral secondary flows and the recirculation zones oscillated in phase with the pulsatile flow velocity, and the locations of the stagnation and separation points situated on the outer walls of the bifurcation moved back and forth along the vessel wall. However, the general flow patterns remained the same as those observed with steady flow. This situation remained true for all five vessels studied. A similar observation was made at an arterial bend located further downstream from the middle cerebral artery bifurcation. Here, a recirculation zone was formed along the inner wall of the bend slightly downstream from the apex at the site of atherosclerotic wall thickening.

Flow Patterns and Atherosclerotic Lesions in Coronary Arteries

The exact anatomical locations of atherosclerotic lesions and flow patterns in the human left and right coronary arteries have been studied in detail using human transparent coronary arterial trees prepared postmortem.[41] It was found that atherosclerotic lesions develop exclusively at the outer wall (hips) of major bifurcations and T junctions and at the inner wall of curved segments, where flow was either slow or disturbed with the formation of slow recirculation and secondary flows and where wall shear stress was low. In no instance were atherosclerotic lesions found at the flow divider where fluid velocity and wall shear stress were high and where the formation of early atherosclerotic lesions have been observed in experimental animals fed high cholesterol diets. In the example shown in Figure 3.18, that of the trifurcation of the left main coronary artery (LMCA) prepared from a 61-year-old male subject, flow separation occurred at the outer wall (hips) of the bifurcation, creating regions of separated flow. They were then filled with spiral and recirculation flows formed as a result of the strong deflection of the flow from the LMCA at the obtuse angle flow divider. Adjacent to the regions of disturbed flow are the sites of the atherosclerotic lesions. Thus, as shown in Figure 3.18, in the left anterior descending branch (LAD) atherosclerotic lesions were found along the inner (lower lateral) wall of the gently curved segment of the proximal portion of the LAD where the measured fluid velocity and wall shear stress were relatively low. The deflection of the flow was

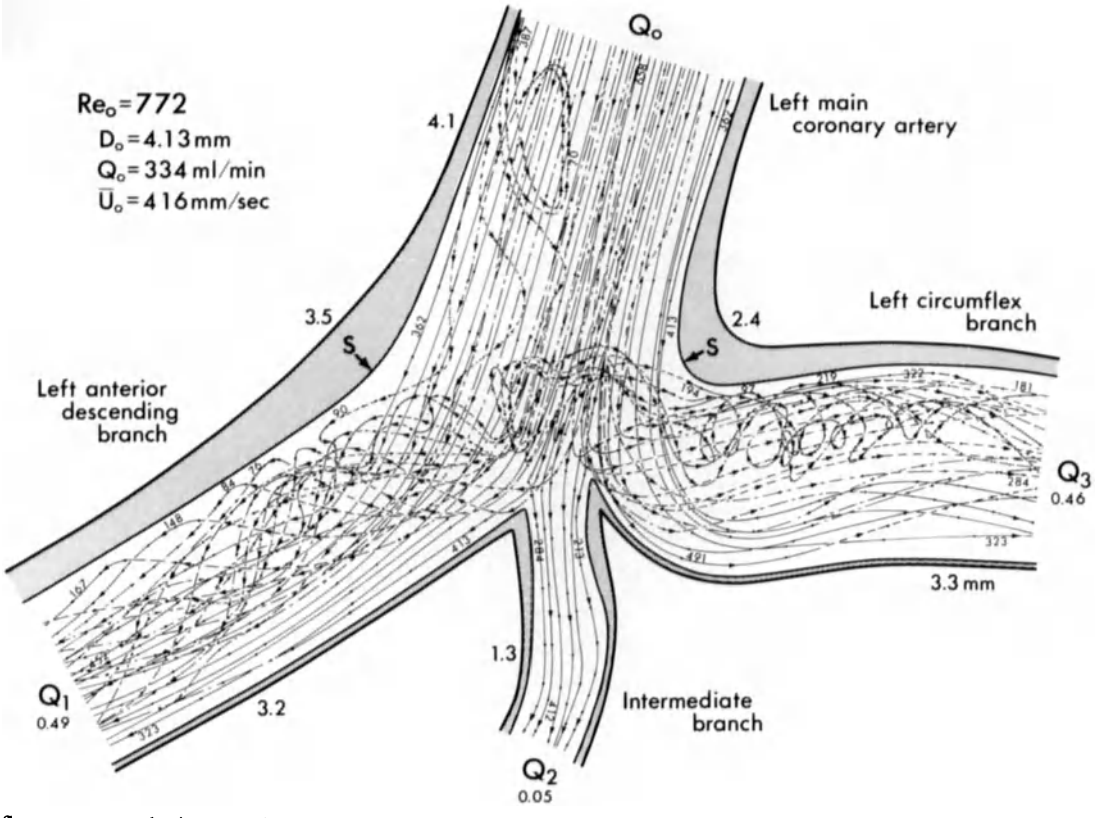

Figure 3.18. Detailed flow patterns during steady flow at the trifurcation of the left main coronary artery (LMCA) in an arterial tree prepared from a 61-year-old man observed normal to the common median plane of the LMCA and its two major branches. Note the formation of recirculation zones and complex secondary flows at the branching site of the left anterior descending branch and left circumflex branch from the LMCA. Atherosclerotic wall thickenings were found at the hips of the trifurcation adjacent to the regions of disturbed flow. (Reprinted with permission of Asakura and Karino.[41])

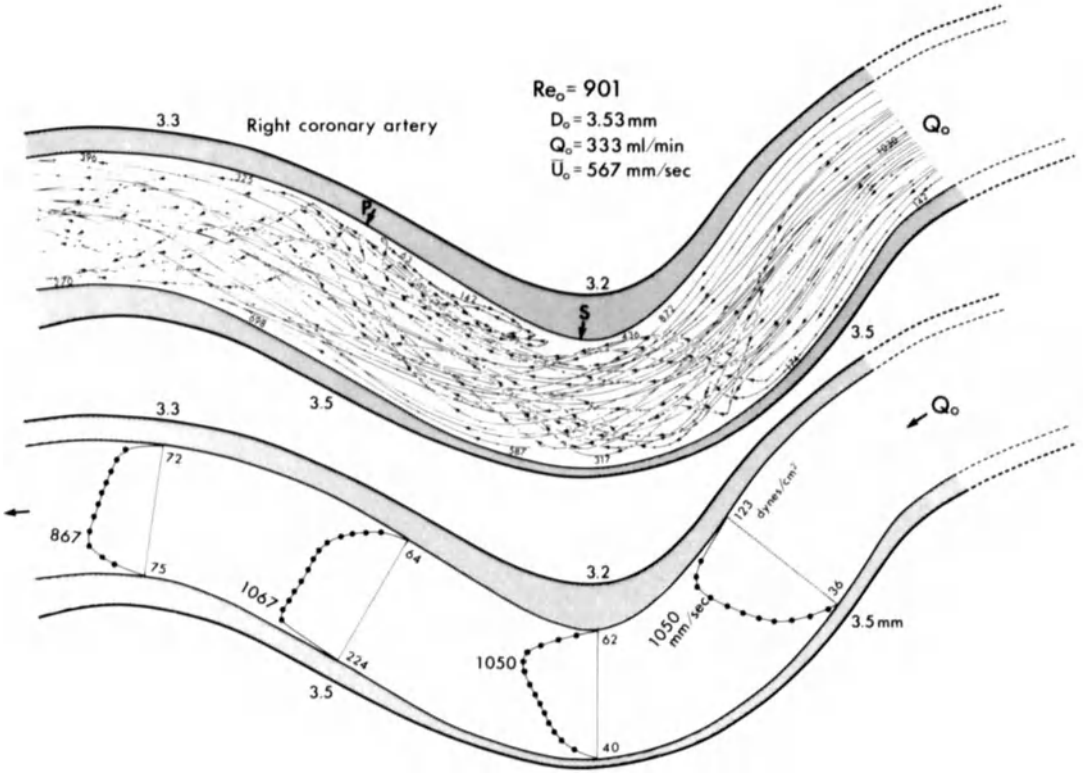

Figure 3.19. Detailed flow patterns (top) and distribution of fluid axial velocity (bottom) as observed during steady flow in the common median plane (parallel to the pericardium) of an arterial segment with multiple bends located in the middle to distal portions of the right coronary artery, prepared from the same subject as for Figure 3.18. Note the development of secondary flows and formation of a recirculation zone adjacent to the inner wall of the middle bend. The lower portion of the figure shows changes in velocity distribution along the arterial segment. The region of high shear rate moves from the inner wall, proximal to the central sharp bend, to the outer wall

much stronger in the lower half of the common median plane in both the LAD and the left circumflex branch resulting in the formation of spiral secondary and recirculation flows along the lower lateral wall of the trifurcation.

In the right coronary artery, as illustrated in Figure 3.19 (top), in an arterial segment with multiple bends most of the atherosclerotic lesions were confined to the curved segments along the inner wall where flow was either disturbed with formation of a recirculation zone or very slow. Figure 3.19 shows that flow separation occurred at the inner wall of the middle and distal bends. The regions of separated flow were filled with fluid from the peripheral thin-layered secondary flow, which traveled along the vessel wall, all the way from the outer wall of each bend. In the middle bend, a thin-layered standing recirculation zone was formed along the upper (pericardial side) inner wall, just distal to the apex of the sharp bend where atherosclerotic wall thickening was localized. Figure 3.19 (bottom) also shows the velocity distributions, which are seen to change drastically within a few vessel diameters between locations proximal and distal to the sharp bend. In the proximal portion, the velocity distributions were skewed toward the inner wall (higher shear rate region), facilitating flow separation and formation of a recirculation zone along the inner wall distal to the apex of the bend. Just distal to the apex of the bend the peak in the velocity distribution gradually shifted toward the outer wall of the first bend and hence toward the inner wall of the second bend, again favoring flow separation at the inner wall of the second bend. Atherosclerotic wall thickenings were localized in an alternating manner at the inner wall of each bend, with a maximum occurring in regions of recirculation where fluid velocity and wall shear stress were low. Thus the results here, as well as in the circle of Willis, indicate that there is a strong correlation between the sites of low flow velocity (low wall shear stress) and the preferred sites for the genesis and development of atherosclerosis in humans.

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Discussion

Blood Flow and Aneurysm Formation

Dr. Fox: What weaknesses in a vessel wall might lead to bulging of the wall and subsequent change in blood flow dynamics? For example, would a small aneurysm attract some type of flow pattern to it that would in turn precipitate further aneurysmal growth, or must we abandon flow concepts for those aneurysms and think only in terms of pressure and vessel wall damage?

Dr. Goldsmith: There was a related question from Dr. Hilal concerning why it is that when the renal artery is ligated close to the aorta that a vortex appears in one of the branches of that stump. Soon thereafter one sees a recirculation zone and formation of a thrombus that occludes the vessel. Why then in an aneurysm is the flow maintained, as is evident from our pictures? If we understood the mechanism of thrombus formation related to flow dynamics that results in obliteration of the aneurysm lumen, we could suggest a method of altering the entry of blood into the aneurysm sac and thereby induce formation of a thrombus. I do not know the answer. I do know that flow through an aneurysm is fairly good and that there are recirculation patterns, but there is no clear zone of stasis or near-stasis that would induce a thrombus to form.

Aneurysmal Shape as Related to Flow Dynamics

Dr. Solomon: One of the problems in your model of the basilar apex is that it is an idealized version. It is more likely that aneurysms developing at arterial bifurcations do not have a normal shape, and they often have an abnormal tilt with respect to the basilar artery. Many of the aneurysms I have seen are neither classical in appearance nor perfectly symmetrical. This point is particularly true at the anterior communicating artery complex, where there is often a dominant A_1 segment artery. Also the varying shapes of the basilar artery apex may predispose to aneurysm development. One cannot simply look at a "normal" classical structure and determine whether the flow characteristics are sufficient for the formation of an aneurysm.

Dr. Goldsmith: In our work to date there are too few examples to be conclusive. My suggestion and that of Dr. Hilal as well is to review a large number of angiograms, compute the geometry of those aneurysms, and then try to determine mathematically what can be said about them. I believe that the geometrical configuration of a particular bifurcation is a determining factor in aneurysm formation. It is still too early to give a definitive answer, however.

Dr. Solomon: Your example of ligation of the renal artery represents more of a right angle takeoff, whereas intracranial aneurysms are more in a direct line of pulsatile arterial blood flow.

Dr. Goldsmith: That is true; but even when the flow comes to a dead end I believe it can predispose to aneurysm formation. In view of the lack of absolute evidence, perhaps my contention is not correct.

Dr. Solomon: In the early literature on aneurysms we often reported performing a hunterian ligation of the proximal common or internal carotid arteries. The result was an alteration in pulsatile flow dynamics and often thrombosis of the aneurysm. It was concluded that if the artery was proximal to the aneurysm the change in anterograde pulsatile flow led to stagnation or near stasis followed by endosaccular thrombus formation.

II. BASIC CONCEPTS

B. SPECIALIZED ENDOVASCULAR TECHNOLOGIES

CHAPTER 4

Doppler Observations in Arteriovenous Malformations

J.P. Mohr

Although well recognized as clinical entities, arteriovenous malformations (AVMs) and other vascular anomalies of the brain and its membranes occur infrequently. Their widely variation in etiology, overall size, location, feeding and draining vessels, histology, and course make it difficult to determine their prognosis and best treatment.

Prevalence

It has been only during the last few decades that AVMs have been identified during life. Sensitive neuroradiological imaging tools have allowed us to detect them more frequently. Entities such as cavernous angiomas could scarcely be studied at all during life prior to the development of magnetic resonance imaging (MRI). Most of the reported cases of AVM come from the experience of large centers with special interest in surgical therapy, making it difficult to determine if these cases, which have been brought to clinical attention through the referral process, are adequate examples of the natural history of the disorder.

The study of McCormick is the best known. It was not population-based but reflected his personal effort to document the prevalence of AVMs in an autopsy series. He found 118 AVMs (60%) in the cerebral hemispheres, 28 (14%) in the brainstem, and 5 (3%) in the spinal cord. Many of these AVMs were rather small and might well have been overlooked in earlier studies.

Incidence

The literature on AVMs remains small; there are clusters of single cases, with only a few large series reported.[2] Because subarachnoid hemorrhage accounts for roughly 10% of strokes, AVMs make up approximately 1% of all strokes. The availability of brain imaging has increased the frequency with which AVMs are being discovered; and now angiography has come on the scene, permitting some insight into possible changes in AVMs over time. In the few studies to date using angiograms, AVMs have been found to enlarge,

to remain static, or even to regress. Increased size has been documented in young patients subjected to follow-up angiograms, but it is not known what role age plays in changes in AVM size. The AVMs shown to enlarge have been in the cerebrum or brainstem and have varied from small, deep lesions to those on the surface with several feeding vessels; they have enlarged from having one to several feeders, sometimes "sprouting" many branches.

Transcranial Doppler (TCD) is is an ultrasonographic technique that permits noninvasive measurement of the velocity of blood in the intracranial arteries, thereby making it an ideal method to study AVMs. Although qualitative studies of TCD findings in AVMs have been previously described, our series is among the largest and most recent, comparing the effects of treatment from embolization and from surgery.

Arteries feeding an AVM typically have normal mean velocities that are higher than normal, occasionally showing turbulence associated with extremes of high velocity. Lower than normal pulsatility indices are seen, reflecting the low resistance to flow that characterizes the AVM. In our hands, TCD has become useful for the noninvasive diagnosis of AVMs and has even been able to distinguish major feeding arteries from nonfeeding arteries.

The equipment we use is a pulsed, range-gated 2 MHz TCD (EME TC2-64B, Eden Medizinische Elektronik GMBH, Uberlingen, Germany) which measures the mean velocity (V) and pulsatility index (PI) of feeding and nonfeeding arteries. We employ the transtemporal or suboccipital ultrasonic windows as described by Aaslid.[3] Measurements are recorded at the same depth of insonation for each artery before and after treatment. The pulsatility index (PI), an index of vascular resistance, is determined by the formula[8]:

$$\text{(systolic velocity} - \text{diastolic velocity)/mean velocity.}$$

In most instances, TCDs were performed within 1 week before and after treatment (range 1–70 days). We have used a two-tailed paired t-test to assess the significance of changes in V and PI for feeding and nonfeeding arteries after therapy. The unpaired two-tailed t-test is used to compare V and PI changes between surgically treated and embolized feeding arteries.

It has been assumed, but not previously documented, that embolization produces hemodynamic changes in AVMs similar to those that occur after surgical resection. Our findings have given support to this thesis by demonstrating that embolization consistently has a therapeutic hemodynamic effect on the embolized feeding artery similar to the effect seen in feeding arteries after surgical resection, with a decrease in mean velocity and an increase in pulsatility index. Such quantitative effects are not readily documented with angiography. Our data also support the commonly held assumption that surgical resection produces greater hemodynamic changes in feeding arteries than does embolization because the AVM shunt is completely or nearly completely removed in one step. After surgery the changes in velocity and pulsatility index are more dramatic in the surgically treated feeding arteries compared to those in embolized arteries. To date, our series of more than 20

cases is too small to show statistically significant differences between the two treatment types, but further study of larger numbers of patients might confirm the impression that the changes after surgery are greater than those after embolization. Our TCD findings certainly indicate that embolization can achieve therapeutically determinable changes in AVMs, at least on hemodynamic grounds.

We have also been able to effect dramatic changes in the nonfeeding arteries using embolization. Successful embolization of arteries feeding the malformation may activate a collateral circulation to the malformation from previously nonfeeding arteries by way of the border zones. These cases suggest that AVMs are capable of recruiting more blood flow from one feeding artery when the input from the other feeding artery is reduced, attesting to the dynamic behavior of these lesions.

An increase in velocity after treatment of the feeding arteries has been seen in some nonfeeding arteries, consistent with the possibility that the AVM had been exerting a "steal" effect on these nonfeeding arteries prior to therapy. However, in our case material to date, there have been no symptoms or signs suggestive of steal prior to therapy in any of these patients, and none of these patients showed improvement in neurological function after therapy, suggesting that if the AVM indeed had been exerting a hemodynamic "steal" effect on nonfeeding arteries prior to therapy it was clinically unimportant.

In some instances, changes in velocity has occurred in arteries that have no anatomical relation to the malformation. This finding is not fully understood at present, but it may mean we have altered some fundamental blood flow regulatory system in the vessels.

Studies on our patients to date demonstrate that TCD is a convenient, reliable method for quantitatively evaluating the hemodynamic changes that occur in feeding and nonfeeding arteries of AVMs after embolization or surgical resection. As further experience is acquired with TCD in this setting, the technology may prove to be useful for planning and monitoring the effects of surgical resection, embolization, or radiotherapy of AVMs.

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Discussion

Technology and Instrumentation of Doppler Ultrasonography

Dr. Taveras: The technology of Doppler ultrasonography has been advancing rapidly because of continuing improvements in instrumentation. As you know, with color Doppler we have now been seeing the reversal of flow that takes place at the carotid bifurcation. We have regularly observed this phenomenon and asked ourselves what was happening, and does reversal of flow really occur? Dr. Goldsmith has demonstrated this finding. I believe we can now say that it does in fact occur and add that we certainly expect there will be major improvements in ultrasound technology and instrumentation in the future.

Dr. Mohr: Six centers including ours are involved in an atheromodification project in patients with nonhemodynamic carotid artery stenosis. The project is providing an interesting opportunity to use the color Doppler to examine changes in the carotid lumen along the boundary zone of the stenosis and observe the apparent velocity of the vortices created distal to the stenosis. In addition, there are wonderful opportunities now and in the immediate future to quantitate what we used to see in a two-dimensional picture.

Dr. Hilal: Two points are obvious but need further emphasis. The instrumentation is small and portable. It can be brought into the embolization suite and used without interrupting or delaying the procedure. Second, there are not other methods of monitoring flow that are real-time, as this is. If one uses xenon gas, it takes at least 10 minutes to get an answer if you have a fast computer, whereas with Doppler ultrasonography you see it immediately. Regardless of whether you have two or three balloons or you occlude one pedicle or a number of pedicles, you can see the changes immediately. Therefore one can obtain a number of studies and make immediate decisions as to how to proceed further.

Dr. Heishima: Are you saying that the Doppler measures only flow?

Dr. Mohr: No, it is measuring velocity.

Dr. Hilal: The pulsatility index is a close relative of flow. Though we are not measuring flow in the index, we have enough of a practical index to give us an idea of the flow.

Dr. Goldsmith: Flow is measured by simply putting together velocities. Therefore you are measuring flow.

Dr. Mohr: You are measuring flow, but you are not quantitating it because you do not have the exact understanding of the diameter of the vessel at the time.

Measuring Flow

Dr. Fox: Dr. Viñuela, I understood from the work your group presented this past year that the pressures they are recording through the catheters are in fact a direct function of flow and are an exact quantified real-time measurement of flow. This may then be a way to compare it to the flow seen at follow-up. Would you comment on the statement?

Dr. Viñuela: We are gathering in situ information about the local changes in pressure when one embolizes an AVM or a fistula. The question is what we are trying to translate in pressure measurements now. Will we be able to complement pressure

measurements in the immediate future with local xenon arterial injections using the portable xenon unit to measure real flow? We are going to have transcranial Doppler data and attempt to use this hemodynamic information to effect a good clinical outcome. In answer to the question: Yes, we are gathering in situ information regarding local pressure changes, not only at the MCA level. We are going to the area of the malformation and coming back because we obtain pressure recordings while both advancing and withdrawing the catheter in order to observe the local and regional changes in pressure. We hope this information will enlighten us about the potential morbidity of interventional procedures including hemorrhage and edema.

I believe that your work on flow is an important adjunct to what we are doing and is ultimately related not only to flow in the great vessels but to flow in the tissue parenchyma, which is the other element. Our efforts are directed to gathering information that might allow us to prospectively predict the outcome of interventional treatments and the disease processes themselves.

Dr. Heishima: If we give you a cross-sectional diameter of the vessel, which we often do by angiography, can you not then calculate flow?

Dr. Mohr: Yes, in fact we are doing that now with Dr. Hilal. We are trying to establish the equivalent of a nomogram that tells us when we have reached the end of probable biological diameters. There are easily predicted limits to the MCA size that we should be able to encompass with a direct velocity measurement.

Dr. Heishima: Adding to that, we have tried to use transcranial Doppler ultrasonography to evaluate and plan therapy for vasospasm. We know that the ultimate outcome is a definable abnormality in an intact patient. It seems as though the curve is brittle, and at some point the patients are no longer intact; yet there has been only a minor change in the velocity measurement.

Dr. Mohr: I could answer that in part by saying that the work we did with hematocrits proved to be interesting. Hemodilution is part of the approach to many patients with spasm; and in the process of reducing the hematocrit one achieves a secondary acceleration in velocity that is entirely a function of reducing the particle size. Hence in some instances what appears on the transcranial Doppler scan to be increasing spasm is in fact accelerating flow secondary to reduction in particle size. The effects of hemodilution therapy are easily documented by the transcranial Doppler method at biologically relevant velocities. Lastly, we recently demonstrated that the anterior cerebral artery is difficult to see on the transcranial Doppler scan and that it is frequently one of the most clinically important vessels affected.

Dr. Murphy-Chutorian: The intravascular Doppler probe that is hooked up to the computer and is used in the pulmonary artery can produce a quantitative flow reading that has been correlated with pressure measurements. Of interest is that there a probe is also available for the coronary artery. It is in the form of a 0.016 inch guidewire.

Dr. Hilal: Is it integrative, or does it measure focally? Does it integrate across the cross section?

Dr. Murphy-Chutorian: Yes, I believe it is an integrative measurement.

CHAPTER 5

Lasers for Treatment of Occlusive Vascular Disease

Douglas Murphy-Chutorian

The object of this chapter is to present two approaches I have initiated that use laser energy to treat occlusive vascular disease: the Eclipse 2100 mid-infrared laser (Eclipse Surgical Technologies) and the SmartLaser (MCM Laboratories). The devices employ distinctly different strategies and technologies in laser therapy. Both are undergoing investigational trials in peripheral and coronary arteries with the hope of improving on the results of conventional therapies (i.e., balloon angioplasty and bypass surgery).

Major Problems to Overcome

The first percutaneous laser angioplasty trial was performed by Ginsburg at Stanford University in 1983. He concluded that the laser was an excellent cutting tool, but he also found that laser energy can remove normal healthy tissue as easily as it removes atherosclerotic plaque. Therefore laser treatment may have the undesirable result of perforating the wall of the artery. The solution to this problem is the essence of this chapter.

Attempts to control the laser energy by visualization (e.g., with angioscopy or fluoroscopy) have been associated with perforations in the arterial wall. The two fundamental problems with this approach are reaction time and resolution.

In this context, reaction time is the time required for the physician to squeeze the trigger to initiate laser firing. Because the lasers are efficient at removing tissue, 0.1 to 0.2 second of laser energy is sufficient time to cause perforations. The fastest reaction time for a human to visually recognize the need to stop firing the laser and to release the trigger is at least 0.3 second. One solution to compensate for this disparity is to create an automatic feedback system to accurately control firing of the laser. A computer firing mechanism can control the laser firing time within a few milliseconds.

The discernible thickness or volume of tissue that is directly in front of the fiber and that can be correctly identified is a measurement of resolution. This measurement is critical because the media of vessels is thin—as thin as 0.1 mm in the carotid arteries. If the detection or visualization system does not distinguish the margin of media underlying the obstructive plaque or thrombus, perforation or dissection is likely to occur.

Neither angioscopy nor fluoroscopy distinguish the media of vessels with adequate resolution. We investigated the use of spectroscopy as a better alternative for identifying tissue signatures, which results in adequate resolution of the target site to safely control laser firing.

SmartLaser

The SmartLaser controls the laser output by utilizing spectroscopy and a computer to provide automatic feedback. The computer "decides" whether to fire the laser based on an algorithm stored in the computer memory, which is derived from tissue fluorescence studies.

The computer can distinguish among tissue types, preventing the laser from firing on intima, media, and blood. All other tissue signals within the artery are recognized as disease, and the computer then triggers the system to fire. There is little patient to patient variablility in spectroscopic signals from normal vessels, which should ensure uniform recognition of diseased versus healthy tissue.

This system was tested in various experiments prior to initiation of clinical trials. Using atherosclerotic arteries obtained at autopsy, the fiberoptic delivery system was placed in the most disadvantageous position, that is, perpendicular to the artery wall. The experiment attempted to "fool" the system into perforating the artery with laser energy. The diagnostic system, however, accurately detected the media and prevented laser perforation.

The initial clinical trials of the system were done on total occlusions in peripheral arteries of patients with symptomatic disease (usually severe claudication or rest pain). The protocol was established to attempt to cross the lesion using standard percutaneous techniques and conventional guidewires. In the event that the guidewire failed to cross the lesion, an attempt would be made to open a small pilot hole through the blockage utilizing the SmartLaser and a 0.035-inch fiberoptic guidewire. If recanalization was achieved with the fiber, the procedure would be followed with adjunctive balloon angioplasty to achieve the goal of less than 25% residual stenosis.

In the series of 126 percutaneous cases, there were 105 (83%) where the SmartLaser did create a narrow channel in a totally occluded leg artery. Balloon angioplasty was successfully performed to achieve definitive recanalization in all cases. Lesion length varied from 1 to 27 cm, with a mean of approximately 10 cm. Lesions were located predominantly in the superficial femoral or popliteal arteries. Clinical improvement was noted in almost all patients with angiographically patent arteries. Complications included perforations in about 10% of cases. Patency rates at 6 months after the procedure were 80%. Patency was confirmed by repeat angiography or duplex scans in most cases.

In conclusion, when conventional guidewires fail to recanalize blocked arteries, the SmartLaser can successfully open small channels in 80% of

cases to allow subsequent definitive balloon angioplasty. Restenosis occurs in 20% of cases, a rate comparable to reclosure rates using balloon angioplasty without laser.

Future Directions in Laser Research

Laser therapy holds promise for further reducing restenosis rates. However, as described above, current laser technology relies on adjunctive balloon angioplasty. Balloon angioplasty is damaging to the arterial wall and is associated with an unacceptably high restenosis rate. Laser researchers hope to use laser energy alone to create openings in arterial blockages. Laser energy may leave behind an arterial lumen that is less thrombogenic and less platelet adherent than the surface resulting from balloon dilatation. To use laser therapy alone without balloon, a pulsed laser source has been developed that can produce sufficient laser energy without being excessively large or expensive. These lasers will be used with multiple-fiber "over-the-wire" delivery systems.

Eclipse Surgical Technologies (Palo Alto, California) is developing such a "stand alone" laser technology system called Eclipse 2100. The laser is one of the new, solid-state mid-infrared lasers that operate at wavelengths near 2 μm and have only recently become available. Currently, these mid-infrared lasers are in clinical trials for gastrointestinal applications; potential applications range from the removal of bone to use in ophthalmology and coronary angioplasty.

The mid-infrared lasers provide controllable and reliable removal of tissue using a clean solid crystal as the lasing medium. The crystal itself is only a few inches long but can produce enough laser energy to remove bone. Remarkably, it is relatively easy to transmit this energy through fiberoptic devices. In contrast, other pulsed laser sources, such as excimer or dye lasers, use hazardous gases or liquids, respectively, to provide laser "fuel." Dye and excimer lasers are large and unwieldy in addition to being fairly expensive. The mid-infrared laser provides the least expensive laser source that can produce clean, precise lesions with only minimal adjacent thermal injury.

Conclusions

The use of highly precise, inexpensive, new energy sources combined with novel catheter approaches is necessary to fulfill the promise of laser therapy for occlusive vascular disease. Certainly, the potential treatment of atherosclerotic cerebral arteries requires precise laser cutting combined with flexible catheters that can track over a guidewire. Presently, laser therapies have limited application for treating peripheral arterial disease, are under investigation in coronary arteries, and probably will be tested in cerebral arteries within the next few years.

Addendum. Since this meeting, our holmium laser system has been used in a multicenter clinical trial to perform more than 1,200 coronary laser angioplasties using over-the-wire techniques. Procedure success rate was 93% with a less than 1% vessel dissection frequency. Balloon angioplasty was used adjunctively in most cases.

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Discussion

Dr. Murphy-Chutorian: You could say that I have taken the "smarts" out of laser and put it into the catheter with these new devices. The devices we are working on are intended to achieve large patent pathways without having to use the balloon. My experience is that once you use the balloon to dilate an artery the result is similar to that achieved with balloon angioplasty—not those seen with earlier methods of dilating the vessel. It is this parameter we are trying to improve.

My goal is to create a device that does not need the smart features of the diagnostic system because it is not directed at treating total occlusion. If an occlusion is total and a guidewire cannot penetrate the vessel, use of the SmartLaser is an excellent way to proceed. Probably about 3% of all the disease in the heart and the legs falls into the category of total occlusion not treatable by guidewire.

Dr. Taveras: When you add the SmartLaser to the Eclipse what happens to its complexity and its price?

Dr. Murphy-Chutorian: The price remains the same as that of the SmartLaser. The SmartLaser sells for about $300,000. It is of course a questionable expenditure if only 3% of your patients are to benefit, but I expect the price to come down over time.

Dr. Berenstein: What is the size of the guidewire catheter?

Dr. Murphy-Chutorian: Laser Plus comes in different sizes. The smallest catheter is in the range of 100 μm, but there are multiple fiber devices. We would use one in the region of a 3F or at a diameter of 1 mm. Theoretically, the catheters could be made smaller. They are highly flexible, like noodles.

Dr. Berenstein: Is it as flexible as the ACS guidewire with the platinum tip?

Dr. Murphy-Chutorian: It cannot be that flexible, but it certainly can be so without disrupting the artery. I wish I could say that these devices were ready and that we have done trials with them. Unfortunately, they are still in the design phase. To give you an example, flexibility within a fiber catheter is a function of the diameter of the largest diameter of any single component. A single fiber of 1 mm diameter has a certain stiffness. If you make the single component 200 μm, or one-fifth the original, you go to the fourth power; that then is the range measure of flexibility.

Dr. Berenstein: Can it negotiate the carotid siphon?

Dr. Murphy-Chutorian: I know it can go down the circumflex artery to the apex of the heart.

Dr. Hilal: Can you ablate a plaque at the carotid siphon?

Dr. Murphy-Chutorian: The SmartLaser is the only *smart* laser on the market; and the Laser Plus is probably the only such device of its kind on the market. At this time we cannot definitely state that it can ablate a plague at the carotid siphon.

Dr. Viñuela: We have the SmartLaser. In one case of complete occlusion of the femoral artery a hole had to be made through the plague before angioplasty. It took about 9 hours. The point was that it was difficult afterward. The computer was not sharp enough. This case occurred during the a period that the computer was indicating that a tissue was plague when it really was not. On the other hand, the SmartLaser is useful for outlining anatomy clearly, precluding the need to perform repeated angiography in order to see where you are.

Dr. Murphy-Chutorian: There have been modifications to the device over time, and the UCLA instrument is what I referred to as the old detection system: It had an 80% success rate and approximately 20% failure rate. I believe they are now using the new device. With the newest device we can actually distinguish the different plaque types.

Dr. Viñuela: I think we will look into the flexibility of the system that is currently available. Our experience thus far has shown that it cannot negotiate the steep curve about the supraclinoid carotid. I have no doubt that future modifications will permit the negotiation of such curves.

Dr. Murphy-Chutorian: I am comfortable with its flexibility for negotiating all parts of the coronary anatomy that would be clinically important and certainly all parts of the leg. I would like to address its use in the cerebral circulation, but the experience is not there.

Dr. Berenstein: Do you have to stop to obtain blood?

Dr. Murphy-Chutorian: No. With this technique we do not stop blood flow.

Dr. Berenstein: If a plague in the carotid causes 95% stenosis, you want to vaporize the plague without permitting cerebral embolization. To accomplish this you must control flow. Do you believe you can achieve the angioplasty in the presence of circulating blood?

Dr. Murphy-Chutorian: We should design the device to eliminate the need for flow control. One of the features of the Laser Plus is its ability to capture particulate material, so the material is removed through the catheter itself. That feature is an advantage, as most of the debris does not propagate distally. Does that eliminate all the debris and fully protect against embolization? No, there is some debris from the site of the slicing. Therefore we have to answer the question: Can the brain tolerate emboli on the order of 10 μm or slightly larger? I do not know the answer. It seems appropriate to perform the experiment using the laser on carotid lesions, measure the size of the debris, and then inject similar size debris into an animal model and section the brain to determine if there are histologically demonstrable lesions.

Dr. Berenstein: Professor Victor Kadish from Riga showed us some balloon angioplasties of cerebral arteries. There was evidence of showers of emboli on every angiogram, and there were multiple branch occlusions.

Dr. Bennett Stein: Does the type of feedback depend on the angle with which the sensor hits the plaque or the wall? In cases with complete occlusion it hits at a right angle; suppose you hit the plaque at another angle?

Dr. Murphy-Chutorian: The angle does not matter because the system remembers it. If the laser hits the plaque at an angle, and there is blood between the device and the plaque, the computer recognizes the blood and refuses to fire. If the device is completely covered by atheroma, it acknowledges that it can fire. If a tiny amount of blood is present, a mixed signal results, which may cause you to fire inappropriately. That situation creates a problem that is not yet solved. That is why I am concentrating on obtaining larger pathways. I do not mean to infer that the SmartLaser is perfect, but it is pretty good.

Anonymous: How many cases have been done?

Dr. Murphy-Chutorian: Probably 10. Some studies have quantified the particle size for each laser type. Approximately one particle in 10,000 is larger than 100 μm, and there are probably fewer than 10,000 particles. It depends, of course, on the lesion length, the laser type, and the aggressiveness of the mechanical technique.

Dr. Berenstein: It may be worth 10 to 20 μm because they close vessels at the capillary level.

Dr. Mohr: Brain capillary diameters are about 90 μm. All these particles disappear into the brain. It is the particles that are larger than 200 μm that are important. The medial lenticulostriate lumens are 40 to 200 μm. It might not be a good idea to embolize them. On the other hand, the lateral lenticulostriates have lumens of 200 to

400 μm. Should you embolize one of them, an easily recognizable complication could result. There may be no disturbance for vessels less than 100 μm in the capillary network in the gray matter.

Dr. Hilal: Are all these lasers forward-shooting? Sometimes the plaque is on one side of the carotid siphon or at the carotid bifurcation, and you would have to "shoot" to the side in order to ablate an asymmetrical plaque. Can you direct the laser or orient it in situ?

Dr. Murphy-Chutorian: Yes. There are various ways of accomplishing that. If you use a very high energy laser, however, you may have a problem with both the cost of the tip and its reliability.

Dr. Hilal: Most of the carotid cross sections of vessels I have seen show a crescentic plaque. One side is nearly normal, and the other side has the plaque. You want to work on the bad side.

Dr. Murphy-Chutorian: In terms of what you are describing I have been designing a device to use in the coronary arteries. One possibility is to have something ensheath the guidewire concentrically except at the tip where it might be eccentric so that it could treat the disease where the disease was located. I know it is possible but not if it is practical. We would have to perform many studies to understand the limitations of this new design.

I might mention that debris is one limitation. I do not know the restenosis rate of the laser alone. I have some in vitro data that *look* good but are meaningless to me. It is a difficult problem to study. It would perhaps be easier to study peripheral vessels first.

CHAPTER 6

Microcoils in Neuroembolization

DeWitte T. Cross III and
Sadek K. Hilal

Microcoils, manufactured using platinum wire and Dacron fiber, or other materials depending on the purpose, can be introduced through superselective embolization catheters. Used for neurointerventional work with arteriovenous malformations (AVMs), aneurysms, and fistulas, microcoils can be used as the primary embolization agent or in conjunction with other agents to cause thrombosis, closure, or obliteration.

Technical Considerations

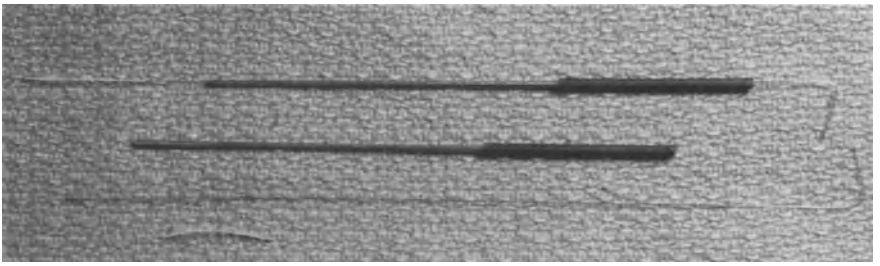
Coils and Technique of Injection

The standard Hilal microcoil, 15 mm in length, is introduced through a superselective catheter with an inner diameter of 0.018 inch. It is made of platinum wire and is constructed so thrombogenic Dacron fibers protrude from the sides of the coil. The head end of the coil, which enters the catheter and vessel first, is rounded; the tail end of the coil is open and may be cut at any point to make the coil the proper length for its intended use (Fig. 6.1A, B). The coil is packaged with a small wire stylet in the tail end of the coil that must be removed prior to use and with an introducer to facilitate insertion into a microcatheter. The coil is marketed by Cook, Incorporated.

Once the coil has been removed from its stylet and cut to length (Fig. 6.1C) it is inserted head end first into the larger end of its introducer, and the smaller end of the introducer is locked into the hub of the embolization catheter. (The introducer is designed to mate with the hub of the Tracker catheter marketed by Target Therapeutics.) A Teflon guidewire, 0.018 inch in diameter, is used to advance the coil within the catheter until the coil reaches a distal point in the catheter that can be seen fluoroscopically but not so distal as to allow the guidewire to alter the position of the catheter tip. In the case of cerebral embolization, the coil is usually advanced to the level of the cervical carotid. Once the coil has been pushed to this position, the wire is removed and the coil is injected into final position with saline-filled 1- or 3-ml syringes locked onto the catheter hub. Coil position can be observed fluoroscopically during and after injection. Roadmapping subtraction can be useful to identify the last coil injected once several coils have been deposited.

Modifications

The length of a coil can be modified from the supplied 15 mm by cutting the coil to as small as 2 to 3 mm. Such changes may be necessary to make the coil land distally or proximally relative to the tip of the embolization catheter, to enable the coil to negotiate curves within the catheter or within the vessel, or to avoid shunting or reflux of coils. In general, the shorter the coil, the more distal it travels from the catheter tip, as to an AMV nidus, and the more easily it can be injected through loops in the catheter. Shorter coils are



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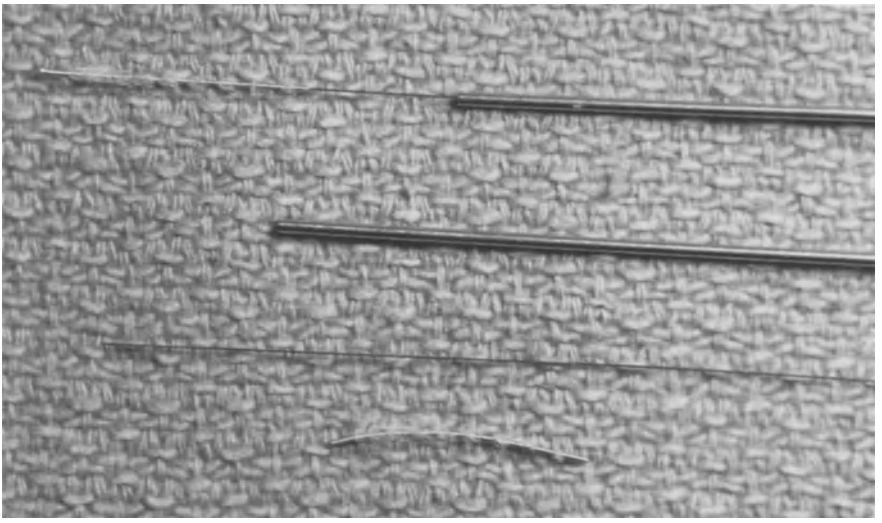
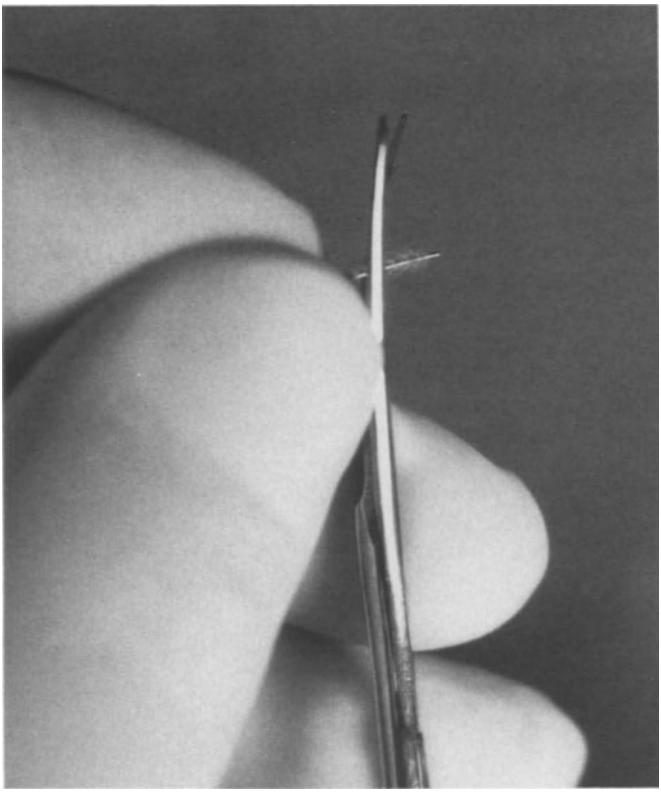


B

Figure 6.1. Preparing microcoils. (**A**) At top, the coil as packaged, with the stylet inside the coil and the coil–stylet assembly inside the introducer. At bottom, the stylet has been removed to allow the coil to be cut or shaped and introduced. (**B**) Close-up view of the individual components. (**C**) Cutting the coil to proper length, shortening the tail end. (**D**) Shaping the coil, if necessary. (**E**) Appearance of a preshaped coil.

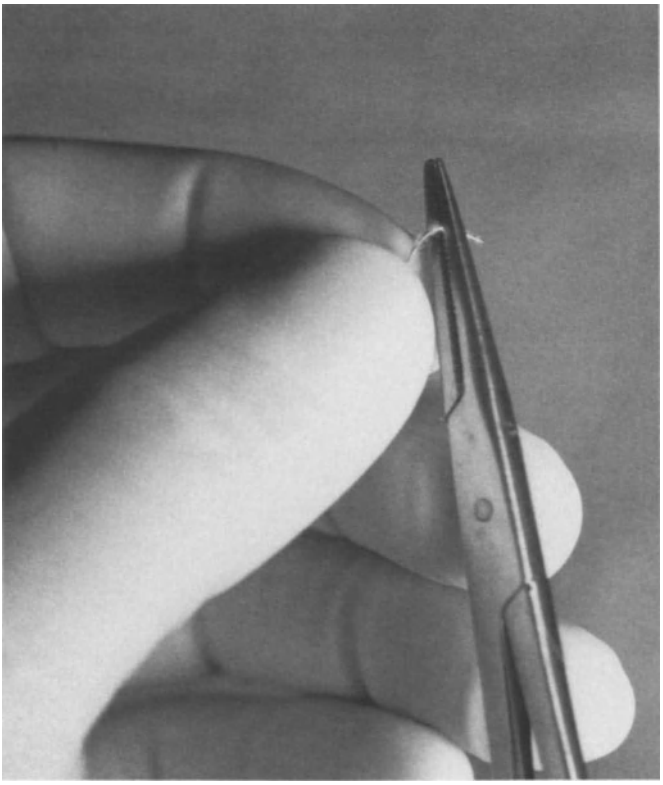


C

Figure 6.1 (*continued*)

more likely to shunt through fistulous connections and to reflux from a proximal location by the force of subsequent coil injections.

For AVM embolizations, small coils are injected initially to close fistulas in the nidus that would shunt particulate embolic material. Coil deposition within the fistulas allows particulate matter to lodge within the smaller channels of the nidus without shunting through larger fistulas to the venous side of the malformation. A coil length should be selected that is small enough to reach the nidus but large enough to lodge without shunting. A 2- to 3-mm length is usually an appropriate beginning size. If 2- to 3-mm coils are seen to shunt, slightly longer coils are tried until a size is found that comes to rest at or near the nidus. Once the fistulas have been sealed, embolization can be carried out with other agents directed to the smaller channels of the nidus. Once flow in the feeding vessel nears stasis, the feeding branch can be sealed proximal to the nidus with larger coils to prevent recanalization. A 7- to 8-mm length is usually appropriate for this purpose.

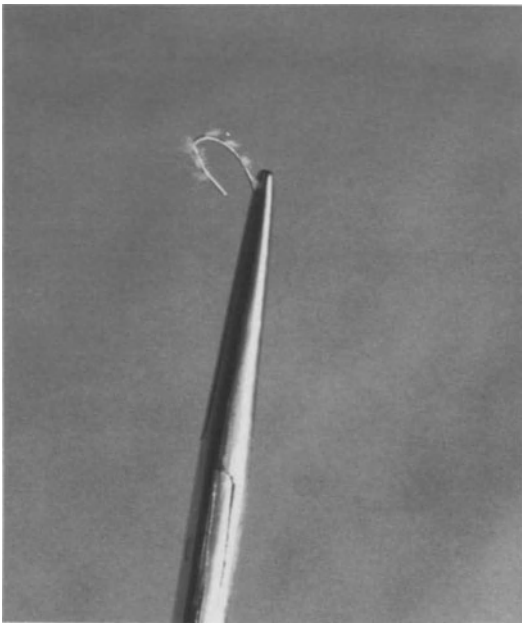


D

Figure 6.1 (*continued*)

Coil shape can also be modified (Fig. 6.1D). The coils are supplied straight but can be preshaped prior to insertion into the introducer and catheter (Fig. 6.1E). For AVM embolization, if one is sealing a feeding branch and coils are seen to reflux from the force of the injection in a stagnant vessel, the coils can be curved using a loosely applied hemostat or the fingers. The complex shape results in a firmer seat. Preshaped coils are also used for microcoil embolization of aneurysms. Circular or spiral-shaped coils leave the catheter tip within an aneurysm and turn into its lumen rather than stressing the wall of the aneurysm, as would be the case if straight coils were injected and the aneurysm wall used to force the coil into a circular or spiral shape (Fig. 6.2A).

Another variable in coil embolization that may be modified is the force of the injection employed for coil placement. Higher pressure can be achieved with saline-filled 1-ml syringes than with 3-ml syringes when coils are being propelled through the catheter and injected into the vessel being embolized.



E

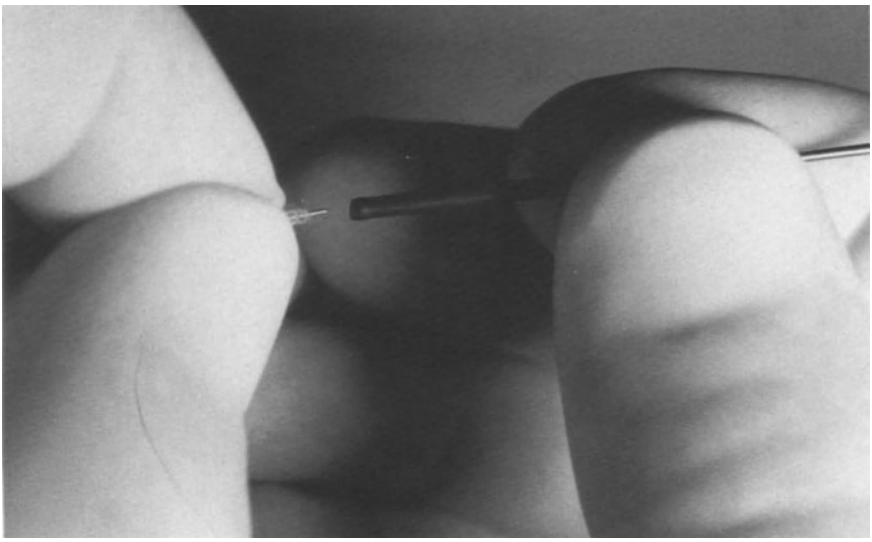
Figure 6.1 (*continued*)

The force applied by the thumb to the plunger of the syringe also affects pressure inside the catheter. Higher force may be desirable to propel small coils through loops and curves in the catheter and to points distal to the catheter tip, whereas lower force may be desirable when working with stagnant vessels or aneurysms. Injection force also becomes critical when the catheter tip can be moved from a desired position by each injection (Fig. 6.2B–E).

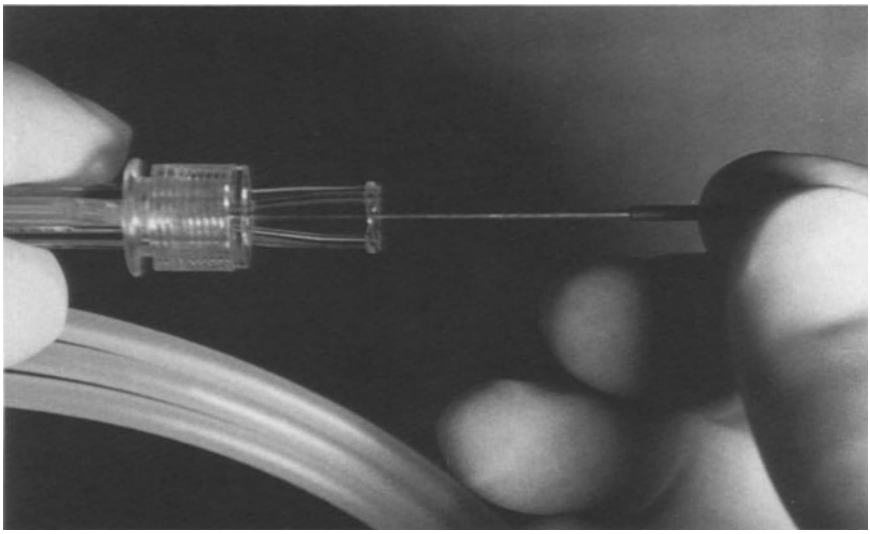
Modifications of coil length, coil shape, and the force of coil injection may therefore be employed to achieve certain ends in microcoil embolization. Specific applications are detailed below following a discussion of potential complications of coil use.

Problems Encountered During Microcoil Applications

One occasionally encounters difficulty introducing microcoils into the microcatheter, with coils sticking at the junction of the hub and the catheter. Gentle repetitive jabs with the introducing wire or rotating and twisting the introducer usually suffice to move the coil along. If these motions are unsuccessful, the soft end of the introducing wire can be removed and the stiff end

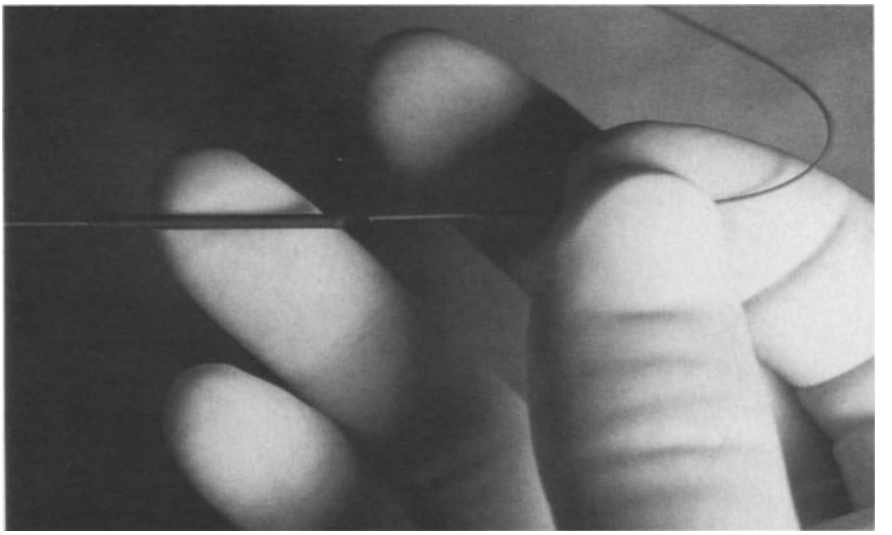


A

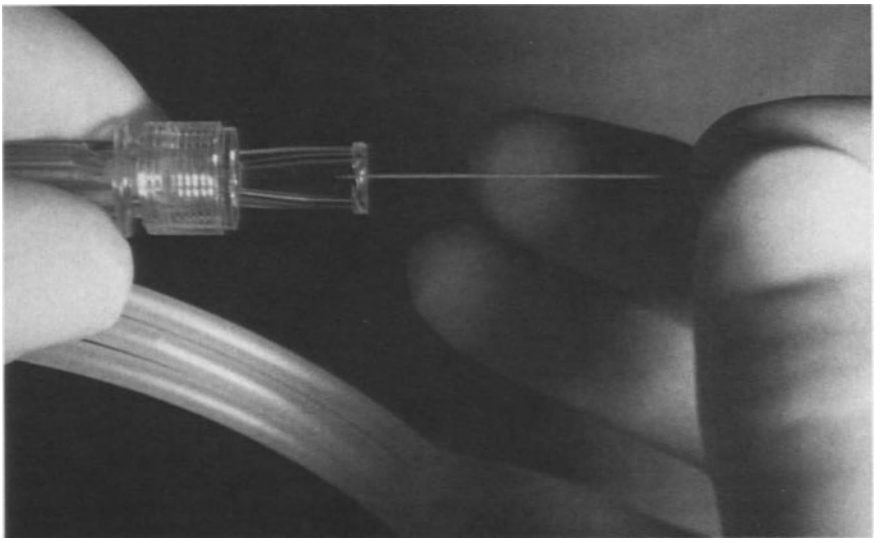


B

Figure 6.2. Injecting microcoils. (**A**) Inserting the coil into the large end of an introducer, with the rounded head end of the coil inserted first. (**B**) Locking the small end of the introducer into a superselective catheter hub. (**C**) Advancing the coil into the catheter with the soft end of a Teflon-coated guidewire. (**D**) Removing the introducer and wire from the catheter, leaving the coil within the lumen of the catheter. (**E**) Injecting the coil into a vessel using a saline-filled syringe.

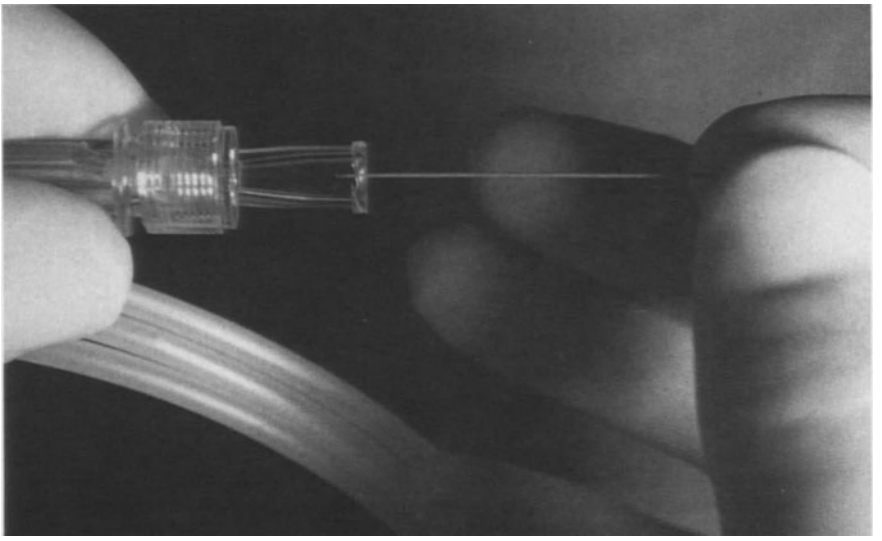


C



D

Figure 6.2 (*continued*)



E

Figure 6.2 (*continued*)

inserted into the catheter hub to advance the coil. Excessive force can result in catheter perforation, so caution should be exercised.

Another catheter-related problem is that sharp turns or kinks in the catheter may prevent coil passage. At times more forceful injection propels coils past a turn, but it may be necessary to pause, opacify the catheter with contrast, determine the cause of the dificulty, and withdraw the proximal end of the catheter until the kink or bend is straightened—and then attempt injection of the coil. One must be careful when doing this that only redundant curves are straightened, and that withdrawal of the catheter does not result in movement of its tip, altering its position for embolization. If withdrawing the catheter does result in movement of the tip, one might not wish to inject the coil that has lodged in the catheter until the catheter is repositioned. Repositioning could require reintroduction of a steering guidewire. One of the most perplexing problems with coil embolization is to have a coil permanently lodged in the catheter, necessitating catheter removal and recatheterization of the vessel with a new catheter.

As discussed in the previous section, optimal coil length is important for preventing problems in coil travel once the coil leaves the catheter. If coils come to rest too proximally during AVM embolization (e.g., falling short of the nidus), coils can be shortened to travel more distally; and if shunting or reflux is encountered, coils can be lengthened or coil shape can be modified.

The geometry of any particular feeding vessel to a malformation may prove unfavorable for coil use if adjustments of coil length and shape do not

achieve desired results, or one may be forced by the geometry to accept less than an optimal result. Assuming that coil placement has been sucessful, a point is reached during the embolization where further coil placement is impossible. This point occurs despite all modifications in length, shape, and injection force and is seen when when there is stagnation of flow. At this point, one must terminate embolization with coils.

Deposition of multiple microcoils within an aneurysm may not result in full obliteration and thrombosis. Coils become more difficult to inject into the aneurysm once little room remains within its lumen. Smaller, more spiral coils can be used to attempt to fill the remaining lumen, but coil reflux from the lumen of the aneurysm to the lumen of the parent vessel becomes more likely. If that risk becomes unacceptable, one may be forced to terminate embolization before complete obliteration is attained. Another potential problem with the use of coils in an aneurysm is the compression or compacting of coils within the lumen over time, resulting in a larger residual lumen after several months than was seen at the conclusion of the embolization procedure. Reembolization with coils can be attempted in such cases, working with the larger residual lumen at follow-up.

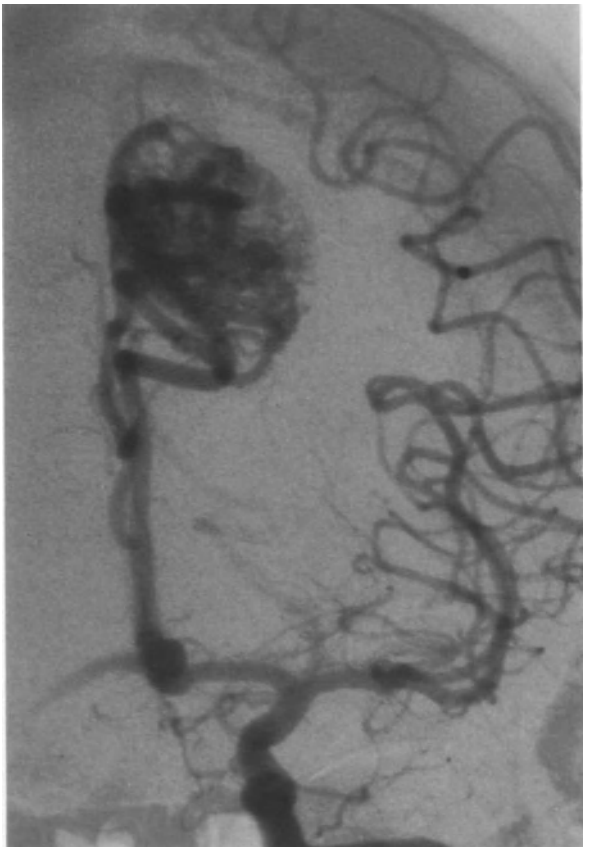
Specific Applications

Arteriovenous Malformations

Embolization of AVMs may be carried out to reduce the size of and flow to a malformation before surgical resection, to reduce the size of a malformation to one acceptable for radiosurgery, to control symptoms related to flow, or, in certain instances, to totally obliterate a malformation. Often specific preoperative goals are set, as eliminating or reducing flow from surgically difficult-to-reach vessels. Microcoils can be used in these cases, with or without the addition of other embolic agents (Fig. 6.3). Our embolization patients are heparinized, and clotting times are monitored to maintain them at 1.5 to 2.0 times baseline during the portion of the procedure that superselective microcatheters are in use. Intravenous sedation is employed rather than general anesthesia whenever possible to allow monitoring of neurological status. Once a feeding vessel has been catheterized with a superselective microcatheter (e.g., the Tracker), the catheter is advanced to a termination point as close to the AVM nidus as can be achieved. If the embolization is to take place in a territory where neurological deficits might be anticipated, injection of the selected vessel with Amytal or lidocaine, depending on location, is performed with a neurologist present to assess altered function. If anatomical definition of the territory at risk is desired with cross-sectional imaging, the patient is transported to the computed tomography (CT) scanner for a dynamic contrast-enhanced study of the area of interest, with contrast medium injected through the microcatheter during imaging. Once

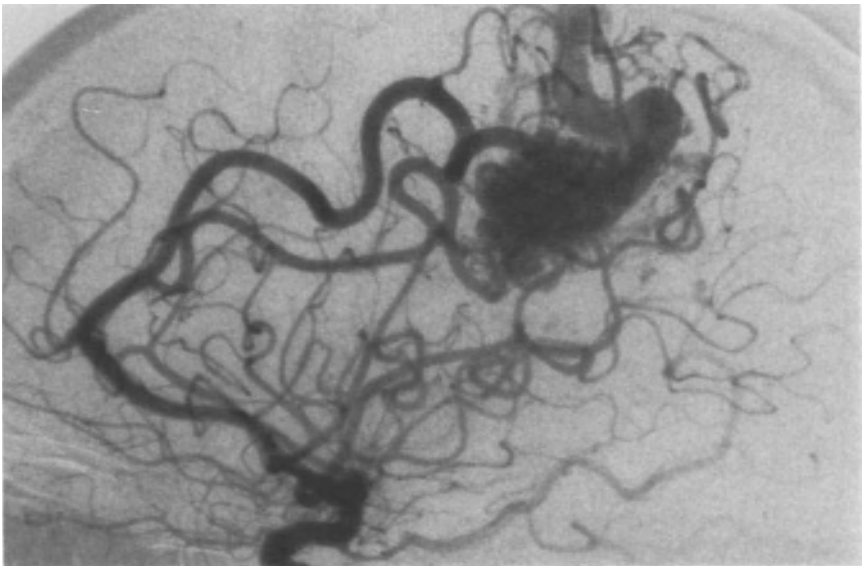
potential deficits have been identified, the decision to proceed with embolization is made or another vessel selected if embolization of the original vessel is contraindicated.

It is desirable to obliterate as much of the AVM nidus as possible before final closure of the feeding vessel selected for embolization (Fig. 6.4). Our current approach is to begin an embolization with particulate material



A

Figure 6.3. AVM embolization using microcoils. (**A&B**) Anteroposterior (AP) and lateral views of a motor strip AVM prior to embolization. (**C**) Plain film obtained after superselective catheter placement in an ACA feeder, with contrast entering the nidus. (**D**) Initial lateral subtracted view before embolization. (**E**) Later lateral subtracted view after placement of initial microcoils to eliminate larger shunts and slow flow. (**F**) Final superselective lateral subtracted injection after injection of a particulate mixture of PVA, collagen, and alcohol, plus additional microcoils. (**G–I**) Post-embolization AP and lateral views demonstrating elimination of the embolized feeder and reduction in the size of the nidus.



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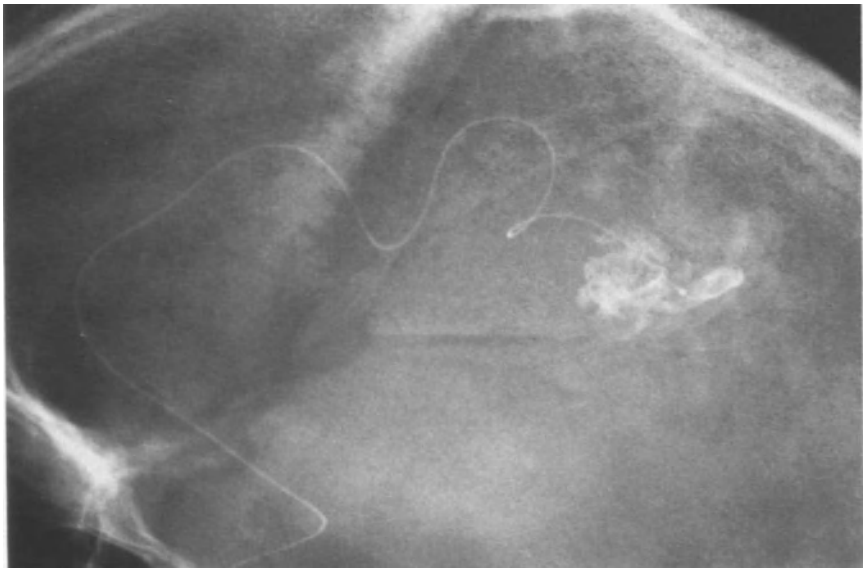
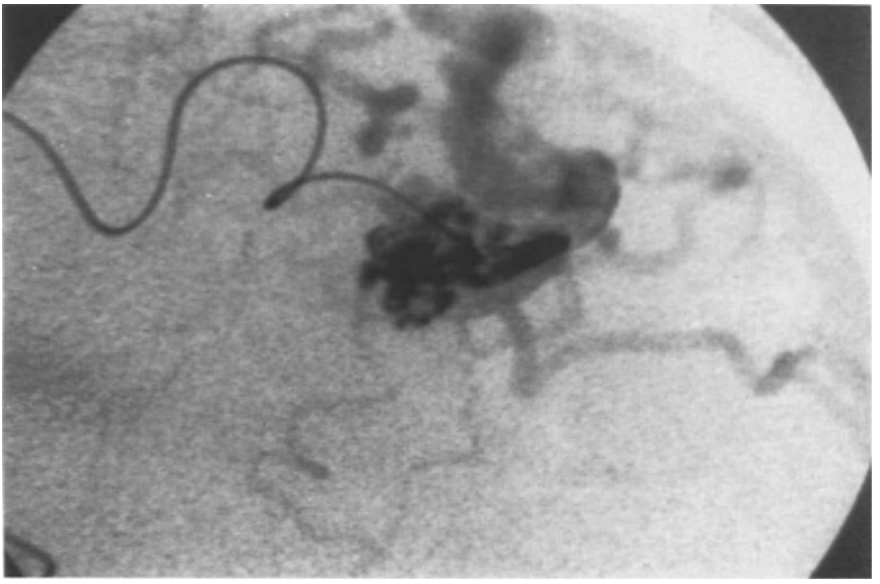


C

Figure 6.3 (*continued*)



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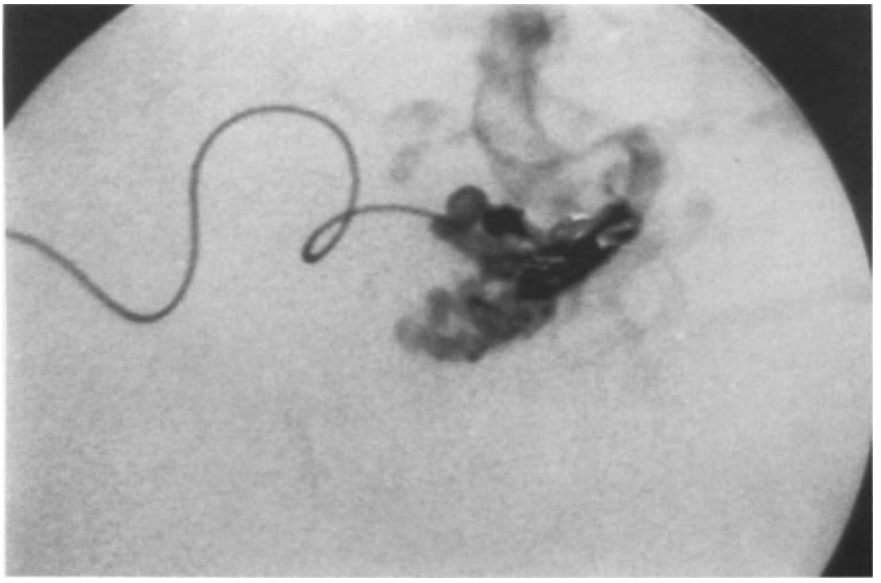

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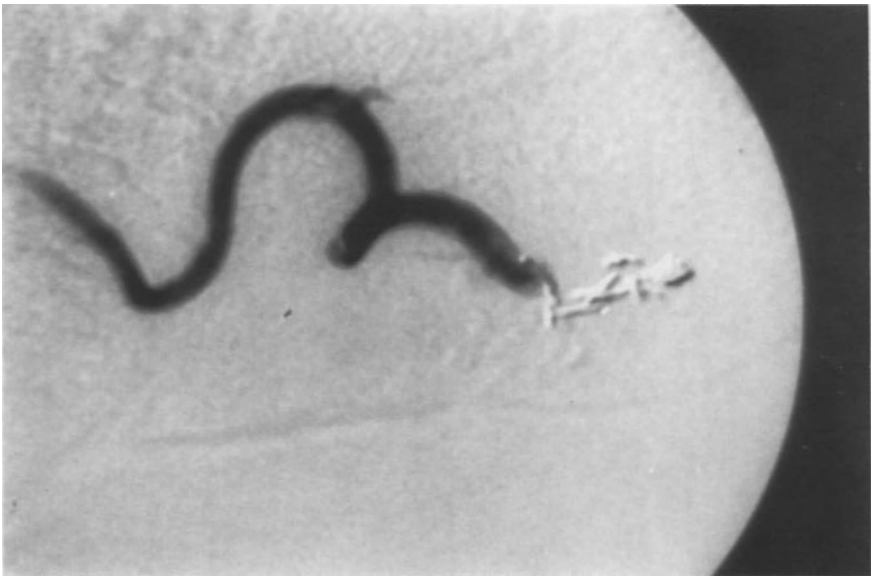

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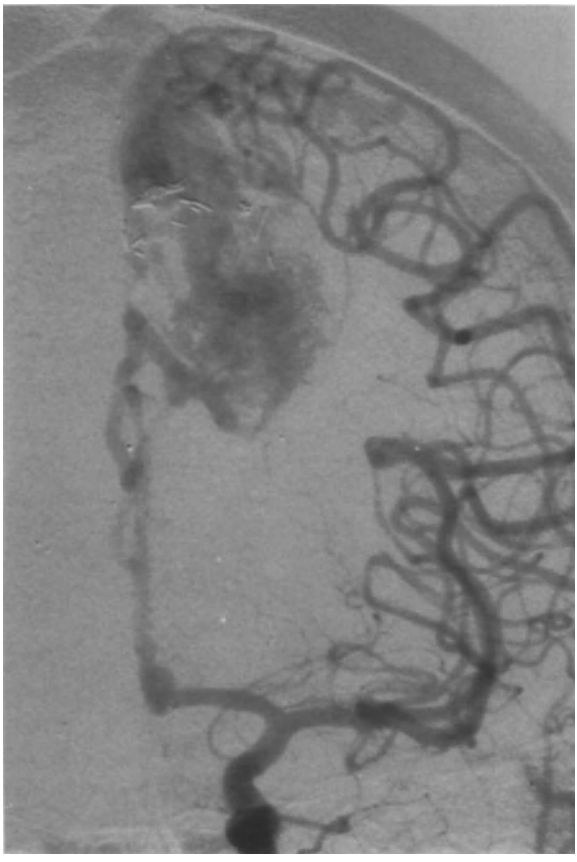
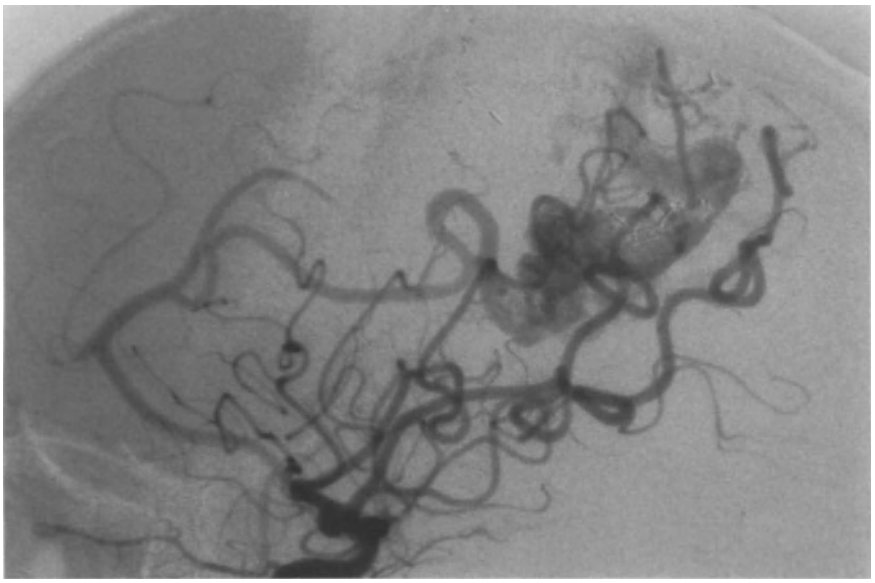
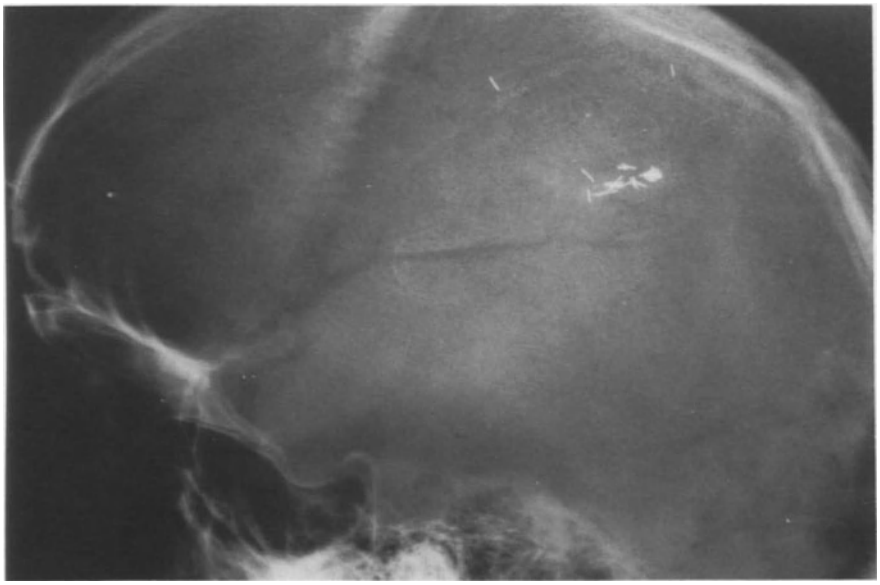


G

Figure 6.3 (*continued*)

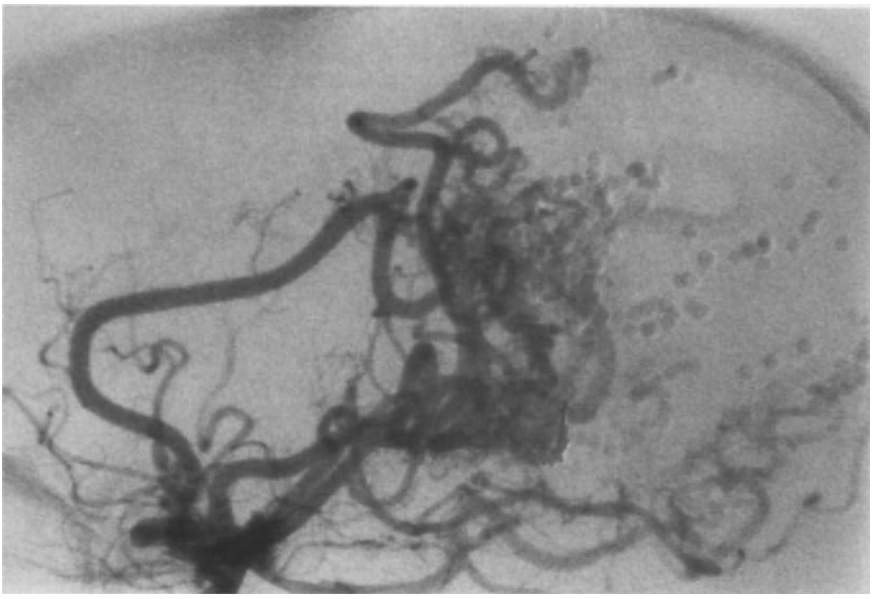


H

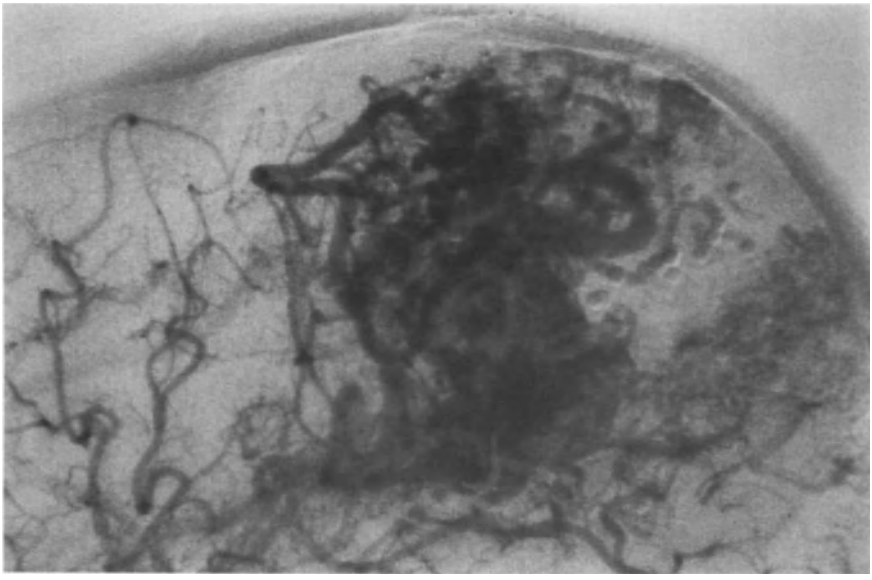


I

Figure 6.3 (*continued*)

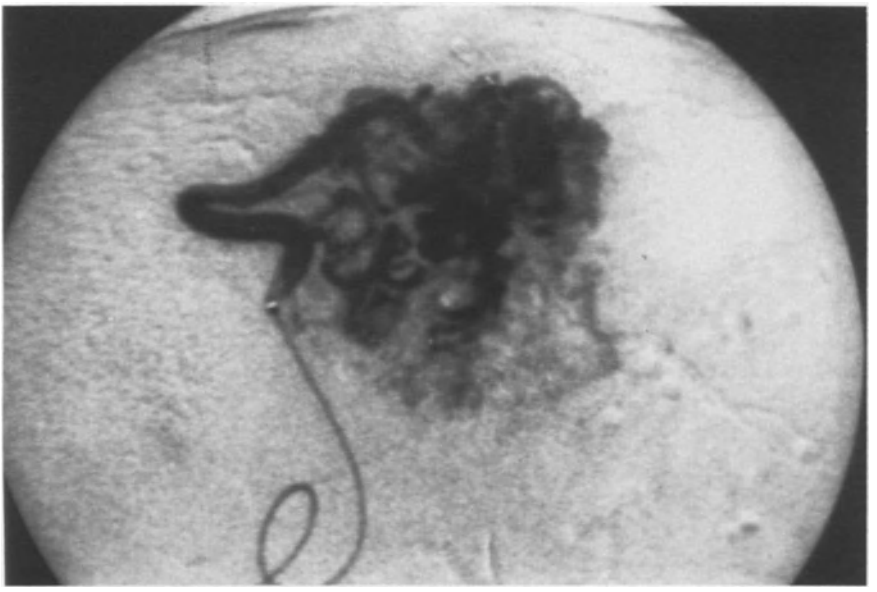


A



B

Figure 6.4. AVM embolization using microcoils. (**A&B**) Preembolization lateral angiogram of a motor strip AVM showing evidence of earlier pellet and coil embolizations. (**C**) Subtracted view from superselective catheter injection in an MCA feeder showing branches filling the nidus. (**D**) Subsequent image showing the initial microcoils injected. (**E**) Postembolization lateral angiogram following further microcoil and particulate embolization, with elimination of the embolized branches and a reduction in the nidus.



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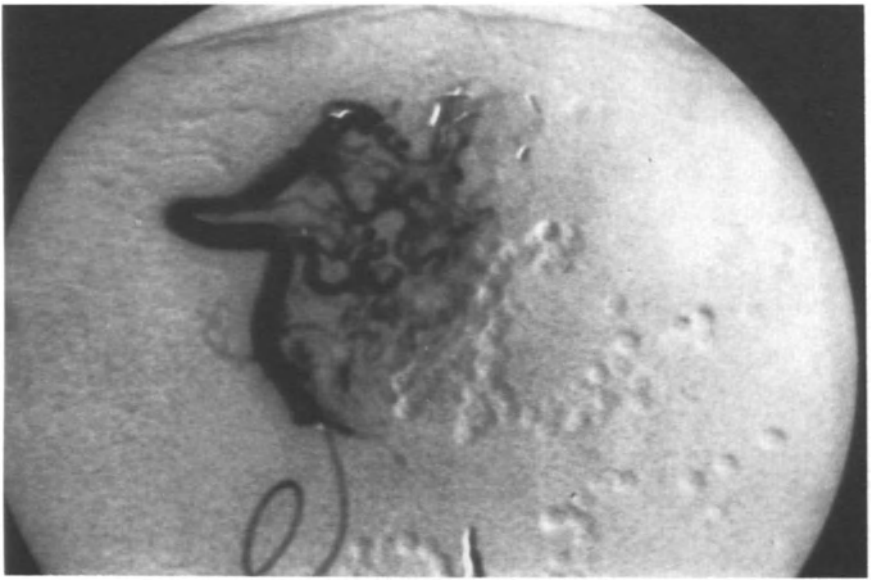

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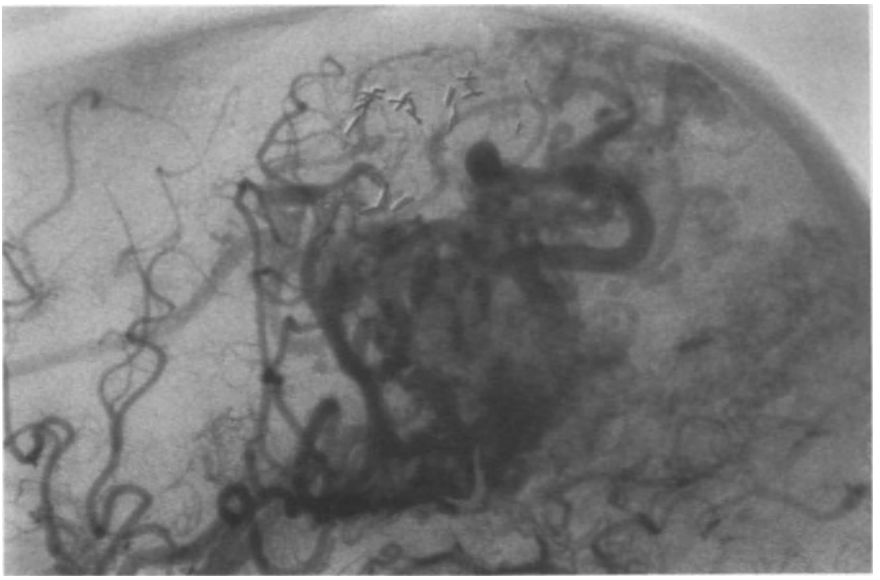


E

Figure 6.4 (*continued*)

(PVA), usually in combination with absolute alcohol and collagen; contrast is added to the mixture for visualization. Particle size should not exceed 500 μm in the standard Tracker catheter to avoid catheter occlusion, and we usually limit particle size to 300 μm. The particles are suspended in nonionic contrast, and absolute alcohol is added to yield and alcohol concentration of 30% to 35%. A small quantity of collagen is added to the mixture, and the mixture is strained through 20-gauge needles to eliminate clumps. Injection is begun into the AVM, and the results are observed on the roadmapping function of digital subtraction fluoroscopy. If injection of the particulate mixture is successful, flow slows in the selected feeding vessel.

If flow slows appreciably, nitroglycerin (25 mg diluted in 250 ml saline) is injected in 2- to 10-ml amounts until systemic effects are seen with pulse elevation. The nitroglycerin counteracts any effects of spasm; if flow then accelerates, additional particulate embolic matter is injected and the same steps repeated until flow remains nearly stagnant. At this point, microcoils are injected to seal the feeding vessel and help prevent recanalization. Medium-length coils are usually selected (7–8 mm) so the coils do not reflux. At times these coils are preshaped into semicircular or spiral forms to prevent reflux from the nearly stagnant vessel and are injected until no flow is seen in the vessel or until coil reflux cannot be prevented.

If particulate embolization results in no slowing of flow, shunting of particles through the larger fistulas of the nidus is probably occurring. One could

then try larger particles (up to 500 μm), though the risk of catheter occlusion would be greater; or one could inject short microcoils to seal the fistulas before resuming particulate embolization. We inject 2- to 3-mm microcoils at this point.

Coils are cut into 2- to 3-mm lengths and are injected to reach the nidus without lodging in the proximal portion of the feeding vessel by the technique described in previous sections. If these coils shunt, slightly longer coils are tried until a size is found that travels distally but does not shunt. Coils are injected until slowing of flow is perceived, well before the point of stasis. Once flow is believed to slow somewhat, embolization with particles is resumed. If shunting is still a major problem, coils are injected until particles lodge in the smaller channels of the nidus. Particulate embolization is then carried out until the flow in the vessel becomes nearly stagnant; the process outlined above is then followed, with the injection of nitroglycerin to combat spasm, the injection of additional particles to reach near-stasis, and the final placement of larger proximal coils for total occlusion.

This process can be carried out in as many separate feeding vessels as can be catheterized and safely embolized, though staging of the embolization may be desirable (Figs. 6.5 and 6.6). Embolization of one feeding vessel per sitting allows the patient to adapt to changing flow patterns and to recover as fully as possible from any potential deficit before additional obliteration is attempted, but the clinical circumstances and ease of additional embolization may influence timing.

In certain cases it is desirable to use only microcoils for an embolization or to eliminate alcohol from the particulate mixture. We avoid using alcohol in vessels supplying the skin, mucous menbranes, or bone so as to avoid necrosis and when swelling of the embolized territory is to be minimized. In cases where geometry is unfavorable, it may be impossible to find a coil length that can travel to and lodge within a nidus to seal larger channels, allowing particle and alcohol embolization to be successful. The only option for that particular feeding vessel may be the injection of coils that lodge proximally and occlude the vessel near the catheter tip. Proximal occlusive coils would eliminate flow from that feeding vessel, perhaps a desirable goal; but they would not reduce the size of the AVM nidus, the ultimate goal.

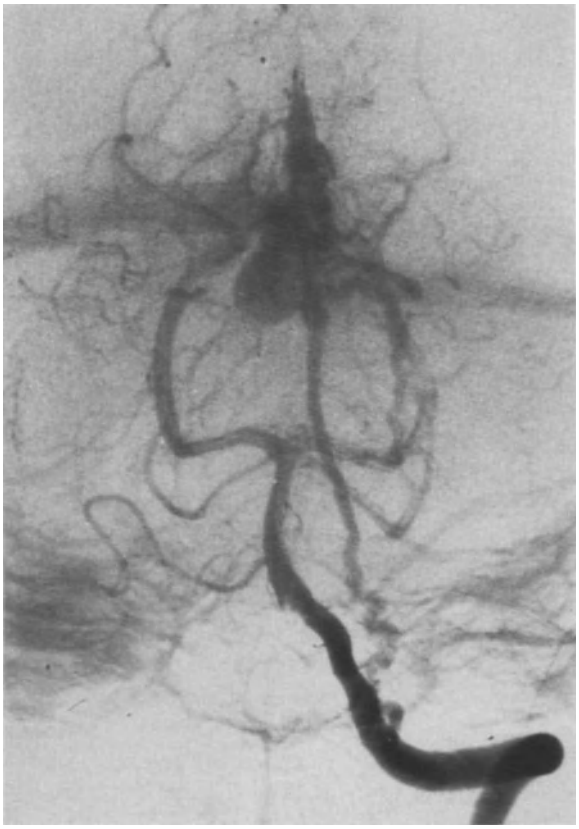
Principles of microcoil embolization as described above for use in brain AVMs are similar to those employed for AVMs in the spine and head and neck, bearing in mind that collateral circulation territories may be at risk and that agent selection may differ from that selected for brain use. Microcoils have proved to be a useful primary agent or an adjunct to additional agents in a variety of neurointerventional settings.

Aneurysms

Aneurysms referred to us for embolization have thus far been giant aneurysms in locations difficult to reach surgically, giant aneurysms that have

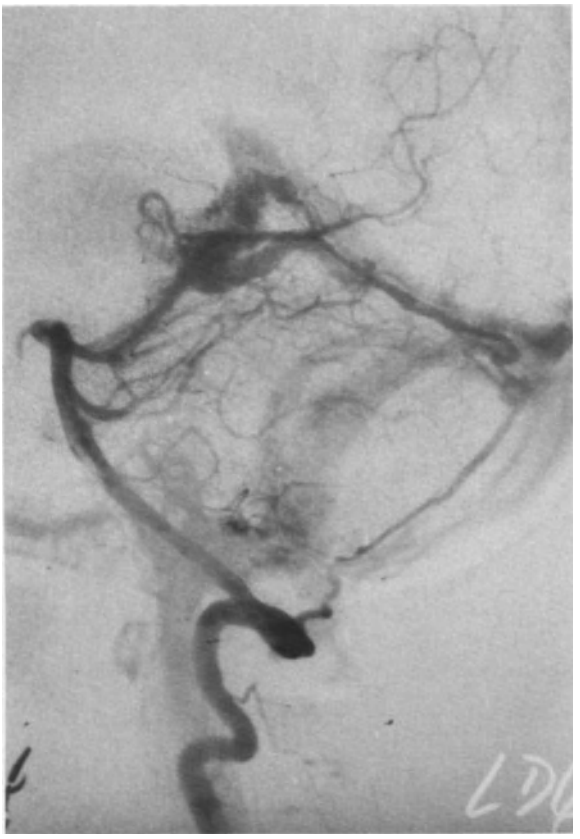
already failed surgical management, or giant aneurysms in patients in whom poor clinical condition precluded surgery. Some success has been achieved in partial or total filling and thrombosis of these aneurysms by the injection of multiple microcoils. Total, permanent thrombosis has not been possible in most cases with current coil technology, and coil modifications are probably required to achieve better results. The concept is promising.

For coil embolization of aneurysms, a superselective catheter (e.g., the Tracker) is directed into the lumen of the aneurysm. It is positioned so the tip of the catheter is stable within the aneurysm for injection of coils. Modification of the tip of the microcatheter may be necessary to achieve stability; it is done by steaming the tip of the catheter over a forming wire at



A

Figure 6.5. AVM embolization using microcoils. (**A&B**) AP and lateral views of a dural AVM demonstrating a large vertebral meningeal feeder. (**C**) Lateral subtracted image of superselective catheter injection into that artery. (**D&E**) Postembolization AP and lateral views showing occlusion of the vertebral supply using particles and microcoils, with the AVM being fed by remaining SCA and PCA branches.



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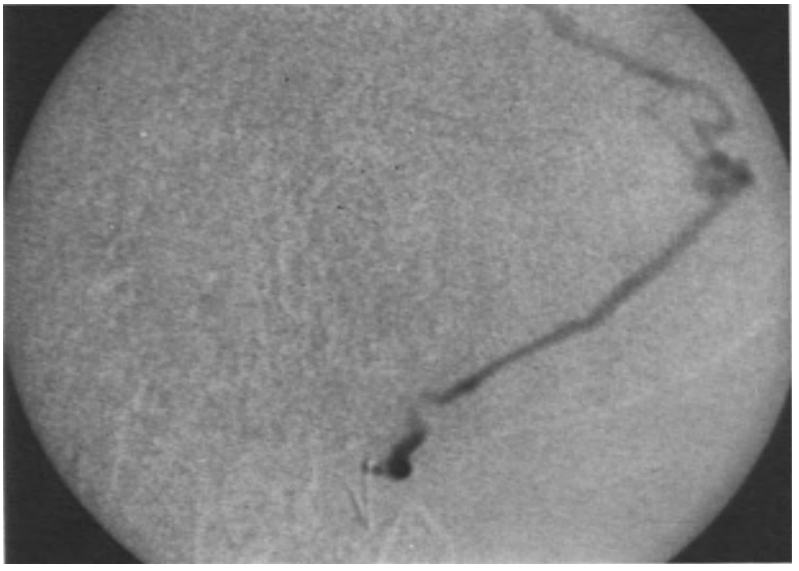

C

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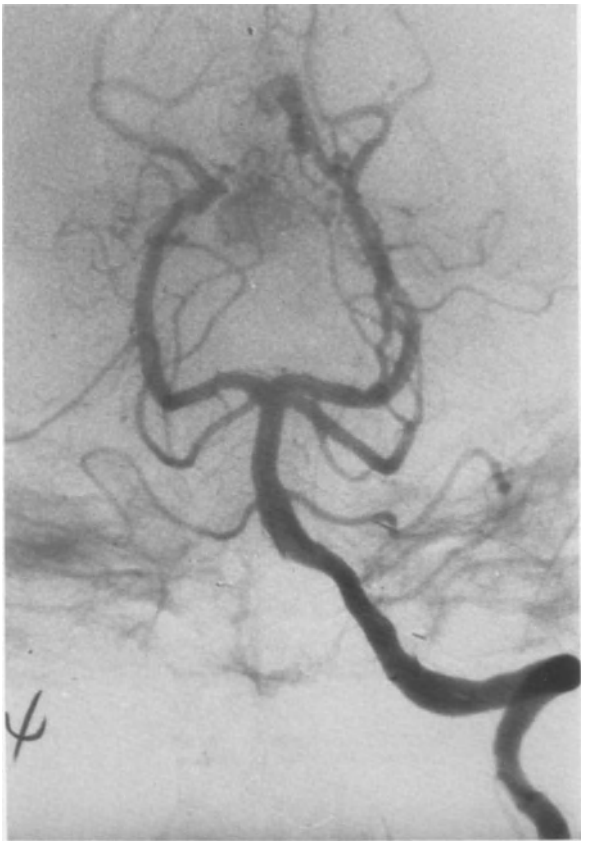
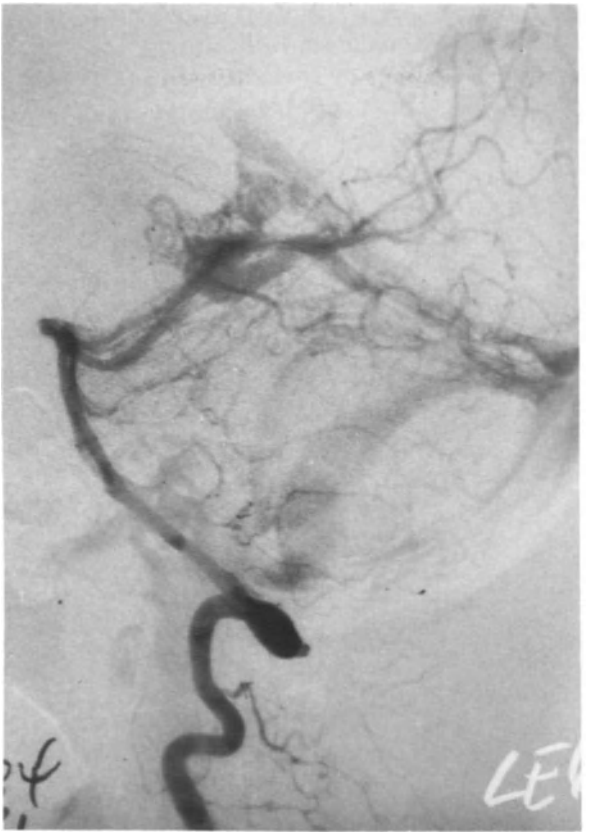


D

Figure 6.5 (*continued*)

its tip before it is introduced into the artery. Once the catheter is seated in the aneurysm, preshaped microcoils are injected (Fig. 6.7).

A coil length is selected that allows the coil to emerge from the tip of the catheter in the aneurysm and reform its circular or spiral shape within the lumen. It should be of a length that fills as much of the aneurysm as possible without projecting significantly into the lumen of the parent vessel, usually 7 to 10 mm, or full length for large aneurysms. Short coils are less desirable, as reflux from the aneurysm lumen into the lumen of the parent vessel is usually to be avoided. As described in previous sections, aneurysm coils are given complex shapes before introduction into the catheter using a hemostat or the fingers, allowing coils to emerge from the tip of the catheter and turn into the lumen without placing undue stress on the wall of the aneurysm; it also helps ensure stability of the coil within the aneurysm. The



E

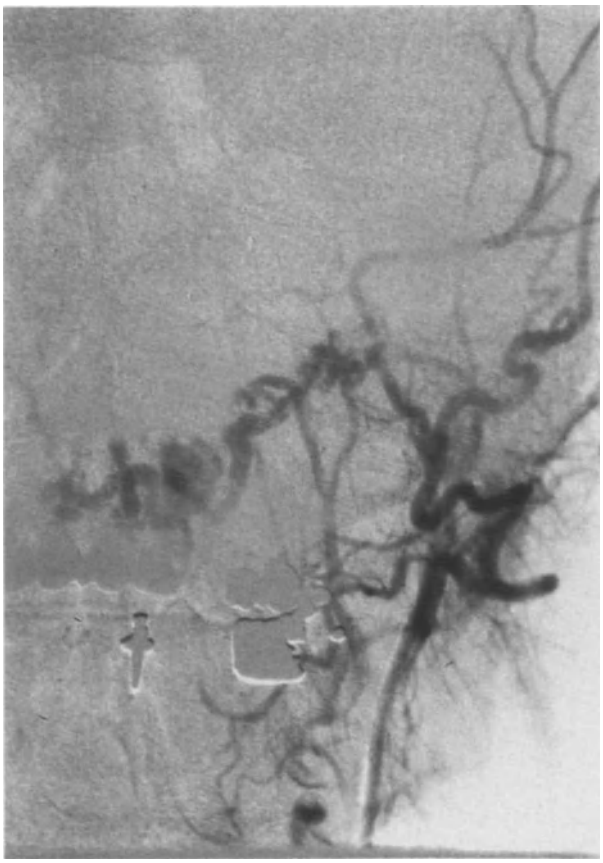
Figure 6.5 (*continued*)

Hilal platinum microcoil is soft and flexible, and no aneurysm we have embolized to date has ruptured as a result of coil injection. The coils are carefully delivered into the aneurysm by injecting saline into the catheter behind each coil using 3- or 1-ml syringes locked onto the catheter hub. The progess of coil placement can be easily monitored by fluoroscopy. Roadmapping digital subtraction helps to identify the boundaries of the aneurysm and its parent artery.

After a number of coils have been placed within the aneurysm, successive coil placement becomes more difficult. With much of the lumen filled by earlier coils, less room is available for later coils to enter the aneurysm lumen and assume their given shape. Later coils lodge within earlier coils, and injection from the tip of the catheter may cause movement of the catheter tip away from its desired position well within the aneurysm. Once coil placement

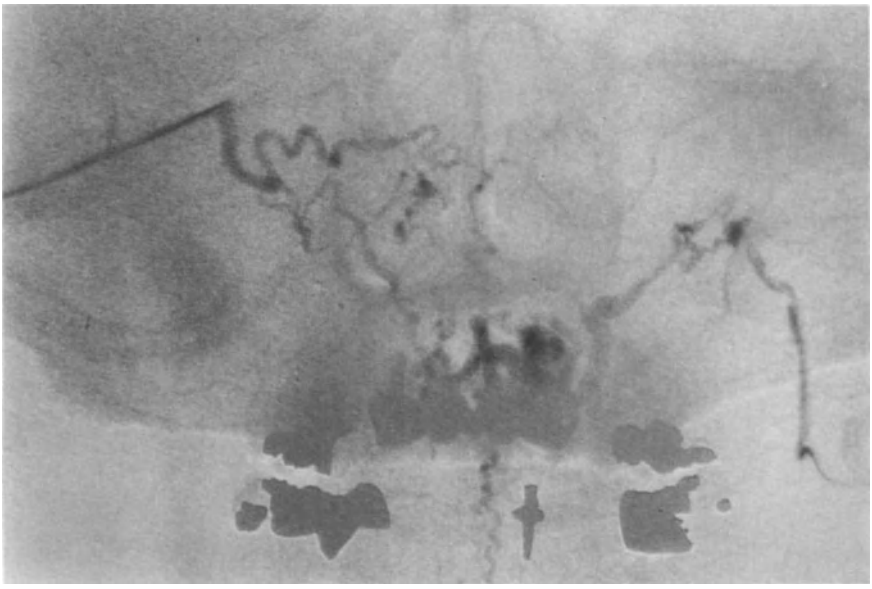
has become difficult, and there is danger of delivering coils outside the aneurysm or of perforating the aneurysm from forceful injection, the embolization is terminated. The microcatheter is removed from the aneurysm, and an angiogram of the parent vessel is obtained to determine the extent of any residual lumen.

Regardless of the appearance of the residual lumen, if any, at the con-



A

Figure 6.6. AVM embolization using microcoils. (**A**) AP view of a dural AVM, showing multiple occipital feeders. (**B**) AP view with injection into a superselective catheter placed in one of the feeding branches. (**C**) AP view after occlusion of the first feeding branch using particles and microcoils. (**D**) AP view with injection into a superselective catheter in the second feeding branch. (**E**) Subsequent image following injection of particles, with slowing of flow and dilatation of the proximal portions of the feeding arteries. (**F**) Final superselective injection following placement of microcoils to seal proximal branches. (**G**) Postembolization angiogram showing elimination of the AVM. (**H**) Plain film appearance of microcoils at the conclusion of the procedure.



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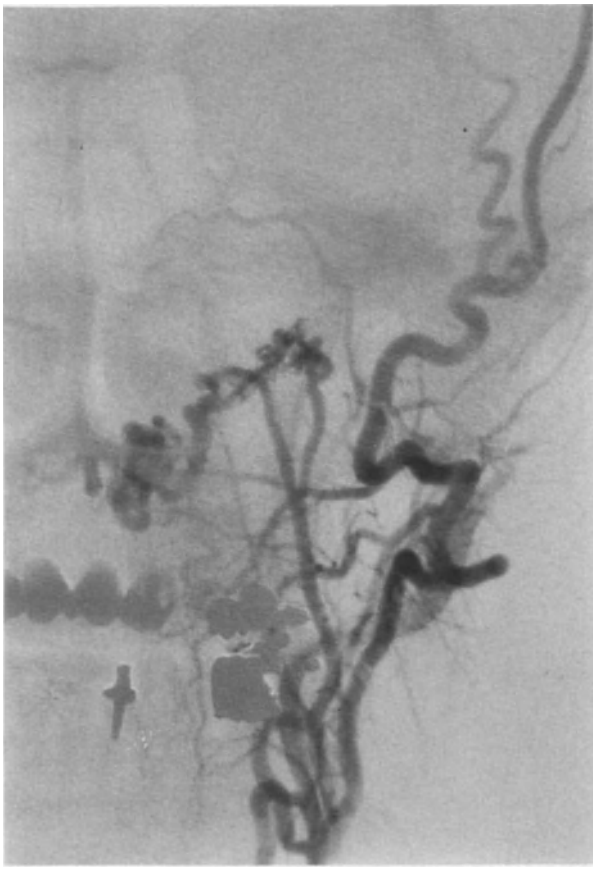

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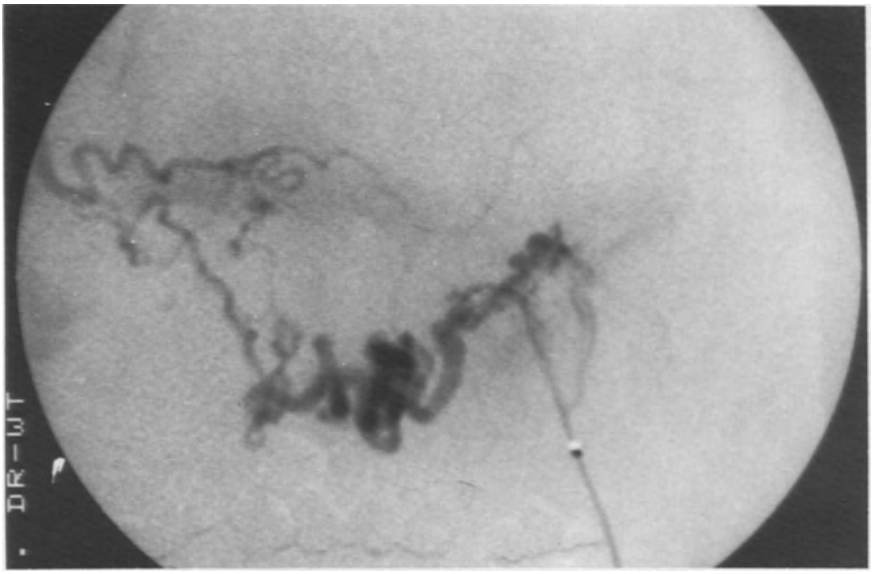

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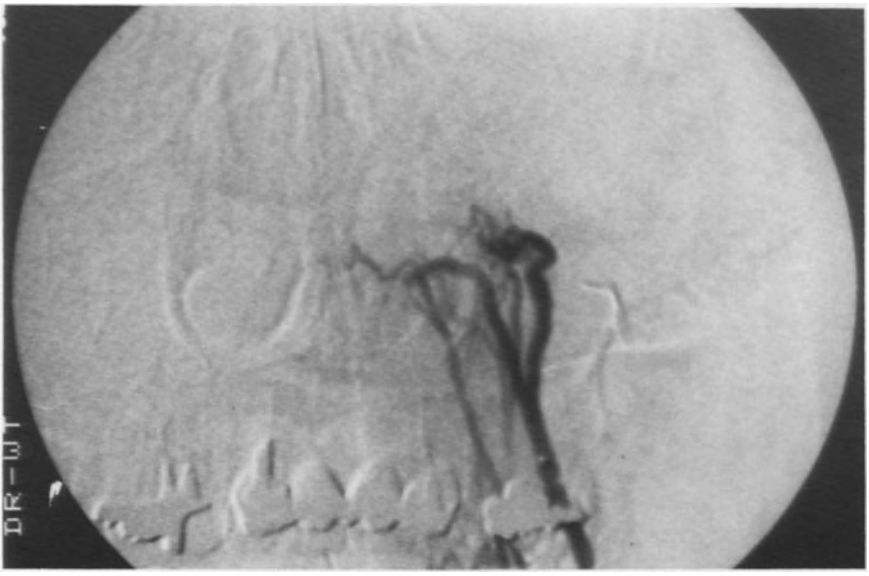

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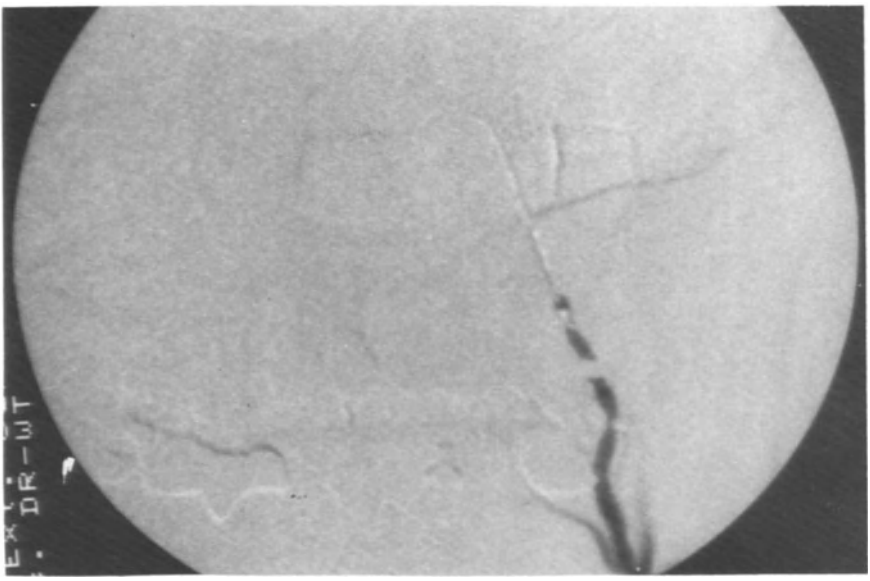

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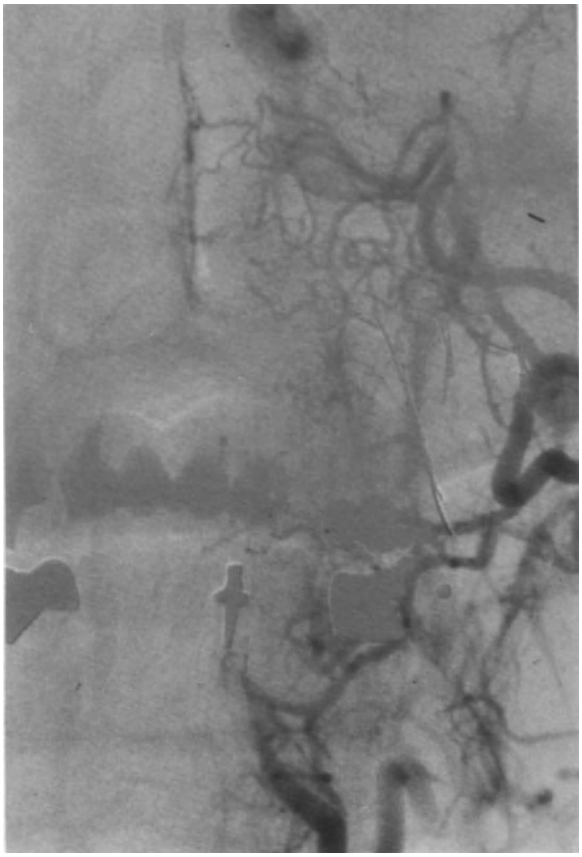

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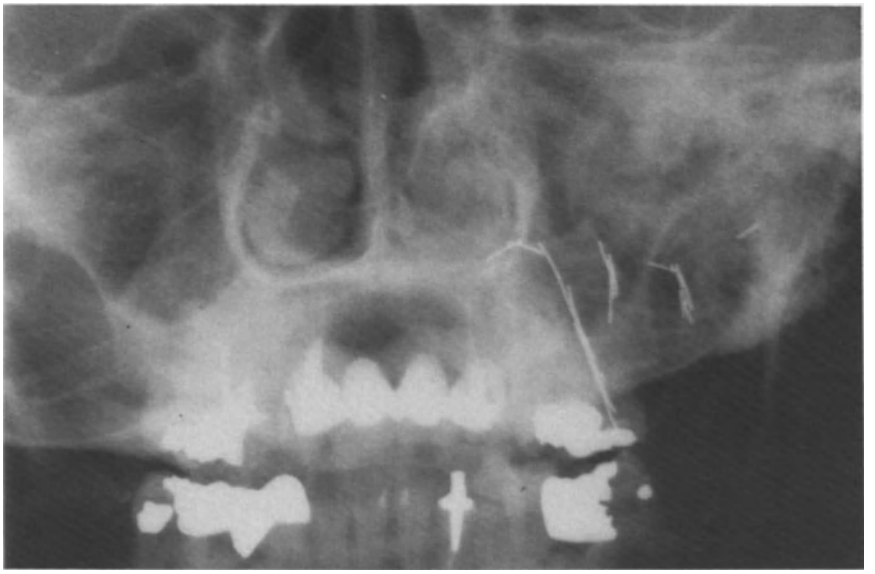
Figure 6.6 (*continued*)



H

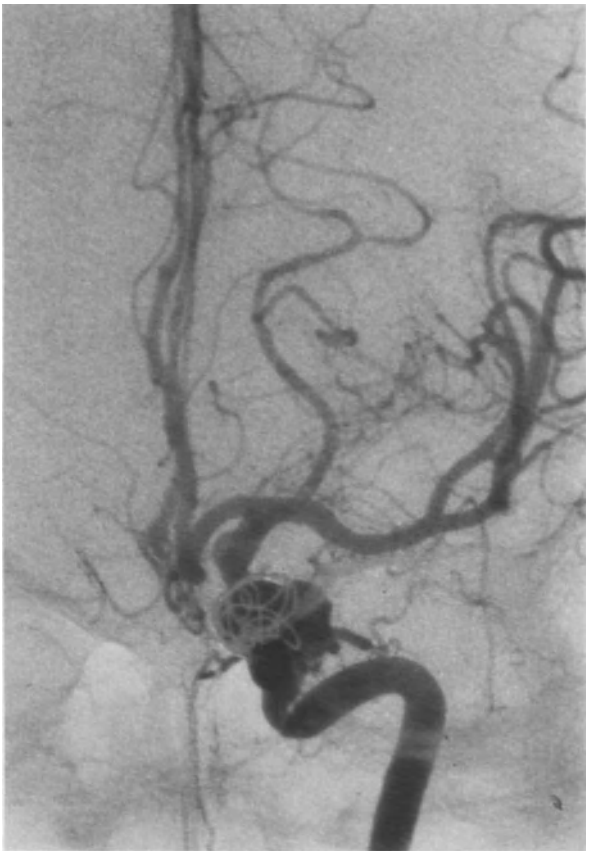
Figure 6.6 (*continued*)

clusion of the procedure, a follow-up angiogram is desirable after several months for reassessment. Further interval thrombosis may have occurred, or the size of the residual lumen may have expanded as a result of compacting of the interwoven coils within the aneurysm over time. Reembolization may be indicated if the residual lumen has enlarged, depending on the therapeutic goals and expected results from reembolization. If the purpose of the embolization was simply to relieve symptoms related to mass effect or pulsation, as in cases of cavernous carotid aneurysms, partial thrombosis may be all that is required for symptomatic relief (Fig. 6.8).

Others have used coils in combination with balloons or balloons alone to effect complete thrombosis of aneurysm lumens. Both coils and balloons have their drawbacks. Either could escape from the aneurysm at the time of embolization: the coil at the point of injection and the balloon at the point of detachment. Each has been associated with later enlargement of residual aneurysm lumens. One method may have advantages over the other for any given aneurysm. Neither is perfect.

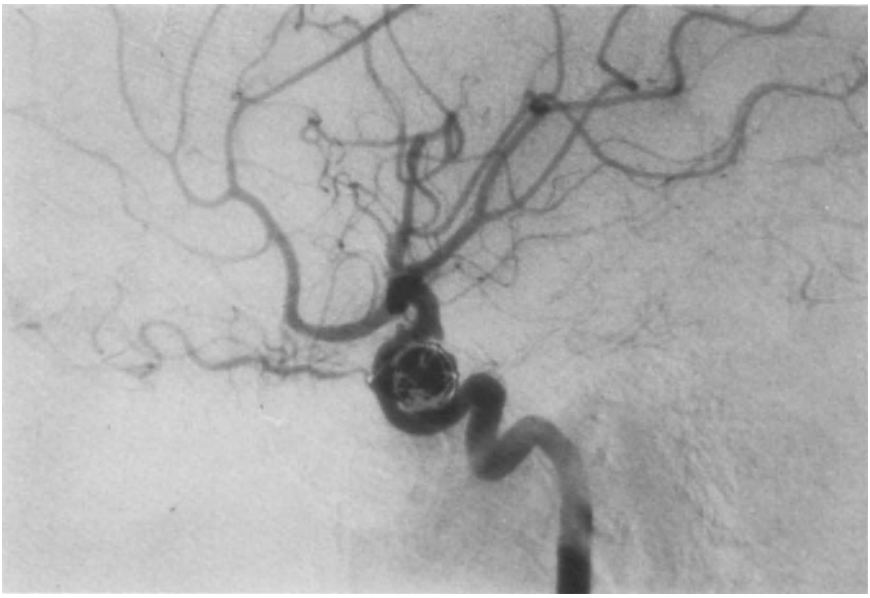
Although we have not lost coils from an aneurysm lumen during embolization and have not ruptured an aneurysm with microcoil injection to date, those potential complications exist. One problem we have encountered is that of thromboemboli. When an aneurysm is partially filled with thrombus, particularly when that thrombus is not organized, it is possible to force

thrombus from the lumen of an aneurysm by placing a catheter in the aneurysm or by injecting coils into the aneurysm. Embolic particles may reflux from the aneurysm into its parent vessel and be flow-directed into normal vascular territories, causing transient or permanent neurological deficits. In our experience, presumed emboli have resulted in complications ranging from transient ischemic attacks (TIAs) to stroke and death. There have been no known complications from emboli forming on small portions of coils



A

Figure 6.7. Aneurysm embolization using microcoils. (**A&B**) AP and lateral views of a cavernous carotid aneurysm after a previous partial embolization using microcoils. (**C**) Lateral view showing superselective catheter placement within the aneurysm to allow further coil embolization. (**D&E**) AP and lateral views after the second embolization showing further packing of the aneurysm lumen with coils and a smaller residual lumen. The patient's symptom, headache, improved.



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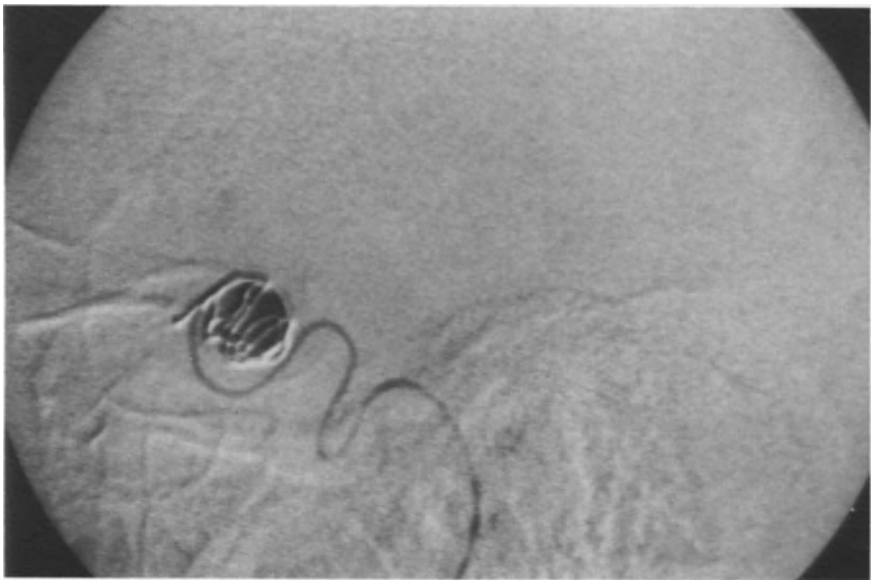

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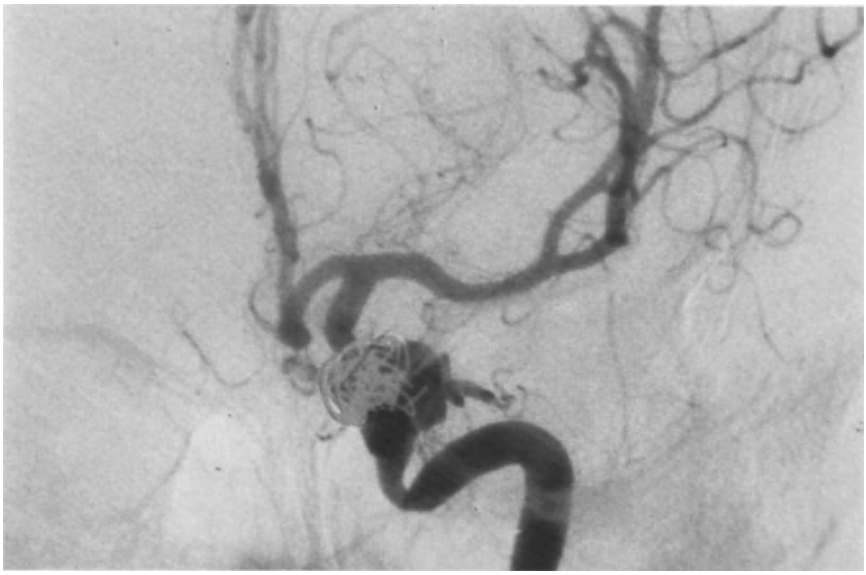
Figure 6.7 (*continued*)



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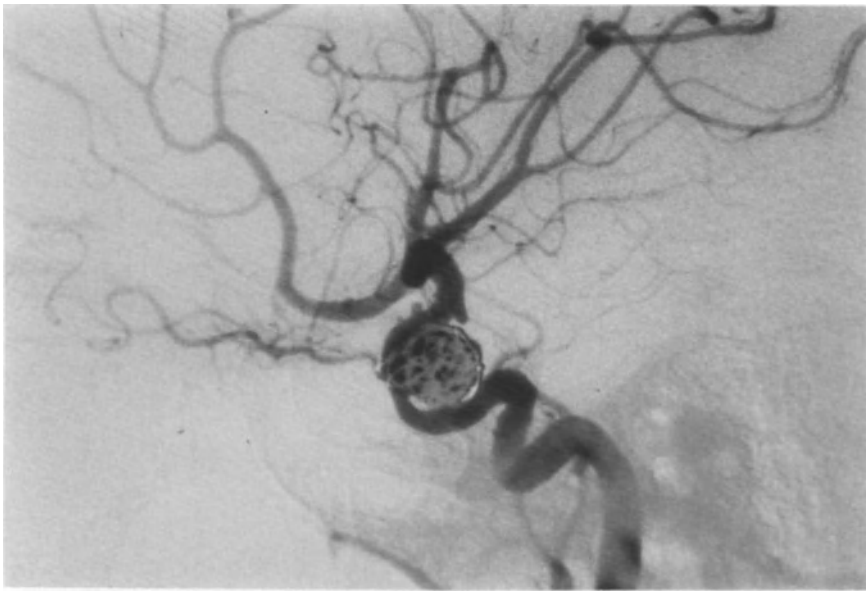

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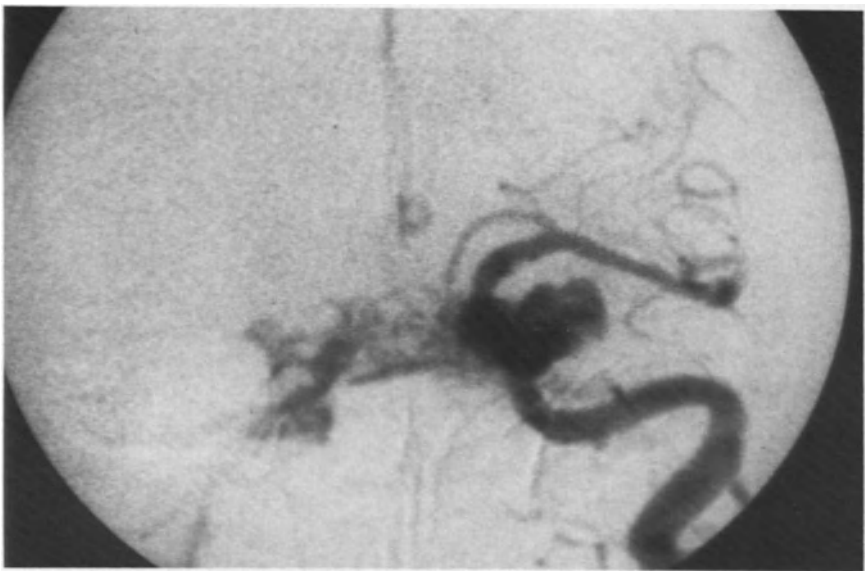
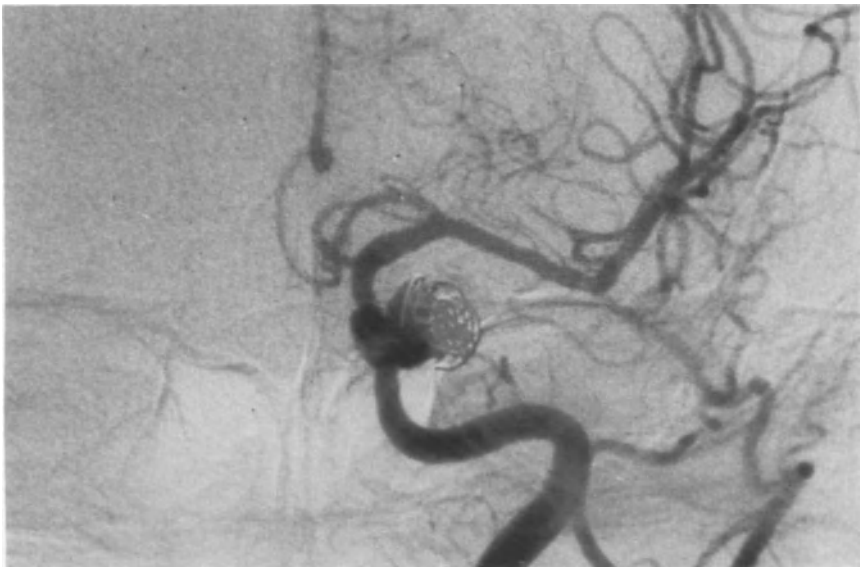
Figure 6.7 (*continued*)



A

B

Figure 6.8. Cavernous carotid aneurysm and fistula embolization using microcoils. (**A**) AP view of carotid injection showing an aneurysm and fistula. (**B**) Superselective catheter coursing through the ICA to enter the lesion, with initial microcoils placed laterally. (**C&D**) Postembolization AP and lateral views showing elimination of the fistula and partial filling of the aneurysm. (**E&F**) Follow-up angiogram after several months showing a more compact arrangement of coils and a slightly larger residual lumen.



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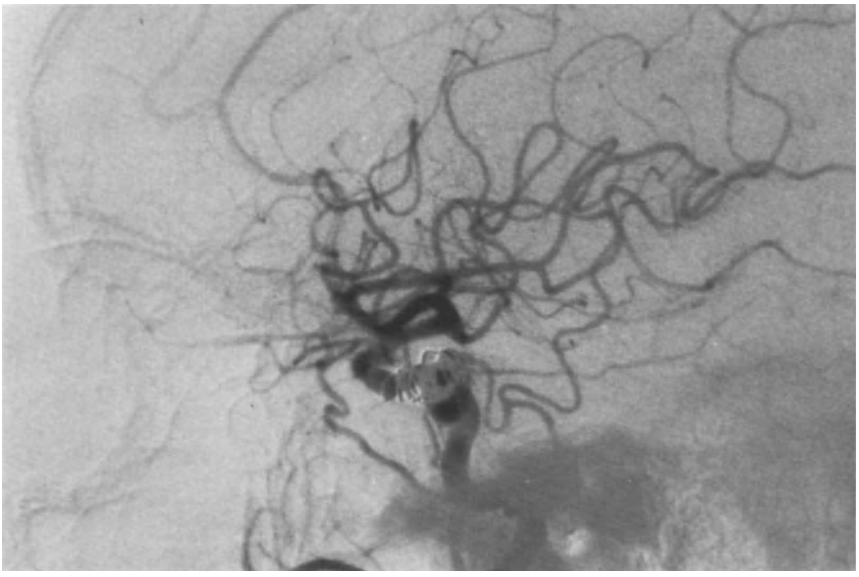

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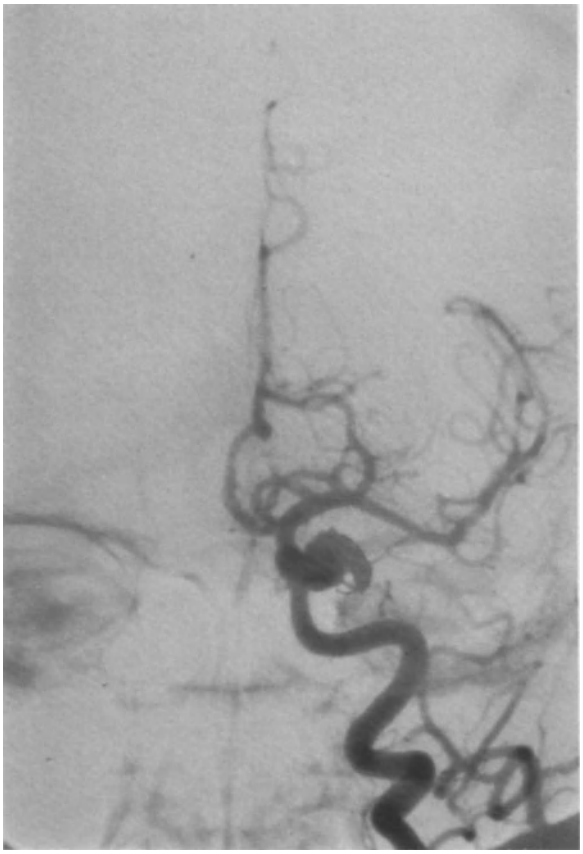
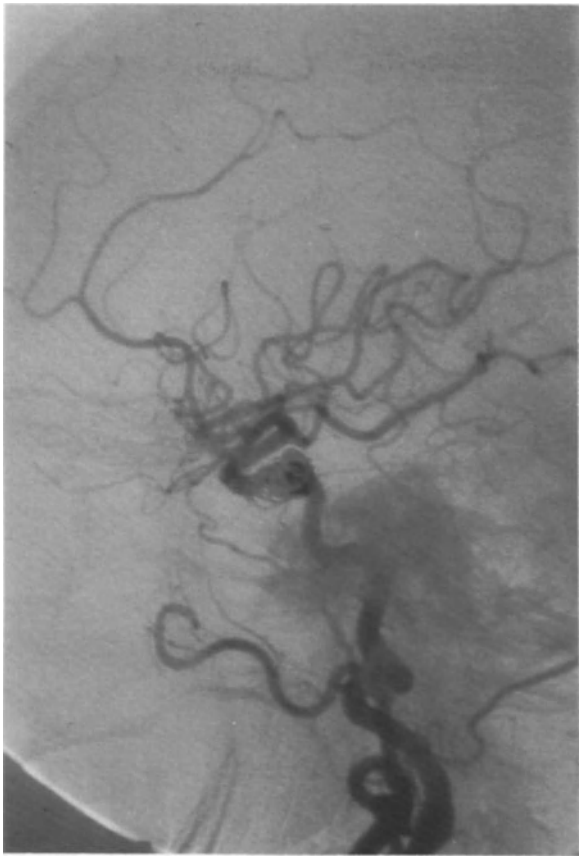


E

Figure 6.8 (*continued*)

projecting into the parent vessel from an aneurysm lumen left to attempt thrombosis of the neck of the aneurysm.

Modifications of the standard Hilal microcoil have been tried for aneurysm embolization. Bipolar coils designed to create a small electrical current to induce thrombosis in the aneurysm were manufactured and injected, but they proved to be much stiffer than the standard platinum and Dacron coils and therefore more difficult to inject safely. Until further improvements are made, injection of Hilal microcoils in the manner described can result in total thrombosis in some cases, partial thrombosis in most, and symptomatic relief in some cases of partial thrombosis. Embolic complications were the most commonly encountered problem but were seen in only a few patients.



F

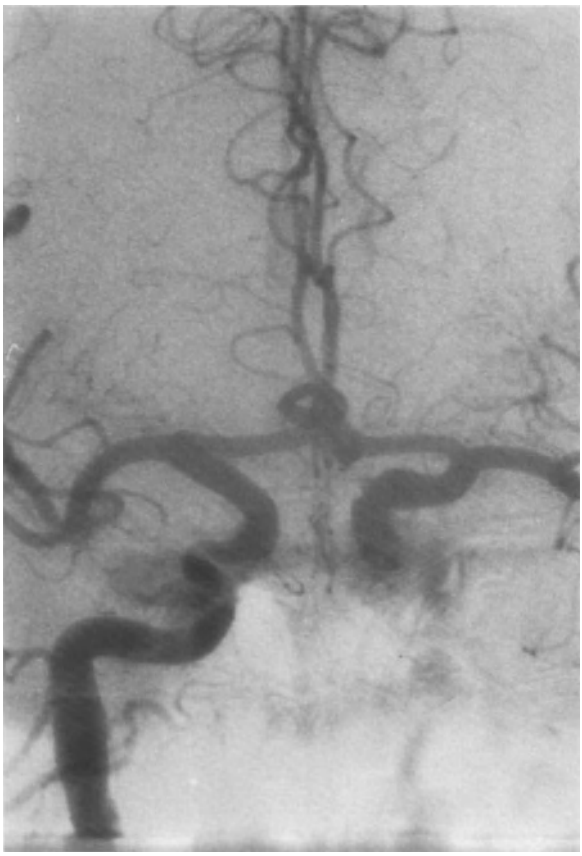
Figure 6.8 (*continued*)

Fistulas

As with closure of fistulous communications in an AVM nidus, microcoils can be used to close other fistulas in the brain or spine. Microcoils are well suited for this purpose (Fig. 6.9).

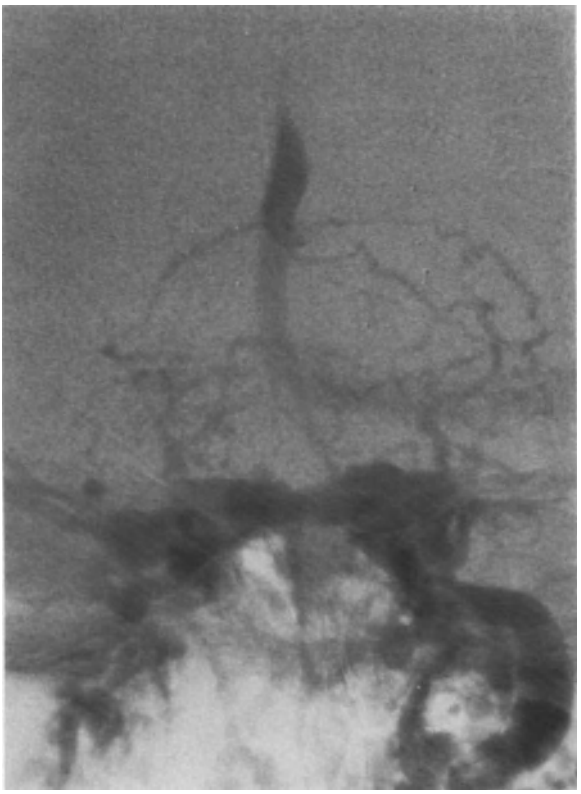
A microcatheter is directed into the fistula and its position confirmed by injection of contrast. The catheter should be well seated if reflux of coils could pose a serious hazard, as in the case of carotid-cavernous fistulas where catheter retraction into the carotid lumen and coil injection into the carotid territory should be avoided. In such cases it may be desirable to preshape the tip of the catheter by steaming it over a forming wire so the tip is better anchored against the wall of the vessel.

Appropriately sized coils are cut, usually of medium length, and injected



A

Figure 6.9. Carotid-cavernous fistula embolization using microcoils. (**A**) AP view of right carotid injection showing the supply of both ICA territories and slight filling of a left carotid-cavernous fistula. (**B&C**) AP and lateral views of the left carotid injection showing that the entire left carotid blood flow is into the shunt. (**D**) AP view with a superselective catheter in the fistula prior to embolization. (**E**) Subsequent image after initial coils are placed, reducing the shunt. (**F**) Final superselective injection after all the coils are placed, with no filling of the shunt. (**G&H**) AP and lateral angiograms of the left carotid artery after superselective catheter removal, showing early partial filling of the petrosal sinus, a small residual shunt. The cavernous sinus syndrome totally resolved in this 81-year-old patient. (**I&J**) Plain film views of the final coil arrangement.



B

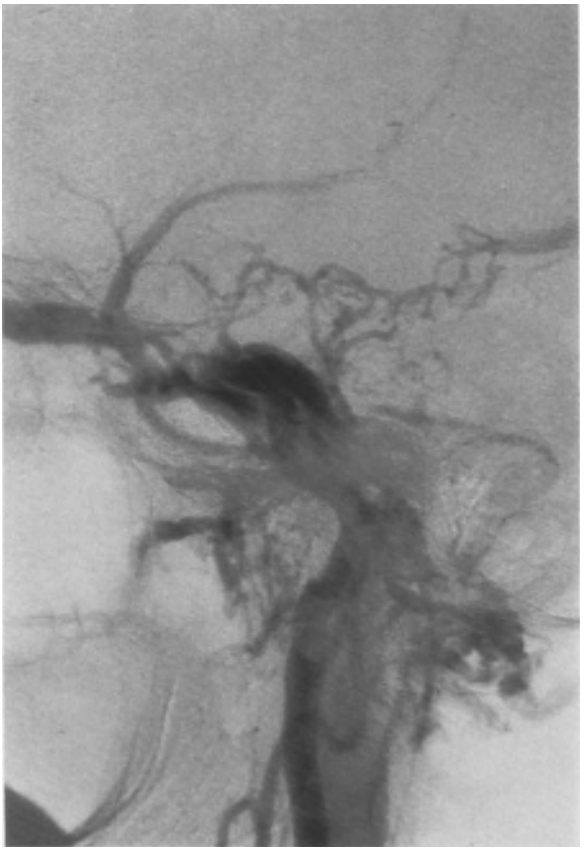
Figure 6.9 (*continued*)

into the fistula by the technique of coil embolization described in previous sections. Coil length and shape may be modified to ensure that the coils lodge within the fistula without shunting, and coil injection is carried out until closure or near-closure of the fistula, depending on therapeutic goals.

Our experience with microcoil embolization of pure fistulas is limited compared to our experience with AVMs and aneurysms. Coils have been used successfully for closure of carotid-cavernous fistulas without complication and can serve as an alternative to the use of balloons.

Conclusions

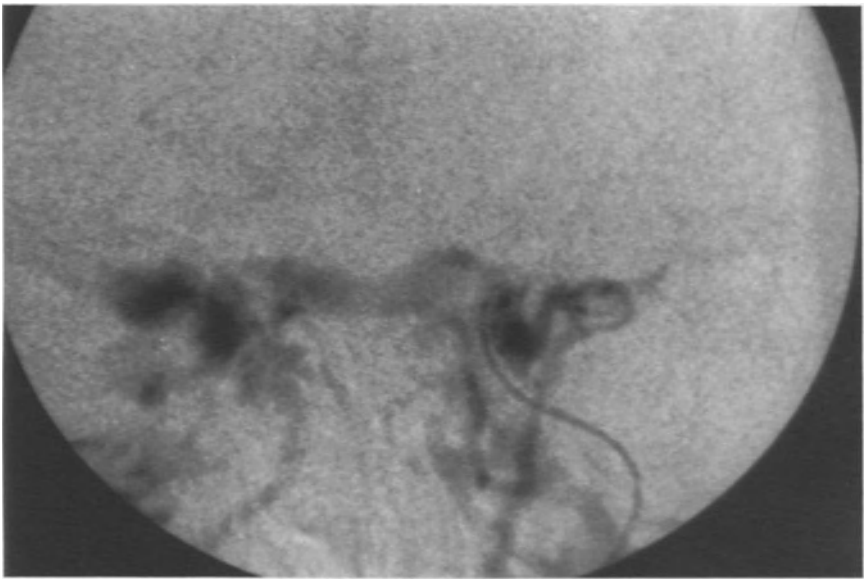
Microcoils have been used with success in a variety of neurointerventional procedures, including embolization of AVMs, giant aneurysms, and fistulas. They may be used alone or in conjunction with other embolic agents or



C

Figure 6.9 (*continued*)

devices, and are now approved by the U.S. Food and Drug Administration for general use. Injection techniques have been developed to achieve optimal results and are outlined above. Familiarity with microcoils—their advantages, disadvantages, limitations, and behavior—is essential prior to use. Improvements in coil technology and delivery systems should continue to occur, resulting in even better outcomes in patients referred for neuroembolization.



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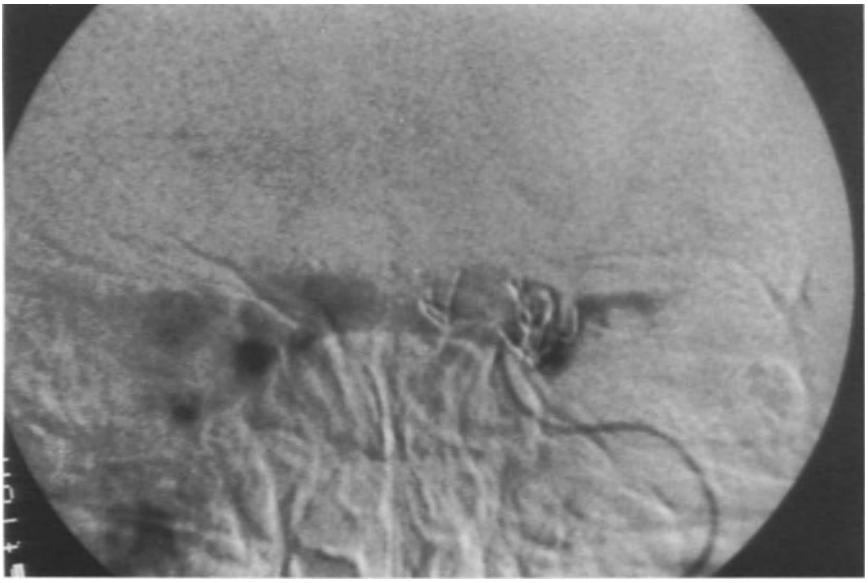

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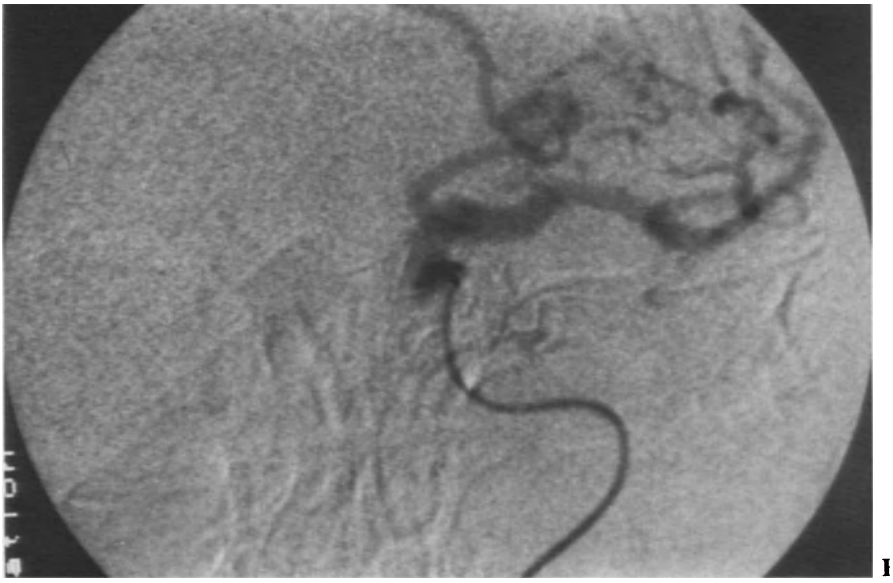

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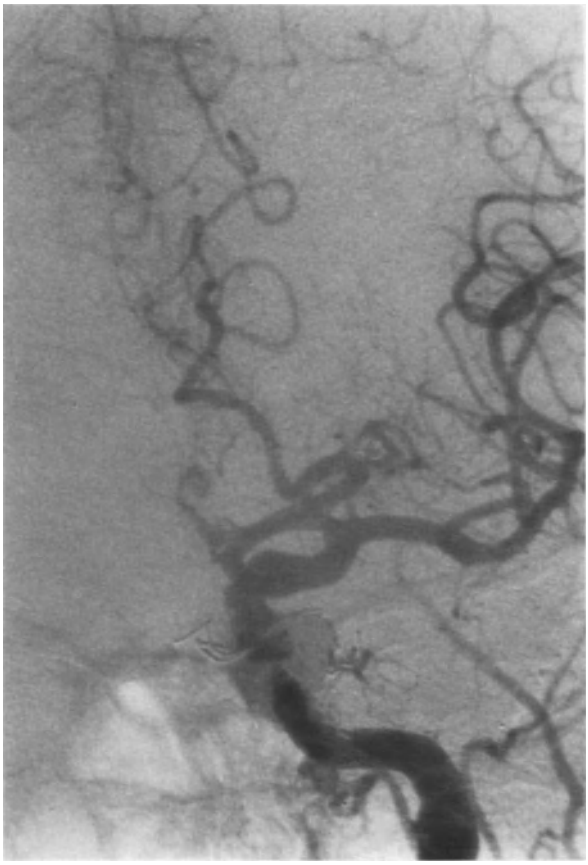

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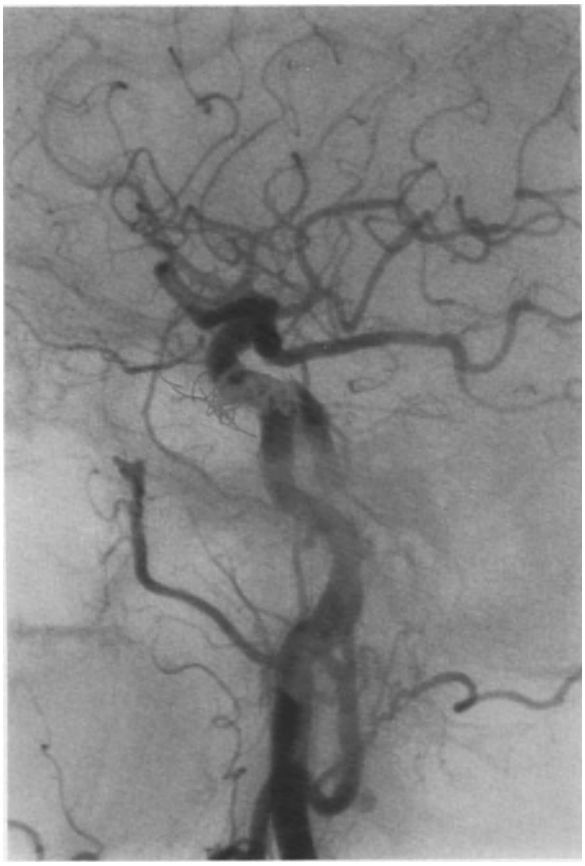

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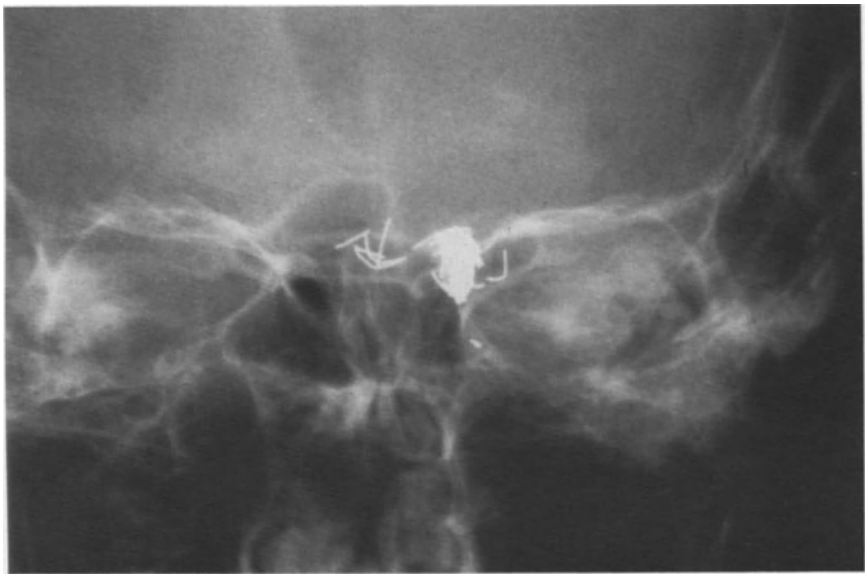

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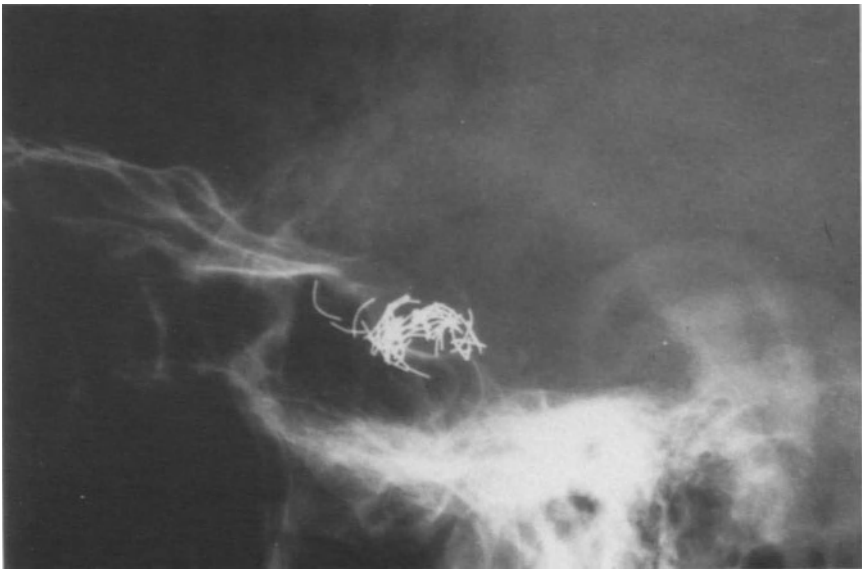


J

Figure 6.9 (*continued*)

Discussion

Aneurysms: Balloons, Coils, and Endothelialization

Dr. Debrun: If we can put balloons into an aneurysm, then certainly coils can be introduced into an aneurysm lumen with similar success.

Dr. Berenstein: Those prongs at the neck of the aneurysm look dangerous to me. They remain when you introduce the last part of the coil.

Dr. Hilal: It is done deliberately. As you are injecting the coil, you withdraw the catheter. This is what I call strengthening the neck of the aneurysm. I plan to have some prongs coming down, for example, into the tip of the basilar artery so that when they become endothelialized they strengthen the wall of the aneurysm.

Dr Berenstein: Do you not believe that they may become the source of emboli?

Dr. Hilal: My theory is that we should keep these patients anticoagulated on aspirin or low dose heparin for several weeks until the coils become endothelialized.

Dr. Berenstein: What evidence do we have that they will become endothelialized?

Dr. Hilal: Anything you place in the vascular system becomes endothelialized. Anything. I know that the pellets become endothelialized and that the coils in the AVMs become endothelialized. I saw them under the microscope with Dr. Stein. If you do not have complete filling of the diameter of the vessel with coils, they are almost exteriorized after a while. Like any foreign body, endothelium grows over them. As I have already mentioned I was trying to take advantage of this fact to strengthen the aneurysmal neck. I am trying to "weave a basket" with the coils inside the aneurysm.

Dr. Berenstein: Perhaps just changing the flow patterns within the aneurysm is sufficient.

Dr. Hilal: I agree. I also do not have the problem of the balloon detaching from the catheter, which, by the way, Dr. Moret tells me is also not a big problem for him. I simply thought that that problem would be avoided with the coils.

Dr. Debrun: I have found when occluding aneurysms of the vein of Galen with coils that sometimes when you start to plug the aneurysm it is easy because all the coils coil into the bulge; but when you reach the endpoint, when you want to complete the occlusion, it is sometimes difficult to avoid having the coil detach and remain in the parent vessel, with subsequent risk of thrombosis of that vessel. In such cases as vein of Galen aneurysms we can often retrieve the coils because they are large. I can attach a thread to the tip of the coil so if its position is not ideal I can pull it out. With the tracker catheter it is impossible to attach a thread to the coil and remove it if its position is not satisfactory.

Dr. Hilal: All my coils are very small. How long is the coil that you place in the vein of Galen aneurysm when you open it up?

Dr. Debrun: You can use any type up to 20 cm.

Dr. Hilal: There is the difference. Hilal coils are 5 to 6 mm.

Dr. Berenstein: Do you shape them with your finger to make them perfect?

Dr. Hilal: I use the clamp and then mount it back into the introducer.

Dr. Pile-Spellman: Platinum is not thrombogenic and its electromotive force is as close to zero as you can get. Therefore it is probably the copper that is causing the thrombosis.

Dr. Hilal: It is both. You need two electrodes.

Dr. Pile-Spellman: One has an EMF of zero. Copper is extremely thrombogenic. Maybe you just need copper?

Dr. Hilal: No, both are necessary. When they are this small you do not see them. Platinum is essential for radioopacity, and you want to know where they are. They also have fibers.

Fibrolysins and Antifibrolysins

Dr. Hilal: Individuals involved in interventional neuroradiology have a certain complication rate, everyone does. Cardiopulmonary rescusitation (CPR) must be available in case of an adverse outcome. We should also have TPA or some other agent available in the event that there is excessive thrombosis that could potentially be reversed.

Aneurysms Amenable to the Introduction of Coils

Dr. Igor Kachkov: Is it possible to use your method for aneurysms of all kinds and in all locations?

Dr. Hilal: We have worked at the base of the skull, and I think today that cavernous sinus aneurysms are a primary target for endovascular surgery. Without question it is the best indication, but I believe we can place catheters anywhere we need to. It is an easy, controllable procedure. For example, we can put them in ophthalmic artery aneurysms that are large and calcified. I do not wish debate the neurosurgical indications versus endovascular indications, but clearly if the endovascular technique is perfected we have the potential to go anywhere in the brain.

Factors Related to Aneurysmal Rupture

Dr. Shalva Eliava: All neurosurgeons are concerned about the rupture of aneurysms during surgery. What do you do if rupture occurs?

Dr. Hilal: Dr. Moret addresses that point. I think we have a better chance of avoiding rupture than does a neurosurgeon. The aneurysm is better protected in its natural habitat before dissection.

Dr. Solomon: It can rupture even in that habitat, though.

Dr. Hilal: Certainly it can rupture, and it can also thrombose. We all experience the same problems. I have no control over the hemorrhage—you are right. Dr. Scheglov has popularized the technique of two balloons. One of its applications is the control of hemorrhage during aneurysmal rupture. Should a rupture occur you can occlude the parent vessel with the second balloon.

Dr. Eliava: Do you use the two-balloon technique?

Dr. Hilal: I used two balloons for the last 10 years when I was using pellets. In fact, I was using three or four balloons in the brain at the same time. At present, I am not using the two-balloon technique, and in the examples I presented I did not use two balloons. Our technique is now sufficiently developed that we are not afraid of rupture even when we use only one balloon.

Dr. Moret: When we are dealing endovascularly with an aneurysm, we do not change the outer atmosphere of the aneurysm. Hence the external pressure on the sac is intact. That is not the case when the skull and the fissures are opened to reach the

neck of the aneurysm. Therefore, in my opinion, even if the aneurysm is fragile and even if the dome of the sac is weak, we do not incur the same risk of rupture as the neurosurgeon during the surgical approach. It is likely that some aneurysm will rupture during endovascular occlusion, but in my experience with more than 40 aneurysms it has not happened. We work carefully and slowly, and we keep external pressure on the sac.

There is another point. We do not try in every case to pack the sac of the aneurysm, and we do not bother the fundus of the aneurysm, which is its weakest point. We just try to occlude the neck. These anatomical factors and our attempts to occlude the aneurysmal *neck*, probably diminishes the chance of rupture.

Dr. Pile-Spellman: Dr. Moret's series is excellent, and to the Western world he is a pioneer in treating "clippable" aneurysms. Yet I disagree with his statement that we do not or should not worry about aneurysmal rupture. Aneurysm surgery and endovascular occlusion are both risky businesses; and because Dr. Moret has been skillful does not mean that a rupture will not occur next week, next month, or next year.

One other comment regards whether an aneurysm should be explored surgically first. When surgical exploration is undertaken but you are unable to clip the aneurysm, and within the next few days balloon occlusion is attempted, the combined procedures probably increase the risk of rupture during the latter procedure.

Dr. Moret: I never said that rupture of an aneurysm cannot occur using the endovascular approach.

Dr. Pile-Spellman: But you did say that we should not worry about it.

Dr. Moret: No, I said that that rupture does not occur as freguently as might be anticipated. At this juncture, all we know about aneurysms come from the surgical literature. We have something to learn about aneurysms and interventional radiology. Of course it will happen, but the frequency of rupture will not be as high as expected.

Dr. Debrun: Neurosurgeons have told me that aneurysms exist in which the neck, not the dome, is the fragile portion, so it is not always the dome that ruptures.

Dr. Berenstein: I would like to propose that any team of neurosurgeons and neuroradiologists who wish to explore aneurysms initially put a little glue around the aneurysm just in case it should rupture.

Dr. Solomon: You have not painted a fair picture of what happens surgically or what the appearance of an aneurysm is for several reasons. First, aneurysms occur in the subarachnoid space. Most aneurysms are not surrounded by brain except perhaps in cases where they have ruptured in one spot and the brain sealed it off. It is possible that one side of the aneurysm is adherent to brain, and that is what may have saved the patient's life. Surgically, it is a mistake to disturb that brain tissue prior to clipping the aneurysm. The second point is that we follow the technique outlined by Dr. Yasargil of working along the cerebrospinal fluid (CSF) cisterns. The idea is to not disturb the brain and to stay in the parent vessel; we follow along this vessel to find the aneurysm neck and clip it, thereby obliterating the aneurysm. You have implied that everything is wide open, the aneurysm is completely exposed, and the field is visualized; and only then is a clip placed on the aneurysm. That is not the case.

Dr. Pile-Spellman: Simply opening the head and removing CSF brings about decompression of the intracranial compartments.

Dr. Holtzman: We now often use spinal drainage during the acute phase of aneurysm rupture in preparation for surgery. CSF release usually accompanies the craniotomy. With this technique there has not been evidence of increased aneurysmal rupture. It

was always contended that maintaining CSF pressure dynamics might be relevant to preventing rupture of an aneurysm; and altering those dynamics was potentially dangerous. In addition, during direct surgery on the aneurysm we clear the field of CSF.

Dr. Solomon: It is not the CSF that holds the aneurysm together. It is one of two things: (1) brain adherent to the aneurysm, or (2) clot that is formed in the cistern around the aneurysm. One should not disturb that clot lest there is a predisposition to rerupture. Therefore the area around the dome of the aneurysm should not be disturbed until the neck is secured.

Dr. Taveras: Do you control the blood pressure during the operation?

Dr. Solomon: Sometimes, but if you are in a situation where the brain is already ischemic you are forced not to. You cannot reduce the pressure because you have to deal with the secondary effects. Sometimes we have to work under full pressure. In situations where we can safely lower the pressure, it is a good thing to do. Most of the time we are not able to do that, and sometimes we utilize temporary clips.

Dr. Moret: It is difficult to understand that you are not changing anything in the physiology of the aneurysm wall as you approach an aneurysm surgically.

Dr. Solomon: We are, but it is not significant.

Dr. Moret: Perhaps. Even if you are changing things very little, though, it changes the risk of aneurysmal rupture during a surgical approach versus an endovascular approach.

Dr. Berenstein: Does an aneurysm usually rupture when it is being dissected rather than during the exposure of the fissure and the drainage of spinal fluid?

Dr. Solomon: In my experience, no aneurysmal rupture could be related to simply draining the CSF. Intraoperative ruptures occur when the surgeon is manipulating the aneurysm and dissecting around it, which of course is necessary in order to prepare the neck for clipping. If it ruptures at this stage of dissection, temporary clips can be used to control the hemorrhage. If the aneurysm should rupture while you are draining the CSF, there is little or almost nothing that can be done. I believe there is no more risk of rupture than in the neuroradiology suite and that simple craniotomy does not cause aneurysmal rupture. I have never seen it.

Dr. Stein: The proof of the pudding lies in the eating, and with experienced surgeons the chance that an aneurysm will rupture before the neck is visualized by current techniques is rare. Once the neck has been exposed and further exposure of the aneurysm is taking place, however, it is possible that rupture can occur. At that point placement of temporary clips or clipping the neck and subsequently altering the clip position is feasible for controlling the rupture. Therefore intraoperative aneurysmal rupture before the aneurysm can be controlled is not a consideration in modern-day surgery.

Dr. Taveras: What percent of the time does aneurysmal rupture occur before the aneurysm is surgically exposed?

Dr. Stein: I would estimate less that 1%. A rupture could not be controlled at the point the surgeon starts to expose the brain or dissects along the parent artery but has not yet reached the neck.

Dr. Berenstein: What about the possibility of rupture with induction of general anesthesia?

Dr. Stein: It would be rare with qualified personnel who do not allow the pressure to get out of control as induction occurs.

Dr. Michael Apuzzo: I second what Dr. Stein has said. We have experts here from

all over the world. Not only those with experience from the endovascular point of view but also from the surgical standpoint. Many lesions are being treated early at this point in time; and even with the lesions treated early the risk of rupture occurring during induction of general anesthesia is close to zero. Similarly, with skilled microvascular neurosurgeons, the risk of seeing blood at the time of dissection is so rare that we report it at our surgical rounds.

In theory, it would be useful for the endovascular radiologists to come into the operating room. If we are to communicate, there should be exposure to the technologies on both sides. A key principle is that the amount of lesion exposed should be minimal, consisting of the parent vessels, the aneurysm neck, and whatever perforating vessels are present.

Dr. Berenstein: You would agree then that for proper resident training time in the operating room to see the actual techniques is important? You would probably also agree that the surgeons should come down to the radiology suites to see what we are doing.

Dr. Apuzzo: I completely agree.

III. ENDOVASCULAR EXPERIENCE

A. SPECIFIC CONSIDERATIONS AT VARIOUS INSTITUTIONS

CHAPTER 7

Surgical Exposure of the Superior Ophthalmic Vein in the Management of Carotid Cavernous Fistulas at Johns Hopkins Medical Institutions

Gerard M. Debrun

Most fast flow carotid–cavernous fistulas (CCFs) are successfully treated with endoarterial techniques.[1] A detachable balloon is advanced into the internal carotid artery (ICA) and detached into the cavernous sinus. However, when the internal carotid artery has been previously trapped or when the endoarterial balloon does not enter the cavernous sinus, the venous route becomes the best alternative. The superior ophthalmic vein (SOV) approach is indicated whenever the cavernous sinus cannot be reached through the inferior petrosal sinus or through catheterization of the jugular and facial veins.

Most CCFs of the dural type have multiple feeders from the external carotid artery (ECA) and the ICA. The ICA feeders are so small no endoarterial balloon can enter the cavernous sinus. Therefore we are left with the alternative of embolizing the ECA feeders or of reaching the cavernous sinus through a venous approach. Here again surgical exposure of the SOV may be indicated if the other venous approaches or embolization of the ECA branches have failed. We have treated eight patients with surgical exposure of the SOV; two had posttraumatic CCFs, and six had dural arteriovenous malformations (AVMs) of the cavernous sinus.

Case Studies

Case 1

A 31-year-old man was involved in a motor vehicle accident at age 20. He was treated by trapping the ICA. A Silverstone clamp occluded the ICA in the neck, and the ICA was clipped intracranially as well as at the origin of the ophthalmic artery. He tolerated the procedure well but continued to have proptosis and to hear a pulsating noise; his right angular veins became progressively enlarged and pulsatile. He remained untreated for 11 years and was then referred to our institution by his ophthalmologist. The angiographic workup demonstrated occlusion of the right ICA and the filling of

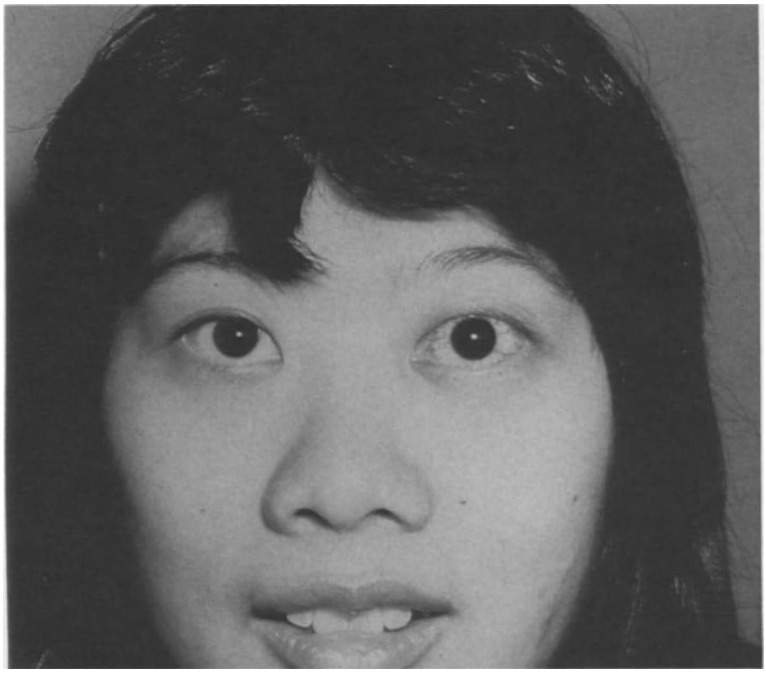
the right cavernous sinus through multiple branches of the right ECA. The cavernous sinus drained exclusively anteriorly into a large SOV. There was no posterior venous drainage through the inferior petrosal sinus. The SOV was surgically dissected at the medial angle of the orbit, and a single balloon was detached into the cavernous sinus, closing all the afferent vessels from the ECA. The patient was discharged a week later, and follow-up angiography showed complete closure of the fistula. He has remained asymptomatic at 2 years.

Case 2

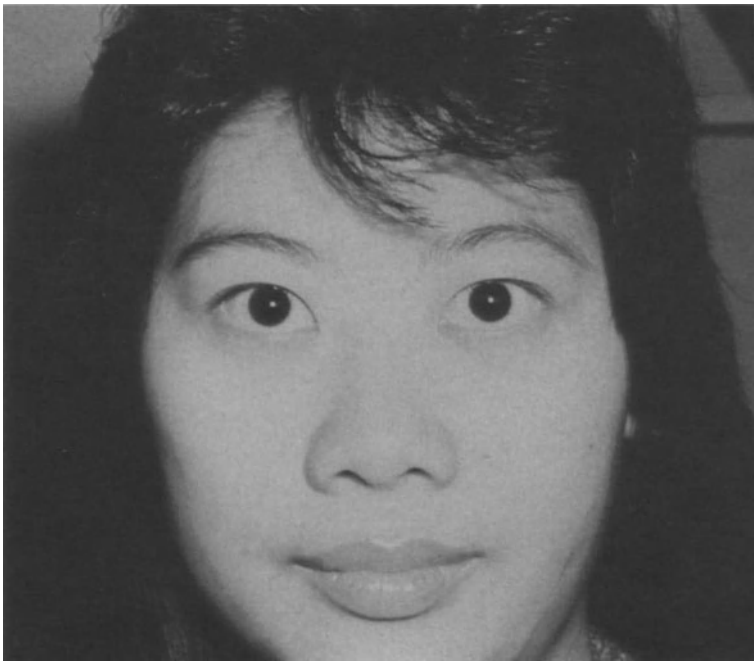
A 26-year-old woman developed a left cavernous syndrome 2 weeks after a motor vehicle accident. She had proptosis, chemosis of her left eye, and VI nerve palsy. The angiographic workup demonstrated a CCF fed exclusively by the left ICA. The cavernous sinus (CS) was fed through a small trigeminal artery, which gave off a cerebellar branch. No balloon, even a small one, could enter this trigeminal artery. A microcatheter could hook the origin of this artery but could not advance far enough for safe delivery of embolizing material. The CS was draining anteriorly into the SOV with no opacification of the ipsilateral inferior petrosal sinus. Therefore the left SOV was surgically exposed, and a balloon was detached into the CS with complete cure of the fistula. There was complete resolution of symptoms at 3 months' follow-up with a normal angiogram (Fig. 7.1).

Case 3

A 70-year-old women had bilateral CS syndrome. She had bilateral VI nerve paresis for several months and red eyes. The angiographic workup showed a bilateral CCF of the dural type with filling of both CSs from both ICAs and several branches of the left ECA. The major feeder was coming from the left ascending pharyngeal artery. The anterior branch of this artery was giving off a CS branch, which was embolized with cyanoacrylic glue. There was no improvement of symptoms, and both CSs still filled from both ICAs. There was no venous drainage through the inferior petrosal sinus. Therefore we decided to expose surgically the left SOV, and two balloons were detached into the left CS. The patient did well. The symptoms resolved on the left side but persisted on the right side. The control angiogram showed absence of filling of the left orbital veins but contralateral drainage of the left CS to the right CS and the right SOV. The patient was scheduled for an SOV approach of the right side several weeks later, but the control angiogram done the day before surgery showed complete closure of the right CCF; hence surgery was canceled. The ophthalmological examination was entirely normal 2 months after treatment, and the patient has remained asymptomatic at 1 year follow-up.



A



B

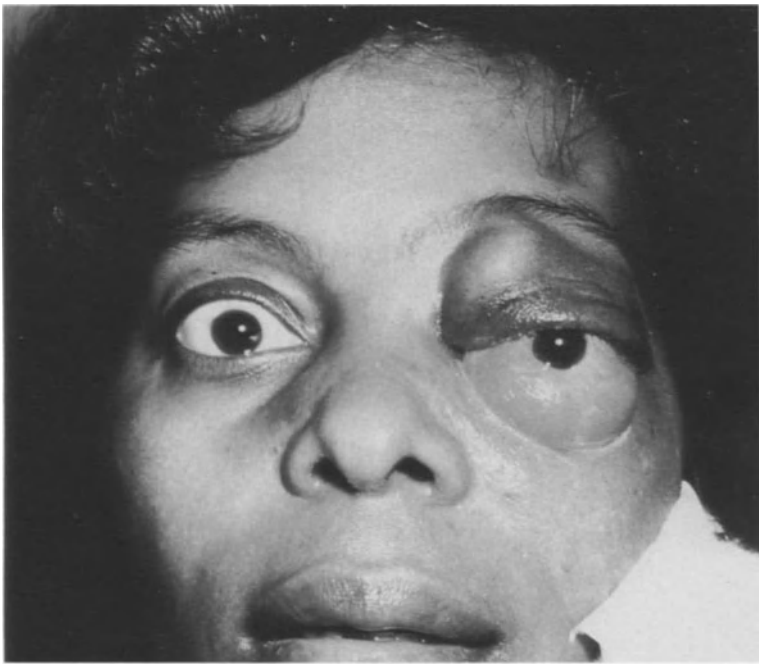
Figure 7.1. Case 2: Traumatic CCF that is impossible to treat via the endoarterial route (the fistula is too small). There is no access to the inferior petrosal sinus. (**A**) Note the left red eye with minimal proptosis. (**B**) Cosmetic result 3 months after treatment using the SOV approach.

Case 4

A 26-year-old man with hemophilia and who is human immunodeficiency virus (HIV) positive developed a left CS syndrome with severe chemosis, proptosis, and frozen eye. The angiographic workup showed multiple branches of the left carotid siphon filling the left CS, which drained exclusively into the left SOV. There was little supply from the left ECA branches. After we failed to enter the CS from the ICA with a microcatheter, it was decided to expose the left SOV. One balloon was detached into the left CS. The symptoms subsided within a few weeks, and the patient has a normal ophthalmological examination 1 year after treatment.

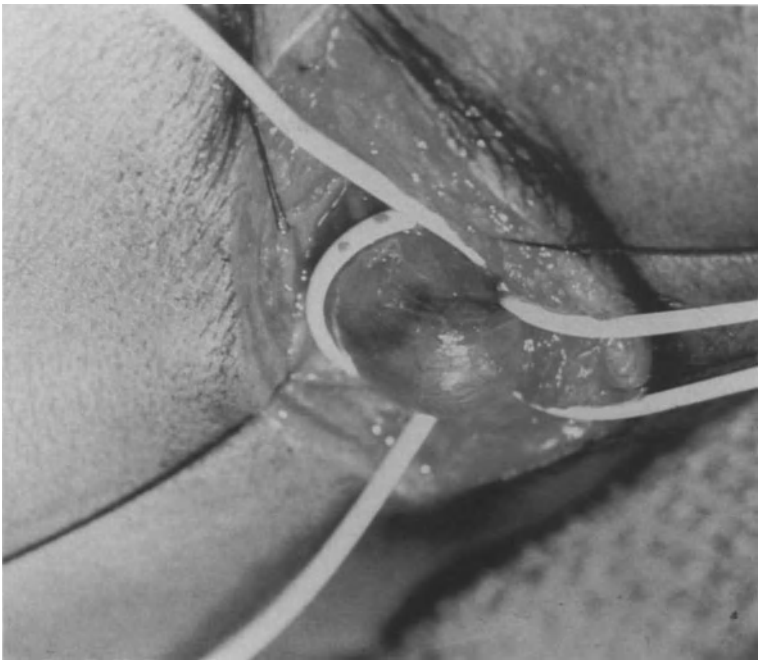
Case 5

A 64-year-old man had a left CS syndrome. He had a red eye and a left VI nerve paresis for months without improvement. The angiographic workup



A

Figure 7.2. Case 6: Dural AVM of the left cavernous sinus not cured by embolization of external carotid feeders. There is no access through the inferior petrosal sinus. (**A**) Note the marked chemosis and proptosis. There is a large pulsating SOV. (**B**) Surgical dissection of the SOV controlled the problem with two-vessel loops. (**C**) Cosmetic result 6 months after treatment.



B

C

Figure 7.2 (*continued*)

showed complex filling of the left CS through branches of both internal carotid siphons and both ECA branches. Both ascending pharyngeal arteries were embolized with polyvinyl alcohol (PVA) particles without clinical or angiographic improvement. The left SOV was exposed, but we could not advance a balloon into the CS. A microcatheter was easily advanced into the CS through the SOV, and platinum coils without fibers were detached into the CS. The patient improved but remained symptomatic for several weeks. He finally completely recovered and had a normal ophthalmological examination 12 months later. He refused to have a follow-up angiogram.

Case 6

A 43-year-old woman had had severe proptosis and chemosis of the left eye for years. She remained symptomatic despite an attempted embolization of the ECA with occlusion of the internal maxillary artery using a detachable balloon. She came to our institution several years later after having been advised that she would need enucleation of the left eye. She had marked proptosis and chemosis (Fig. 7.2) but normal vision. The left angular vein was large and pulsatile. The angiographic workup showed filling of the left CS through ECA and ICA feeders. The ECA feeders were embolized with acrylic glue, but the ICA still filled the CS and the SOV. There was no drainage into the inferior petrosal sinus. The SOV was surgically exposed, and one balloon was detached into the CS. The control angiogram showed anatomical cure of the CCF. Six months later the ophthalmological examination was normal. There was a minimal residual proptosis. The cosmetic result was excellent (Fig. 7.2C).

Case 7

A 49-year-old man had right CS syndrome. He had minor proptosis, a red eye, and diplopia with right VI nerve paresis. The angiographic workup showed a right dural type of CCF fed by both the ICA and the ECA. The branches of both ECAs filling the right CS were embolized twice with particles of PVA without clinical improvement. The right inferior petrosal sinus was not draining the CS. The right SOV was exposed surgically, and one balloon was detached into the CS. Complete clinical and anatomical cure were seen 3 months later.

Case 8

A 50-year-old man had had right CS syndrome for several months. The angiographic workup showed a right dural CCF with feeders from the carotid siphon (ICA) and from branches of the ECA. The CS drained anteriorly into the SOV, and there was cortical venous drainage through the sylvian vein and the vein of Labbe. This situation was considered reason enough to

treat this patient rapidly. We decided to treat the CCF exclusively through the SOV without first embolizing the ECA branches. After surgically exposing the SOV, one balloon was inflated into the CS. Intraoperative angiography of the ECA showed that the CS was still filling from the ECA and draining into cortical veins; however, the SOV did not fill. It was impossible to position the balloon in the CS and obtain complete occlusion of the ECA feeders. Therefore the balloon was detached; and embolization of the middle meningeal artery, accessory meningeal artery, and artery of the foramen rotundum was done with acrylic glue. Clinical cure was obtained in 1 month and anatomical cure confirmed with an angiogram 3 months after treatment.

Discussion

We have reported a subgroup of eight patients from our complete series of CCFs that includes 137 fast-flow CCFs and 62 slow-flow CCFs of the dural type. Only 8 of 199 CCFs were treated after surgical exposure of the SOV; in other words, 4% of patients with CCFs could not be cured with other techniques, and the easiest access to the CS in those patients was the SOV approach because we could not reach the CS through the inferior petrosal sinus (IPS). It is more important to note that the SOV approach was used in 2 of 137 fast-flow CCFs (1.4%) and in 6 of 62 slow-flow dural type CCFs (10.0%). These data illustrate that all traumatic CCFs can be treated using the endovascular detachable technique and that the SOV approach is only exceptionally necessary. There are two situations where it must be considered: One is after a trapping procedure of the ICA when the only access to the CS is the venous route and when the IPS cannot be used. The SOV approach is easier and faster than surgical exposure of the CS. The second indication is the rare case where no balloon enters the CS through the endoarterial route and no catheter can be positioned safely into the CS.

Dural CCFs have always been more difficult to cure than traumatic CCFs because of the multiplicity of feeders filling the CS, generally from one or both ICAs and one or both ECAs. The indications for treatment depend on the symptomatology and on the venous drainage of the CS. Progressive decreased vision, high ocular pressure, progressive glaucoma, and invalidating diplopia from a VI nerve palsy are indications for aggressive therapy. In my experience, compression of the cervical vessels by the patient has not significantly increased the percentage of spontaneous cure, which occurs in approximately 10% of the dural CCFs.

As it is contraindicated to permanently occlude the ICA of these patients, and as the ICA feeders are too small to allow penetration of the CS with detachable balloons or with microcatheters in most cases, the only treatment offered is embolization of the ECA branches. This embolization can be done with solid material or with liquid polymerizing substances. There is more chance of cure with liquid adhesives than with solid particles, but there are

more risks associated with liquid agents than with solid material. The reason is that the branches of the ECA that need to be embolized supply blood to several cranial nerves, and liquid agents can reach the capillary barrier, whereas solid particles of known size cannot reach it and decrease the risks of severe ischemia or tissue necrosis.

These dangerous anastomoses between ECA branches and the cranial nerves are well known and require the attention of the interventional neuroradiologist. They cannot always be avoided. It is said that any embolization of the ECA should not carry more than 1% risk, but the true percentage of complications (even in the hands of well trained neuroradiologists) is probably higher. I discourage people from using acrylic glue or particles soaked in pure ethanol in the middle meningeal artery (MMA) if the microcatheter cannot be advanced into the branch of the MMA, filling the CS far beyond the foramen spinosum, because there is always a recurrent branch of the MMA at the level of the foramen spinosum that supplies blood to the VII nerve.

A VII nerve palsy secondary to embolization with acrylic glue or alcohol may be permanent and is a major complication. The same precautions must be taken when embolization of the ascending pharyngeal artery is required. The posterior neuromeningeal branch of division supplies the VII, IX, X, XI, and XII cranial nerves. It is also often connected with the vertebral artery. Embolization of the anterior branch of the ascending pharyngeal artery should be done with exceptional carefulness if one uses liquid agents because of the potential risk of reflux of the liquid agent into the posterior neuromeningeal branch. Finally, the distal internal maxillary artery often fills the CS through the artery to the foramen rotundum, which is itself often anastomosed with the inferolateral trunk of the carotid siphon. Therefore there is a potential risk liquid agents migrating from the ECA into the ICA. Embolization must be done under flow-control digital subtraction fluoroscopy, and it is wise to have a nondetachable balloon transiently inflated in the carotid siphon during selective embolization of the artery to the foramen rotundum. This measure prevents reflux of liquid adhesive into the ICA with its catastrophic consequences. The potential risks, even low, of embolization of the ECA branches added to the relatively high failure rate of this embolization (more frequently with particles than with liquid adhesives) have gained our attention to such a point that we believe that the venous approach to the CS should be considered the first choice for treatment—before embolization of the ECA branches. The SOV is the chosen venous route if the IPS cannot be used. Embolization of the ECA branches becomes the best choice if the venous approach has not allowed anatomical closure of the CCF. We used this approach in cases 1 and 8 (see Case Studies, above).

We consider surgical exposure of the angular vein at the medial angle of the orbit a simple, easy, controllable surgical procedure with excellent cosmetic results. A 2-cm incision is made along the medial portion of the eyelid.

The vein is meticulously dissected, and two-vessel loops are placed around the vein. The surgeon then performs a small venotomy. There is perfect control of the arterialized vein thanks to the vessel loop. The balloon catheter or the microcatheter is introduced directly through the venous opening; the size of the catheter should be the same size as the venous opening, thereby avoiding any leakage of blood at the opening site. Under intraoperative digital subtraction fluoroscopy, the balloon catheter is easily advanced toward the CS into the SOV. Gentle pulling on the proximal part of the vein with a one-vessel loop may help open the sharp angulations of the vein and ease the advancement of the balloon catheter. We were unable to advance the balloon catheter into the CS in only one case, where we easily advanced a microcatheter into the CS and treated the patient with coils rather than with the balloon. We use latex balloons, but Silastic balloons would work as well. The latex balloons are inflated with iodine contrast material. They shrink with time and are deflated after a couple of months. Therefore the risks associated with compressing the cranial nerves (VI and III) are not permanent.

The SOV approach has been used by other authors.[2–7] Some prefer direct puncture of the angular vein at the medial angle of the orbit. We consider this technique dangerous, with the risk of uncontrollable intraorbital bleeding. Others have thought that the SOV approach is risky in recent cases of CCF because the arterialized vein does not have a thick wall, as do long-standing cases. We think that if the surgical dissection is done by a vascular neurosurgeon assisted by an ophthalmological surgeon there is total security and perfect control of any blood leakage that might occur after the venotomy. A meticulous dissection of the vein must be performed, however, for at least 1cm, which allows easy passage of two-vessel loops around the vein. Eight cases is a small series, but we have not faced any technical difficulties and the cosmetic result has always been perfect.

In conclusion, we recommend without reservation the use of the SOV approach in the management of: (1) traumatic CCFs and other fast-flow CCFs when there is no other access to the CS; and (2) dural AVM type CCFs when the IPS cannot be used and when embolization of the ECA branches has failed to cure the patient. It is controversial to consider the SOV approach as the first treatment and to reserve embolization of the ECA branches in case of incomplete anatomical cure of the CCF through the SOV approach.

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Discussion

Dr. Bebrun: Is the SOV approach a good alternative to external carotid artery embolization? This point is debatable, and I am sure that Dr. Moret is totally against this approach because he considers that the patient can be cured with embolization of the external carotid artery. If we add up the number of embolizations of the external carotid, seeking a number indicative of potential risks, I know that Dr. Moret would say that embolization of the external carotid is 100% safe in the hands of someone who knows the anatomy of the external branches well. Despite his opinion, complications can occur. I must therefore emphasize that with one balloon positioned in the cavernous sinus and with an elegant approach to the cavernous sinus through the exposure of the SOV we can treat patients without submitting them to several embolizations. It is not a bad approach.

Dr. Viñuela: Do you have an arterial line in place all the time to confirm the results?

Dr. Debrun: Not always, because for the cases we have already done we did not have the transparent holder and the transparent table. Now, however, we plan to double up intraoperative angiography and to have an arterial line in position so we have control until the fistula is effectively closed.

Dr. Viñuela: If you have an arterial line with that type of fistula, should one consider having a temporary balloon occlusion of the internal carotid during the procedure and drop the pressure in those huge veins?

Dr. Debrun: What is your thinking regarding temporary balloon occlusion?

Dr. Viñuela: You are working in a high-flow arterialized vein. The possibility of morbidity must be considered and whether it will result from a temporary balloon occlusion such that the vein becomes a completely pulseless outlet. Do you perform the procedure in that manner? If you have an arterial line, which I assume is important to have, and if you perform a temporary balloon occlusion of the internal carotid artery and that vein becomes pulseless such that when you puncture it no blood escapes, it should be easy to introduce a balloon directly.

Dr. Debrun: With the two-vessel loop it is completely bloodless. The surgeon makes the incision, and there is not a drop of blood. We completely control the exit of blood; then, as soon as the catheter is introduced, there is no bleeding.

Dr. Viñuela: Are you saying it is not necessary?

Dr. Debrun: I think it is not necessary. We have done seven cases so far, and the only failure was a patient who was treated with coils. Despite the SOV exposure in that patient I could not advance the balloon through the loops of the anterior part of the SOV; I could, however, advance a tracker in the cavernous sinus and so detached 25 platinum coils into the cavernous sinus. Unfortunately, the patient was not cured.

Dr. Berenstein: Why not put Crazy Glue in?

Dr. Debrun: Because of the risk of reflux of Bucrylate. Such reflux could be avoided with transient occlusion of the internal carotid artery.

Dr. Hilal: If you had an arterial line, why inject only 25 platinum coils? Why not 40?

Dr. Debrun: We used flower coils at the time; I did not have the "magic" Hilal coils.

Dr. Pile-Spellman: What I have done in the most recent cases is to put in two or three flower coils and two Hilal coils, and then stack them. The flower coils are useful because of their large shape.

Dr. Kachkov: In how many instances was it possible to preserve the function of the internal carotid artery in cases of traumatic carotid–cavernous fistula?

Dr. Debrun: I have now treated more than 100 cases over the past 14 years. At the beginning of my experience only 50% of internal carotid arteries were preserved. Among the last 20 cases we preserved the internal carotid in more than 90%. I think that now everyone who has experience with the treatment of traumatic carotid–cavernous fistulas achieves 90% to 95% preservation of the internal carotid artery. The remaining patients must be treated by another technique.

Dr. Hilal: Why did you not use the femoral vein? If you have, what do you think of the femoral vein approach?

Dr. Debrun: It is a good one if the inferior petrosal sinus is patent. The chances of success, though, are not high. and if the microcatheter can reach the compartment of the cavernous sinus (CS) which needs to be treated. However the use of balloons is more difficult than the use of coils through the inferior petrosal sinus. The superior ophthalmic vein can be catheterized from the femoral vein, external jugular vein, facial vein, angular vein and superior ophthalmic vein. I have done it on one occasion and I think that the San Francisco team has also done it in one case. However it is a difficult catheterization, and once again it precludes the use of detachable balloon which is for me the best material to use for a fistula.

CHAPTER 8

Current and Future Perspectives in Interventional Neuroradiology at New York University

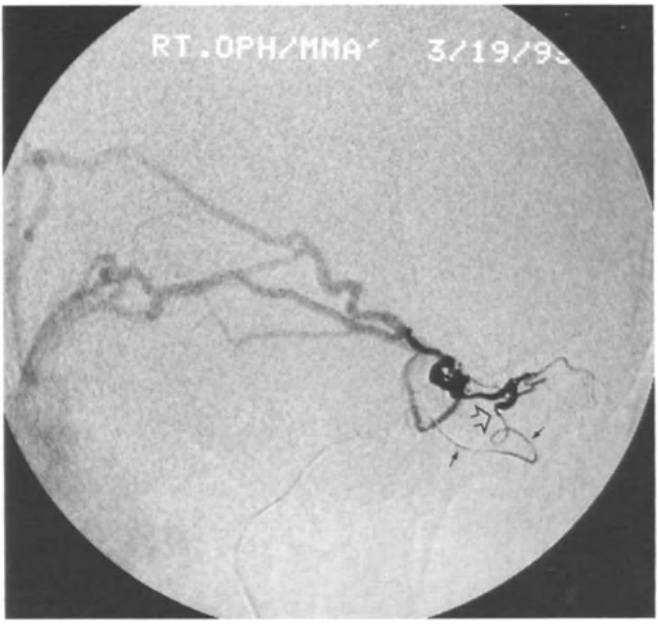
Alex Berenstein, Gary R. Spiegel, and Peter K. Nelson

Interventional neuroradiology, referred to as intravascular surgery in the Soviet Union or endovascular surgery in Japan, is a discipline that has evolved from diagnostic angiographic techniques and has culminated largely in transarterial embolization operations. The method was first used for the treatment of an arteriovenous (AV) fistula 56 years ago. Thirty years later, transarterial embolization was applied to treat some vascular malformations of the brain. At present, improvements in techniques and the development of microcatheters permit the safe and reproducible catheterization of intracerebral, extracerebral, and spinal arteries in the fifth and sixth divisions (Figs. 8.1–8.9). Subsequent refinement in embolic materials and infusion cytotoxic agents, in conjunction with a better understanding and knowledge of functional vascular anatomy in the craniofacial, spinal, and cerebral circulations, have permitted application of neuroangiographic techniques to the management of increasingly complex problems (Table 8.1). These procedures can be used as the sole form of treatment or can be combined with other modalities.

Throughout the body and particularly within the nervous system, endovascular interventional procedures can be divided into categories aimed at reducing or obliterating regional blood flow (embolotherapy), reconstruction (fistula and aneurysm repair), revascularization (thrombolysis or transluminal angioplasty), and intraarterial infusions (chemotherapy, cytotoxic infusion, functional superselective amytal testing (Table 8.1).

The inherent risk of central or peripheral neural injury when treating lesions of the brain, base of the skull, spinal cord, and adjacent tissues accentuates the need for meticulous case selection and evaluation. Optimal care for patients with complex lesions may best be obtained by the cooperative effort among all physicians involved. Overlap among the disciplines of radiology, neurosurgery, neurology, head and neck surgery, plastic surgery, and other neuroscience specialties is creating new demands and responsibilities. The radiologist and radiology staff should be ready to meet the stresses and demands of intensive interventional care, as the procedures are surgical endeavors, not just diagnostic "procedures."

The neurosurgical staff must be prepared to face the challenges related to



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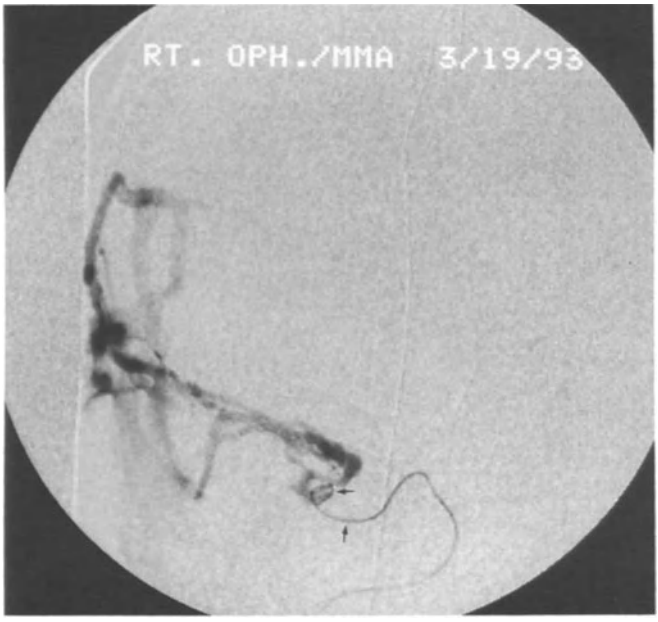
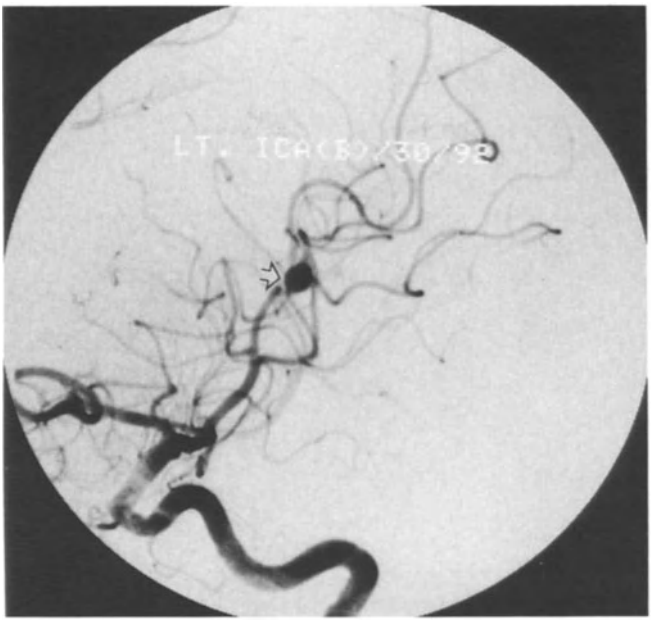


B

Figure 8.1. Digital subtraction angiography (DSA) demonstrates superselective catheterization of the ophthalmic artery using a variable-stiffness microcatheter (black arrows) in lateral (**A**) and AP (**B**) views. Ophthalmic artery origin of the middle meningeal artery is present and supplies a complex dural AVM. Open arrow indicates the catheter tip.



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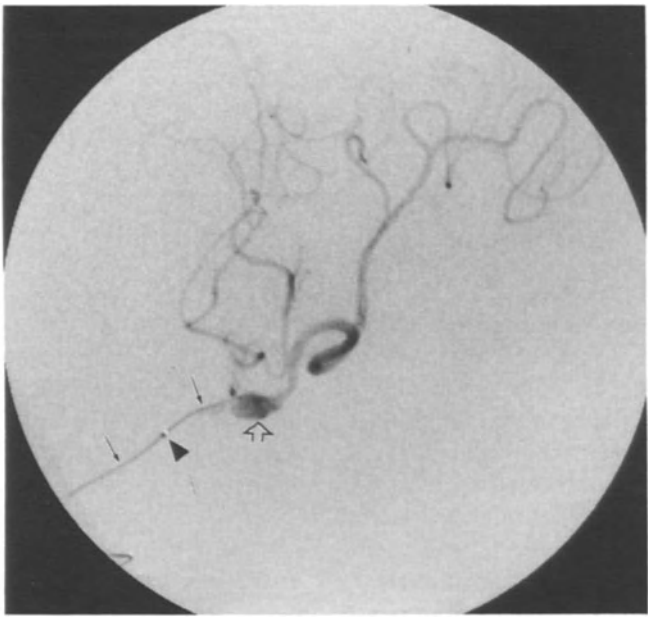

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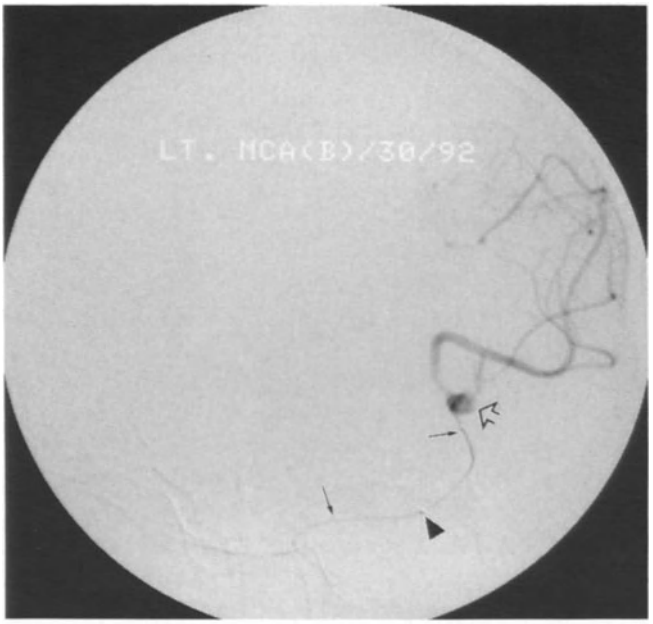
Figure 8.2. (**A**) DSA of a mycotic aneurysm (open arrow) arising from a tertiary branch of the middle cerebral artery. (**B & C**) Superselective catheterization of this branch using a variable-stiffness microcatheter (black arrows), seen in lateral (**B**) and AP (**C**) views. Arrowheads point to an artifact of a prior catheter tip position. Normal appearance of the vessel is noted beyond the fusiform-shaped aneurysm (open arrow).

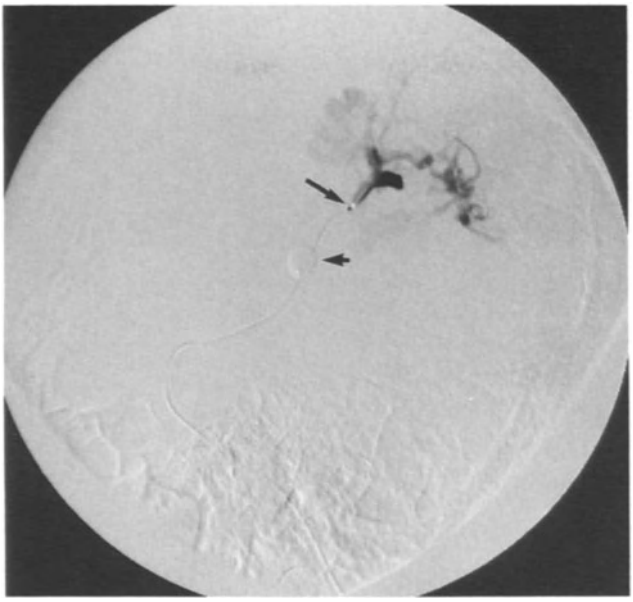


C

Figure 8.2 (*continued*)

new opportunities and problems that these procedures may create. The neurology staff must become adept at recognizing the sometimes unusual clinical presentations of these patients and the changes in neurological function sometimes produced by these new interventions, as well as achieve a better understanding of the natural history of the various neurovascular disorders. There are few instances in medicine where such a multidisciplinary approach has been more useful than in the management of neurovascular problems.

The experimental nature of some embolic agents and techniques, alternative modes of management, the potential risks, and expected results, as well as the need for several stages or a combination of procedures, must be explained in detail to the patient and family. The development of a good patient-physician relationship is essential for safety and success. Radiologists involved in these procedures are now active participants in the decision-making process of patient care and follow-up. They must assume and share the clinical responsibility for their patients. The new discipline emerging from this evolution is what we are calling surgical neuroangiography.



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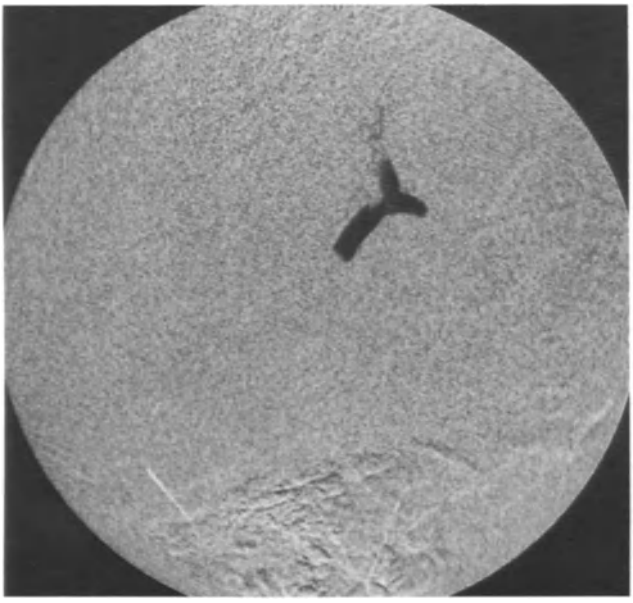


B

Figure 8.3. (**A**) Lateral DSA showing a double-lumen Berenstein balloon catheter (arrow) inflated in a main MCA branch proximal to a high-flow double fistula of an AVM. The inner microcatheter extends more distally (long arrow). (**B**) NBCA glue cast of both fistulas.

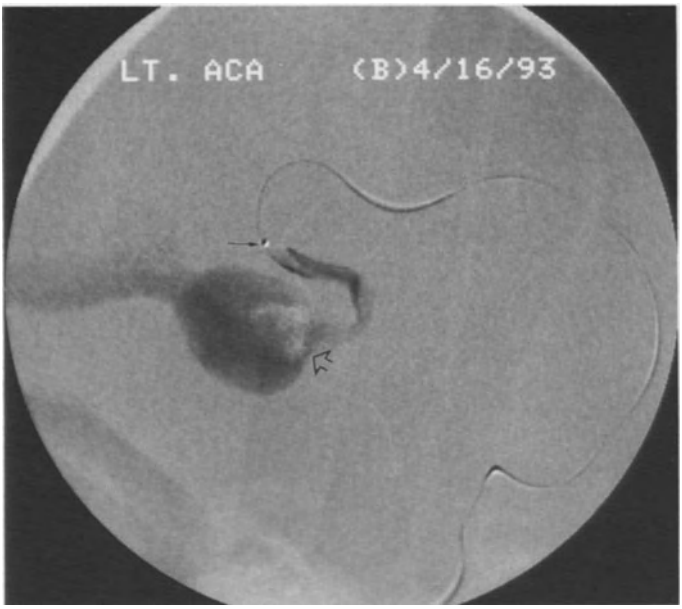


Figure 8.4. DSA in lateral projection of superselective catheterization of the pericallosal artery in an infant, which supplies a direct arteriovenous fistula of a galenic malformation. Solid arrow indicates the catheter tip; open arrow points toward previously deposited NBCA.

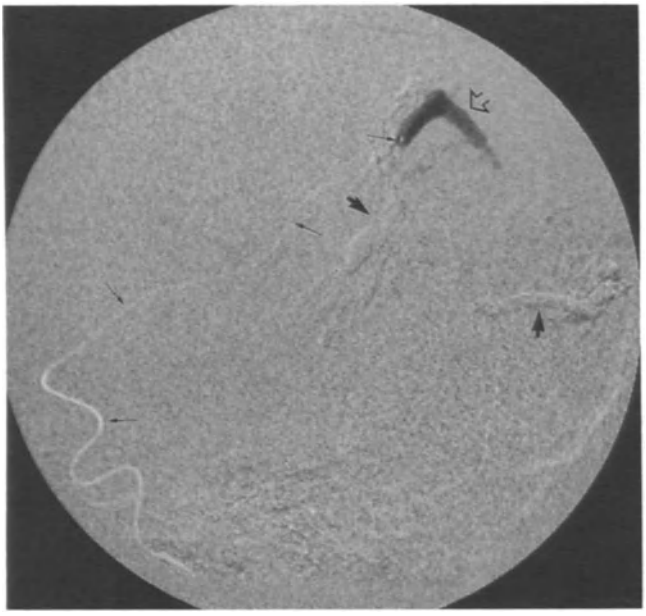
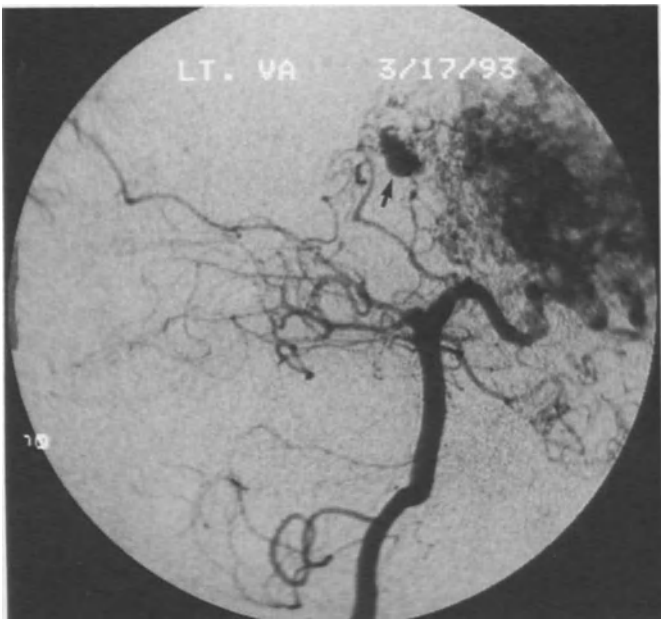


Figure 8.5. Lateral DSA immediately after IBCA deposition in a posterior MCA branch supplying an AVM. The IBCA is radiopaque (open arrow). The white line (thin arrows) represents the original position of the microcatheter prior to the IBCA deposition. A great advantage of DSA is its ability to subtract the previously injected IBCA (thick arrows).



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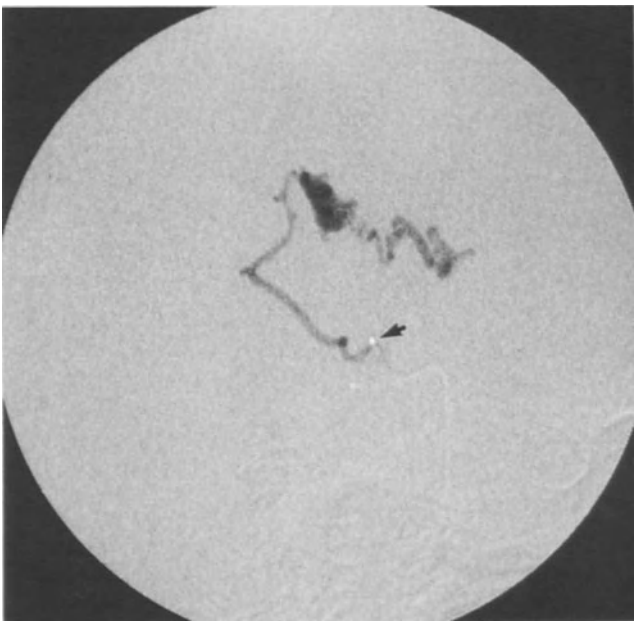

B

Figure 8.6. (**A**) Lateral vertebral artery DSA of a complex AVM harboring an arterial aneurysm (arrow) within a posterior feeder. The patient had a recent hemorrhage localized to this area. (**B**) Superselective embolization of this pedicle using radiopaque NBCA. Arrow shows prior catheter tip position. (**C**) Postembolization control DSA demonstrating complete occlusion of the aneurysm and its pedicle; arrows indicate glue cast.

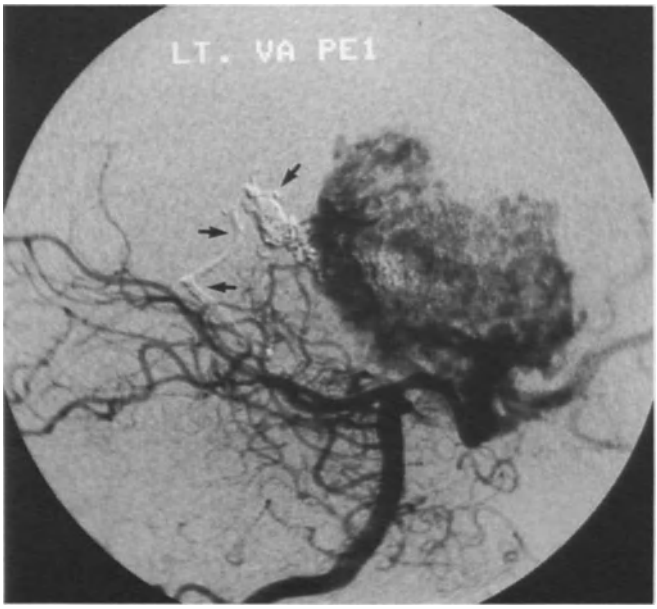

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Figure 8.6 (*continued*)

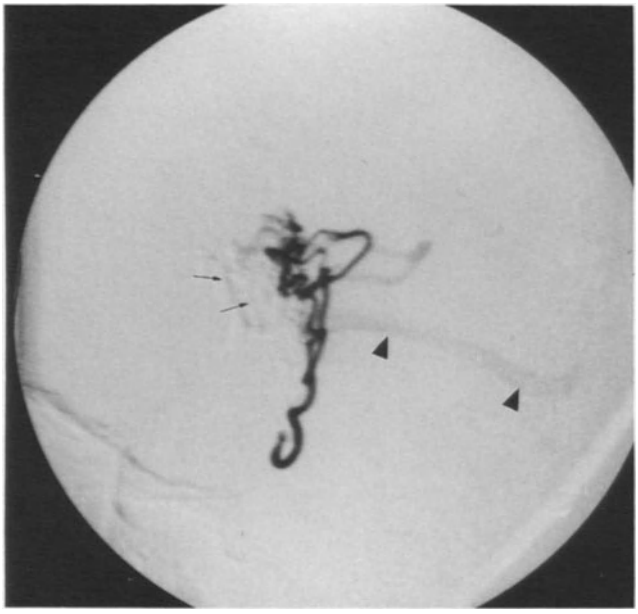


Figure 8.7. Lateral DSA of superselective catheterization of a lateral lenticulostriate artery involved in a multipedicular AVM (same patient as in Figure 8.13); previous IBCA is subtracted (arrows). Venous drainage is indicated by arrowheads. (Reprinted with permission of Berenstein and Lasjaunias, Surgical Neuroangiography, Vol. 4.)

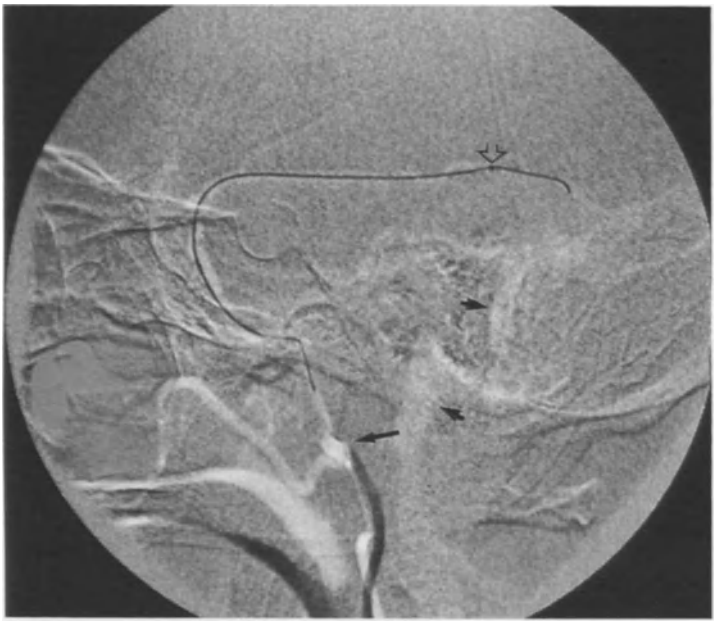


Figure 8.8. Lateral DSA of a dural AVM draining to the transverse sinus. The guiding Berenstein 7F catheter is seated at the middle meningeal artery origin (long arrow). The tip of the variable-stiffness microcatheter has superselectively catheterized the temporosquamosal branch (open arrow). The guidewire is extended further toward the transverse sinus. Short arrows indicate the sigmoid sinus and internal jugular vein on this "roadmap" image.

Embolotherapy

Embolization as a therapeutic modality is used preoperatively for hypervascular tumors and vascular malformations. It may allow surgical resections in cases that had been considered inoperable prior to the advent of embolization. In many patients the results of the technique are only palliative, as eradication of the problem is not possible. Embolization is curative and highly successful treatment for high-flow arteriovenous fistulas in most locations. It has proved to be a successful emergency treatment for many cases of intractable bleeding, primarily in the area of the head and neck. For inoperable and malignant tumors, embolization or cytotoxic infusions may offer palliative relief from pain, bleeding, pulsatile tinnitus, and discomfort due to mass effect.

A variety of catheters or delivery systems and embolic agents have been used for embolizations. For best results thorough familiarity with a selected group of delivery systems (Table 8.2) and embolic materials (Table 8.3) provides flexibility and safety in techniques. Delivery systems are chosen for

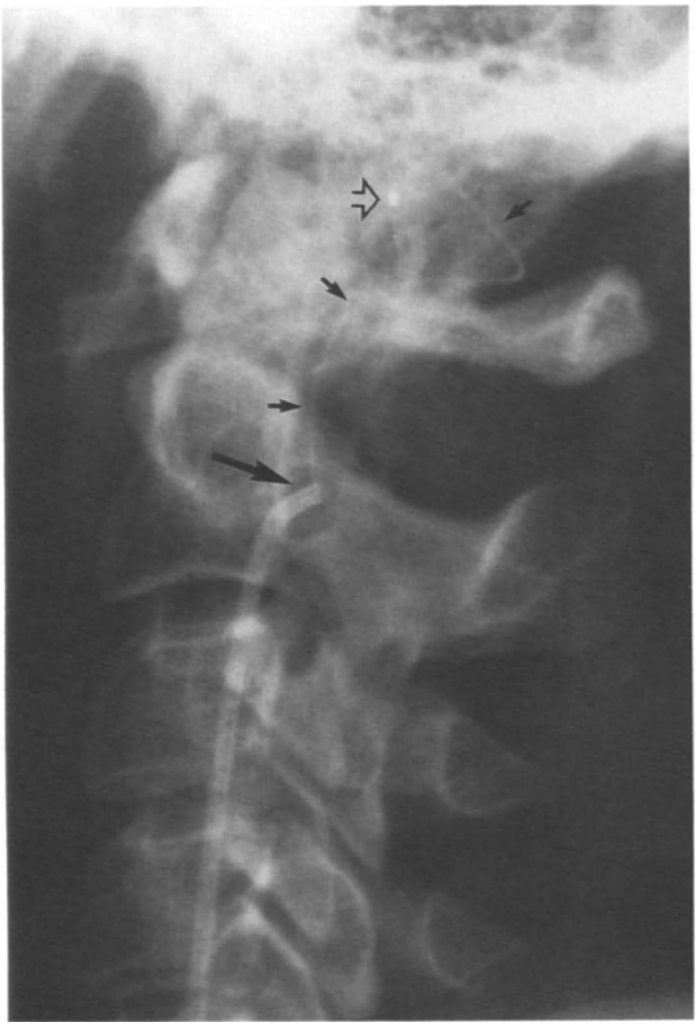


Figure 8.9. Lateral radiograph of superselective catheterization of the anterior spinal artery originating from the distal vertebral artery. Note the coaxial system. A larger catheter has been placed at the C2 level (large arrow); coaxial introduction of a variable-stiffness catheter (small arrows) can be seen. The radiopaque microcatheter tip (open arrow) is at the level of the malformation (same patient as in Figure 8.15). (Reprinted with permission of Berenstein and Lasjaunias. Surgical Neuroangiography, Vol. 5)

Table 8.1. Applications of surgical neuroangiography

Embolotherapy
Vascular tumors (e.g., meningiomas, paragangliomas)
Dural arteriovenous malformation
Brain vascular malformations
Spinal arteriovenous malformations
Vessel occlusion (epistaxis, laceration, aneurysms)
Chemoembolization (microcapsules with hormone or cytotoxic infusions)
Reconstruction
Large-hole arteriovenous fistula (e.g., CCF, VVF)
Aneurysm repair
Revascularization
Angioplasty
Thrombolysis
Cytotoxic infusions
Chemotherapy infusion
Alcohol ablation
Thermal ablation
Functional testing
Amytal testing
Xylocaine testing

CCF = carotid–cavernous fistula; VVF = vertebrovertebral fistula.

Table 8.2. Catheter and delivery systems

Conventional tapered angiographic catheter (1F to 7F)
Nontapered (thin-walled, 1F to 9F)
Modified superselective torque catheter
Single- and double-lumen balloon catheters
Flow-guided single-lumen balloon microcatheters
Detachable balloons: silicone and latex
Calibrated "leak" detachable balloon microcatheters
Steerable microguidewires
Variable stiffness microcatheters
Angioplasty balloon catheters

Multiple catheters and delivery systems have been reported. The ones listed in this table represent the ones with which the authors are familiar and use.

their superselectivity, and their ability to produce flow control. They now include a variety of flow-guided and guidewire-directed variable-stiffness microcatheters.

The choice of embolic materials is based on the superselectivity achieved, nidus location, size, angioarchitecture, pattern of venous drainage, velocity of blood flow, and vulnerability of surrounding tissues to ischemia. The selected embolic agent should be able to reach the nidus of the lesion beyond

Table 8.3. Embolic agents

Absorbable solid particles
Autologous blood clot[a]
Gelatin sponge and/or powder (Gelfoam)
Oxidized cellulose (Oxycel)[a]
Microfibrillar collagen (Avatine; Angiostat)
Glutaraldehyde cross-linked collagen[a]
Nonabsorbable solids[b]
Lyophilized dura (Lyodura)[a]
Polyvinyl alcohol foam (PVA; contour microemboli)
Detachable balloons (latex, Silastic)
Metallic coils (with or without fibers)
Fluids
Low-viscosity silicone rubber[c]
Isobutyl-2-cyanoacrylate (IBCA)[c]
N-Butyl-cyanoacrylate (NBCA)
Ethanol 95%
Ethanol in lower concentrations
Hot (boiling) contrast material[a]
Opacificants
Tantalum dust (1–2 μm)
Tantalum oxide (1–2 μm)
Retardants
Iophendylate (Pantopaque)[c]
Acetic acid[a]
Lopiodol

Multiple agents have been introduced. Most agents presented in this list are ones with which the authors are familiar and use.
[a] Not in routine use.
[b] Particulated agents can be obtained in numerous sizes, from 40 μm to several millimeters.
[c] No longer in routine use.

the point of potential collateral flow. Materials are also chosen for their familiarity, efficacy, and safety. The clinical goal (preoperative, palliative, or curative) may influence the type of agent used. Distal migration of embolic materials to the venous side or to the pulmonary circulation must be avoided. Embolic materials are limited by size, velocity, adhesiveness, and toxicity.

Vascular Neoplasms

Vascular neoplasms in the external carotid distribution, as in other territories, are usually embolized with particulate agents. These lesions usually have a capillary bed, some with small arteriovenous shunts, which may be

Table 8.4. Dangerous vessels in the craniocervical territories

Injected artery	Collateral route	Risk of embolization
Occipital	C1, C2, to VA	Posterior fossa stroke
Internal maxillary a. orbital branch of MMA	Ophthalmic a. ICA	Blindness, stroke
Ophthalmic a. originating from the MMA	Ophthalmic a. ICA	Blindness, stroke
Anterior deep temporal a.	Ophthalmic a. ICA	Blindness, stroke
Foramen rotundum a. (ILT)	Cavernous (C4) internal carotid	Stroke
MMA, ILT (foramen spinosum)		
Accessory meningeal a. (foramen ovale)	Cavernous (C4) internal carotid	Stroke, IV nerve palsy
Petrous branch of MMA	Supply to cranial nerve VII	VII nerve palsy
Stylomastoid a.	Cranial nerve VII	VII Nerve palsy
Ascending pharyngeal a.		
Carotid branch	Internal carotid (C5)	Stroke
Neuromeningeal branch	Supply to cranial nerves; cervical vertebral a. (C3 anast.)	IX, X, XI, XII Nerve palsy; posterior fossa; stroke
Blood supply to spinal cord		
Vertebral a.	ASA, lateral spinal artery, artery of the cervical enlargement (ASA)	Spinal cord infarction
Thyro- and costocervical trunks	Artery of the cervical enlargement (ASA)	Spinal cord infarction

a. = artery; MMA = middle meningeal artery; ILT = inferior lateral trunk at C4; ASA = anterior spinal artery.

occluded by particulate embolic agents of the appropriate size (generally 50–250 μm). Consequently, there is less potential for persistent supply from collateral vessels than that obtained after proximal embolization or vessel ligation. As with other embolic procedures, strict attention must be paid to the presence of dangerous collateral pathways that supply the cranial nerves or serve as potential connections to the intracranial circulation (Table 8.4). Table 8.5 lists the vascular tumors that can be approached by embolotherapy.

Intracranial and spinal meningiomas may be devascularized by particulate embolization (Fig. 8.10), which reduces blood loss and simplifies removal. It is of particular benefit in the case of lesions located at the base of the skull. For maximal effect, surgery is generally recommended 2 to 10 days following embolization.

Table 8.5. Tumors fed by the external carotid artery

Paragangliomas
Meningiomas
Vascular neurinomas/schwannomas
Hemangiopericytomas
Esthesioneuroblastomas
Aneurysmal bone cyst
Hemangiomas
Giant cell tumors
Sarcomas
Squamous cell carcinomas
Hypervascular-metastatic tumors

Dural Arteriovenous Malformations

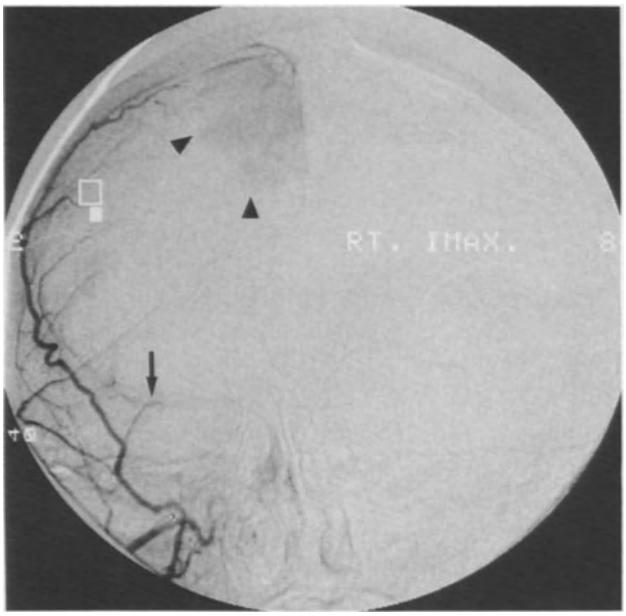
About 10% to 15% of all intracranial arteriovenous malformations (AVMs) involve the dura exclusively. They consist of a network of small multiple fistulas and may involve the cavernous sinus, sigmoid sinus, tentorium, falx, or anterior cranial fossa. Dural AVMs must be differentiated from dural fistulas, which consist of a single direct high-flow AV fistula, such as often occurs at middle meningeal artery.

Dural vascular malformations most likely represent an acquired lesion that follows the pathological recanalization of a thrombosed sinus. This has been well documented in dural vascular malformations of the sigmoid sinus as well as those in the spinal cord.

In the cavernous sinus, the major signs and symptoms include secondary glaucoma, visual disturbances, cavernous sinus distension, and variable dysfunction of the oculomotor nerves, resulting from abnormal venous drainage of the ophthalmic venous system. Approximately 30% to 40% of these lesions resolve spontaneously, and there is no indication for therapy. However, relatively urgent treatment is indicated in cases where increased intraocular pressure is uncontrolled or there is rapid deterioration of visual acuity.

Most dural AVMs in the sigmoid sinus are clinically innocuous. The main complaint may be subjective pulsatile tinnitus that is disturbing to the patient. The exception to this clinically benign picture are the lesions that drain into cortical veins. This subset of dural AVMs may present with subarachnoid hemorrhage, seizures, or both and should be treated expediently (Fig. 8.11).

In another group of patients, primarily with posterior fossa dural AVMs, the lesions are associated with significant thrombosis of the venous drainage of the brain. These patients may present with increased intracranial pressure and progressive papilledema, which may be irreversible even after treatment.



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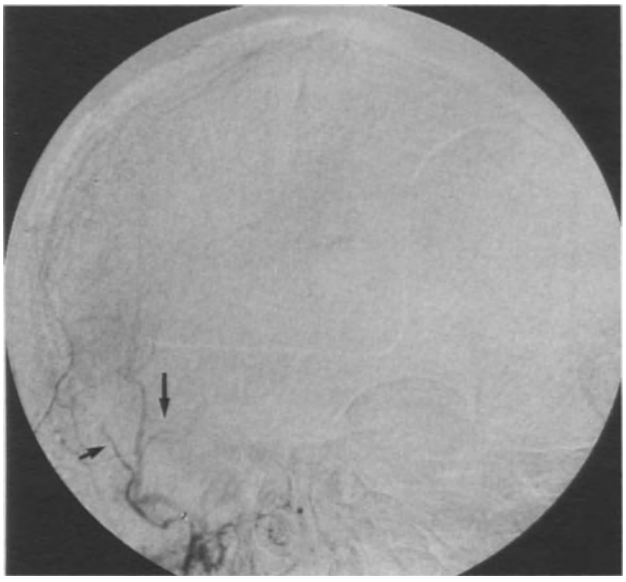

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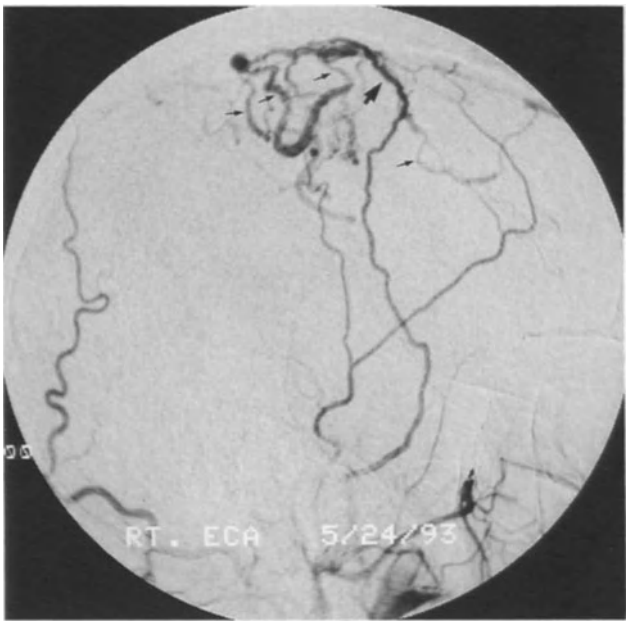
Figure 8.10. Preoperative embolization in a parasagittal meningioma. (**A**) DSA, AP view in midarterial phase demonstrates a hypervascular meningioma (arrowheads). Note the lacrimal anastomosis (arrow). (**B**) Following embolization using Gelfoam powder and a proximally occlusive Gelfoam pledget, tumor blush is not seen and the lacrimal branch is preserved (long arrow). Short arrow indicates the middle meningeal arterial stump.



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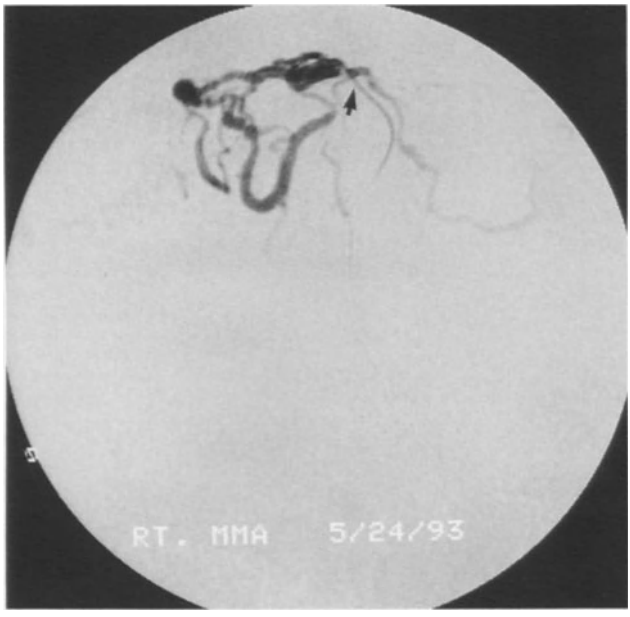
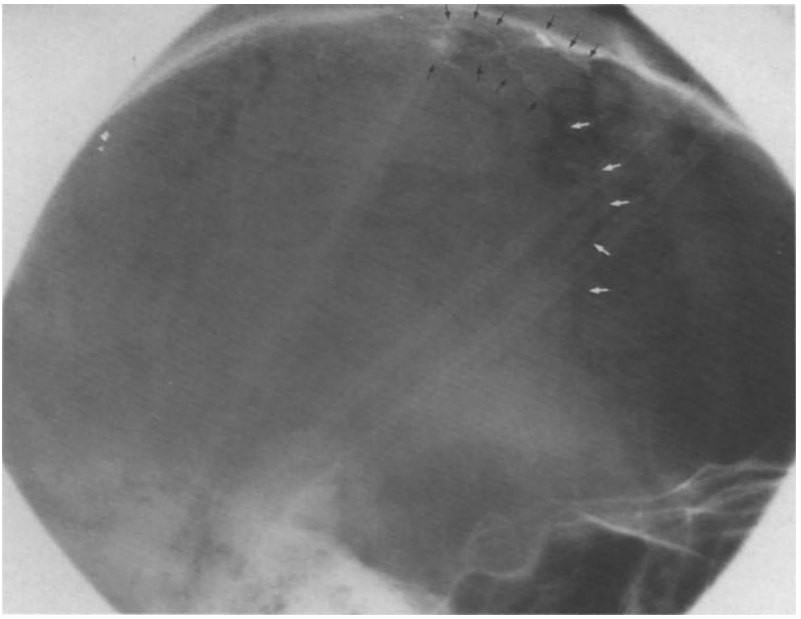


B

Figure 8.11. (**A**) Lateral DSA of a convexity dural AVM with cortical venous drainage (small arrows) and supplied by both middle meningeal arteries (large arrow: distal right MMA). (**B**) Superselective catheterization of the right MMA (arrow indicates catheter tip). (**C**) Plain lateral radiograph after embolization. White arrows delineate the groove of the MMA; black arrows delineate the branching, radiopaque glue within the distalmost portion of this vessel. (**D**) Lateral DSA after embolization demonstrates complete occlusion of the AVM.



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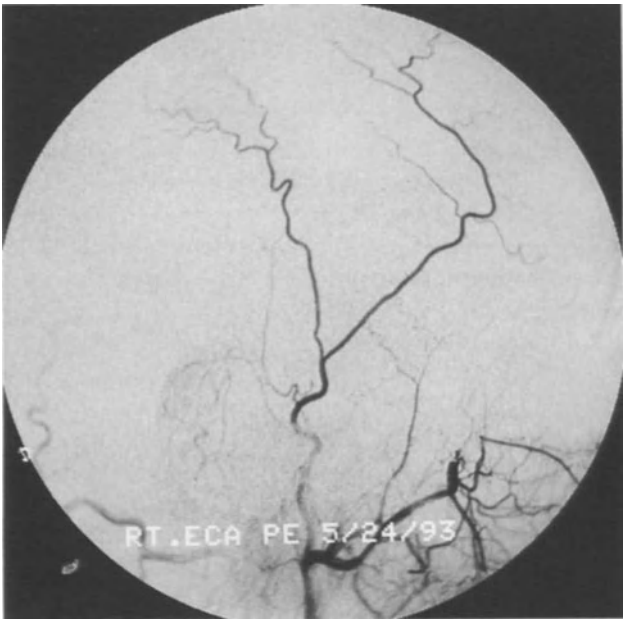


D

Figure 8.11 (*continued*)

Dural AVMs of the anterior cranial fossae, tentorium, and falx often present with intracranial hemorrhage, as they frequently drain into cortical veins. In the dural AVMs involving the superior sagittal sinus, the clinical presentation may vary depending on the venous drainage and degree of AV shunting.

Embolization has become the treatment of choice for dural AVMs in the cavernous sinus. Among 52 patients we treated through 1989, symptoms improved in 94% of cases. The lesion was occluded in most patients, with only one transient complication secondary to embolization to the middle cerebral artery. In cavernous sinus lesions incomplete embolization (leaving dural branches of the C4 and C5 internal carotid artery untreated) is often followed by delayed secondary thrombosis, resulting in complete obliteration of the lesion. It is frequently facilitated by a protocol of carotid compression (performed by the patient using only his contralateral hand) during the postembolization period. In addition, a number of cases may be treated by cavernous sinus packing via a venous approach employing macroembolic agents such as coils. This treatment promotes retrograde thrombosis in the dural AVM nidus, resulting in occlusion of the malformation.

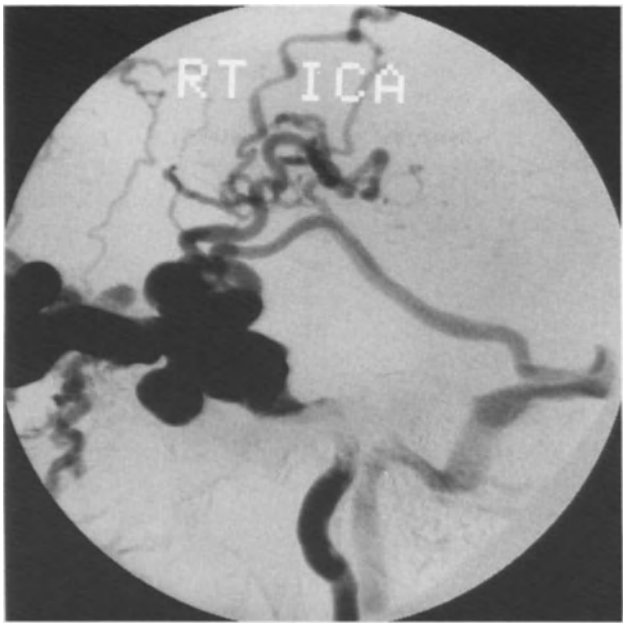
In 36 patients with a posterior fossa dural AVM requiring treatment, the success of treatment in terms of alleviating symptoms was more than 90%. However, total anatomic obliteration of the lesion was accomplished in only 70% of cases. A serious complication (ipsilateral blindness via middle meningeal-ophthalmic anastomosis) occurred in one patient. The results of embolization and its risks compare favorably to those of surgery.

Brain AVMs

The natural history of symptomatic brain AVMs suggests that treatment should be aggressive. Surgical resection is recommended for lesions not involving neurologically eloquent areas of the brain. Treatment is especially indicated in patients with documented intracranial hemorrhage.

Embolization techniques have evolved from the surgical introduction of embolic agents via cutdown of the carotid artery to the use of percutaneous transcatheter techniques utilizing either particulate embolic agents or liquid tissue adhesives. At present, the usual mode of endovascular treatment of cerebral AVMs at NYU is that of superselective catheterization and the injection of liquid *n*-butylcyanoacrylate (NBCA). This treatment is effective primarily in cases where embolization is the only treatment modality or if embolization is combined with stereotaxic radiosurgery.

Three approaches to the use of embolization for treatment of AVMs of the brain can be distinguished. In some cases complete obliteration of the malformation is achieved by embolization alone. More commonly, embolization is employed preoperatively (in conjunction with conventional surgery or stereotaxic radiosurgery) to treat lesions otherwise considered untreatable because of their size or location. Lastly, for highly complex inoperable



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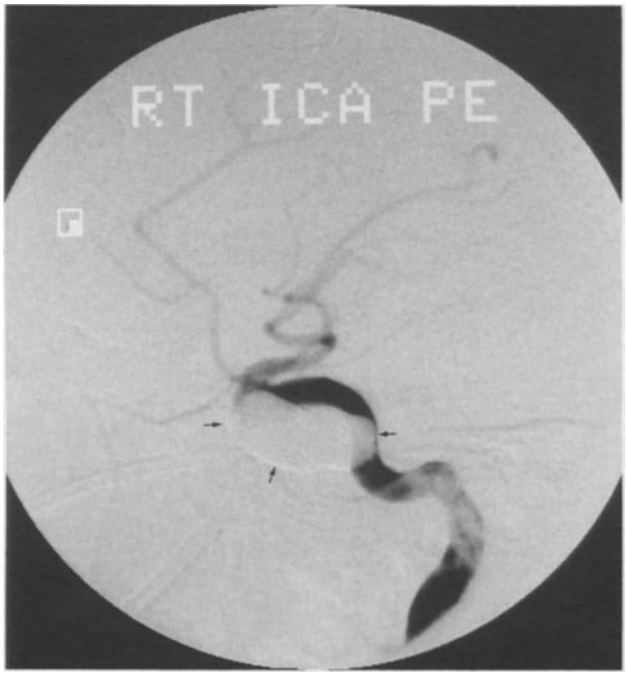
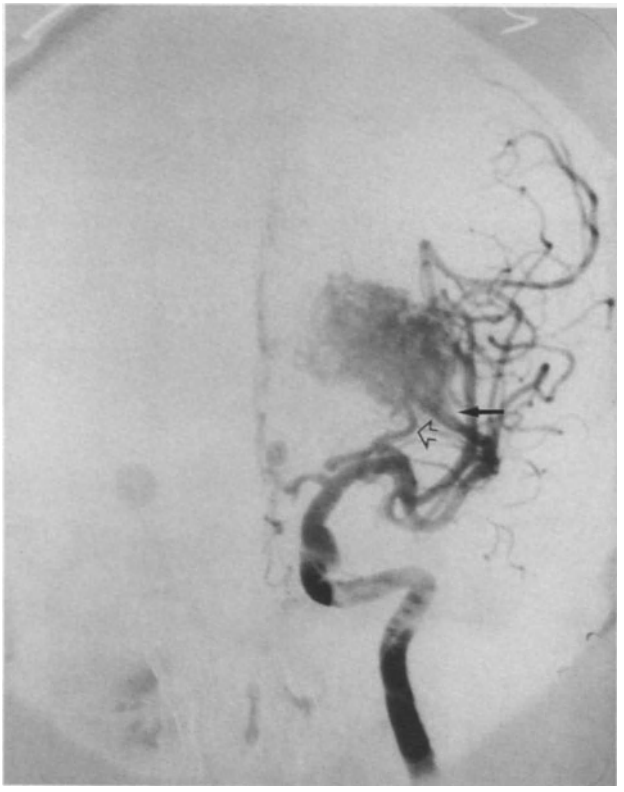


B

Figure 8.12. (**A**) Lateral subtraction angiogram of the left internal carotid artery demonstrates a CCF with anterior and cortical venous drainage. (**B**) Post embolization control angiogram of the internal carotid artery shows complete obliteration of the fistula and preservation of carotid flow. Two overlapping balloons are subtracted (arrows).

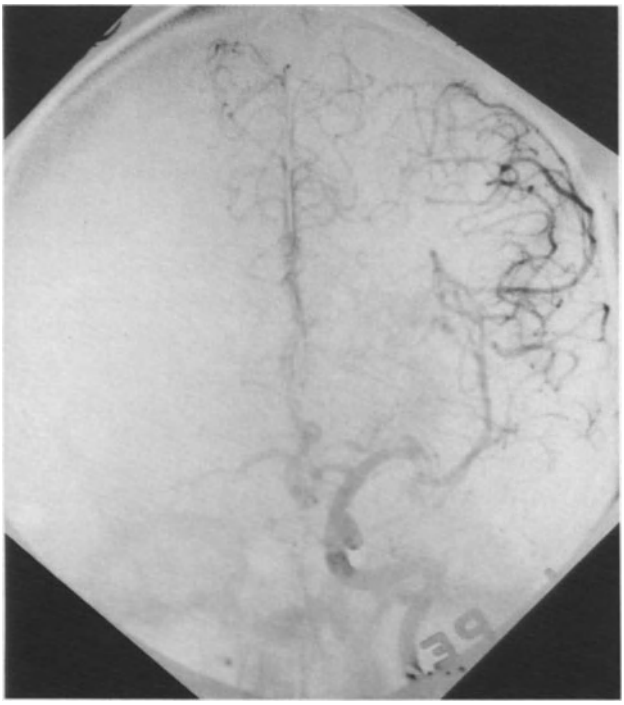
AVMs embolization may be used alone for the palliation of headaches or other neurological symptoms (seizures) related to the localized hemodynamic disturbances affecting surrounding areas of the brain.

When complete obliteration is not expected from the preliminary angiogram, and attempt is made to select pedicles that are involved in the highest-flow fistulas (Fig. 8.3) or those that harbor an arterial or venous aneurysm in their course (Fig. 8.6). If a venous ectasia or area of venous outflow constraint is primarily supplied by one AVM compartment and it can be occluded, partial embolization is acceptable, as this area may represent angioarchitectural weakness and be a site for potential hemorrhage.



A

Figure 8.13. (**A**) Frontal subtraction angiogram of the left internal carotid artery demonstrates a basal ganglia AVM supplied by the middle cerebral artery (black arrow) and two lenticulostriate arteries (open arrow) (same patient as in Figure 8.7). (**B**) Postembolization control angiogram of the left internal carotid artery demonstrating complete obliteration of the malformation, which was accomplished without complication. (Reprinted with permission of Berenstein and Lasjaunias. Surgical Neuroangiography, Vol. 4.)



B

Figure 8.13 (*continued*)

In patients presenting with progressive neurological deficits in whom total obliteration is not possible, partial treatment may be beneficial for arresting or alleviating symptoms.

Successful embolization with NBCA depends on superselective catheterization just proximal to or at the nidus of the AVM and beyond normal arteries. Accurate delivery of NBCA to the nidus requires experience (Fig. 8.13). The experience of the centers performing significant numbers of cerebral embolizations for AVMs of the brain have a morbidity rate of 5% to 7%, and a mortality rate of 1% to 6% (data presented at the VII International Working Group of Interventional Neuroradiology, Val D'Isere, France, 1987).

Galenic AVMs affecting the pediatric population once had a dismal prognosis with conventional surgical therapies. Endovascular embolization is now the standard treatment for these difficult lesions. Up to 1990, we have had experience in treating 25 patients with midline AVMs draining into the vein of Galen. The results (Table 8.6) are favorable in this specific group of patients when compared to those of untreated or surgically treated patients.

Although NBCA has become the agent of choice for embolic therapy

Table 8.6. Vein of Galen malformations: 25 patients treated by embolization (1984–1989)

Patients	No.	Normal	Impaired[a]	Dead
Neonates	12	7 (58%)	3 (25%)	2 (17%)
Infants	8	6 (75%)	1 (12.5%)	1 (12.5%)
Older children and adults	5	3 (60%)	1 (20%)	1 (20%)
Total	25	16 (64%)	5 (20%)	4 (16%)

[a] Includes 12% morbidity due to treatment.

of AVMs of the brain, concern exists as to the malignant potential of the cyanoacrylates. Among available data there is only one report of the carcinogenic potential of the alkylcyanoacrylates. This report referred to a weak mutagenic potential of these compounds in bacteria using the Ames test. Its extrapolation to specific clinical settings is not well established. A large body of literature exists as to the histotoxicity of the alkylcyanoacrylates. During the 20+ years that these agents have been used in medicine, no report exists of an associated tumor in humans. Furthermore, there is no documentation of an allergic or otherwise toxic effect in relation to the use of isobutyl-2-cyanoacrylate (IBCA) or NBCA.

In view of the questions that still surround the use of NBCA, embolotherapy is performed when we believe that the expected natural history in the individual situation is worse than the combined morbidity and mortality of the technique. Factors such as age, presenting symptoms, previous number of hemorrhages, location, and angioarchitecture are taken into account when making this decision.

At present, most malformations referred for treatment solely with NBCA embolization are large, deep, multiple-pedicle lesions in eloquent areas of the brain (Figs. 8.3 and 8.13), lesions considered inoperable, and large brain AVMs unlikely to benefit from radiosurgery primarily. The therapeutic strategy in these cases is to (1) attack focal angioarchitectural weaknesses such as aneurysms arising within the nidus or feeding pedicles, and (2) reduce the size of the AVM nidus, rendering it amenable to stereotaxic radiosurgery.

Spine and Spinal Cord Lesions

In the spinal territory, endovascular therapeutic procedures can be performed for lesions that involve the spinal column and cord. Endovascular embolizations in the spine are primarily performed for tumors as listed in Table 8.7. For most lesions the procedure is done preoperatively or prior to percutaneous biopsy. In some selected cases, such as metastatic tumors, aggressive treatment with a cytotoxic agent (e.g., 95% ethyl alcohol) can be an effective palliative measure.

In the spinal cord, surgical neuroangiography plays a significant role in

Table 8.7. Spinal tumor embolization

Hemangioma
Osteoblastoma
Aneurysmal bone cyst
Giant cell tumor
Plasmacytoma
Ewing sarcoma
Metastatic kidney
Metastatic thyroid

Table 8.8. Spine and spinal cord AVMs

Spinal cord AVMs
Anterior spinal artery
Posterior spinal artery
Metameric AVMs[a]
Spinal cord
Dura
Bone
Muscle
Subcutaneous tissue
Skin
Spinal dural AVMs
Extraspinal arteries draining to medullary veins

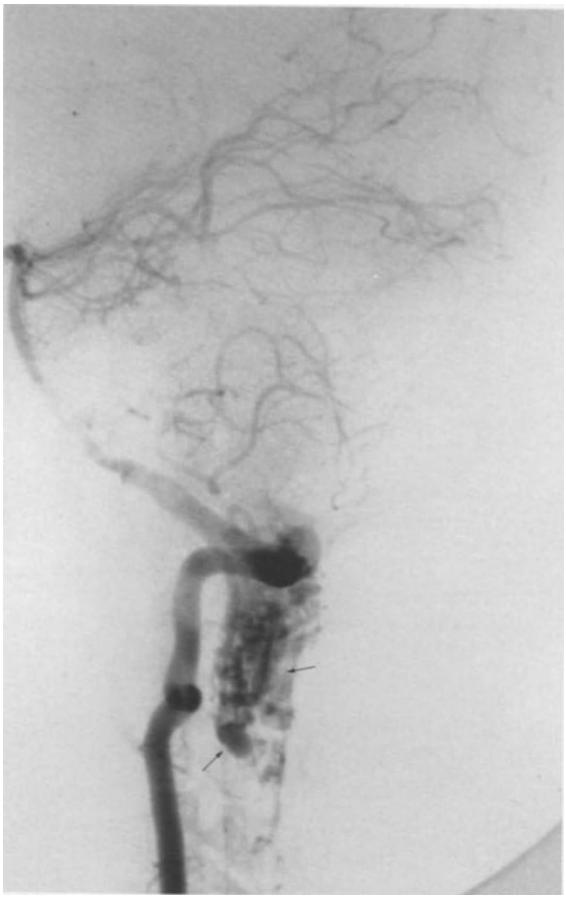
[a] Metameric AVMs can involve all or part of these structures and be associated with systemic disease such as Osler-Weber-Rendu syndrome.

the diagnosis and management of AVMs. There are three main types of AVM of the spinal cord (Table 8.8).

The first group consists of high-flow AVMs, which are usually intrinsic to the cord and supplied by the anterior (ASA) or posterior (PSA) spinal arteries (or both). These lesions usually become symptomatic before the fourth decade of life. Approximately 60% present with subarachnoid hemorrhage (SAH), 25% of patients present with radicular pain or weakness, and the rest present with a progressively developing myelopathy. At angiography, a high-flow malformation supplied by multiple pedicles is found. AV fistulas are frequently present with prominent and usually aneurysmally dilated venous channels (Fig. 8.14). Treatment with conventional surgery may be difficult or impossible. Embolization generally involves superselective catheterization of the supplying vessels under physiological monitoring of spinal cord functions through the use of somatosensory evoked potentials, with or without provocative testing with intraarterial sodium Amytal (Fig. 8.14). In our expe-

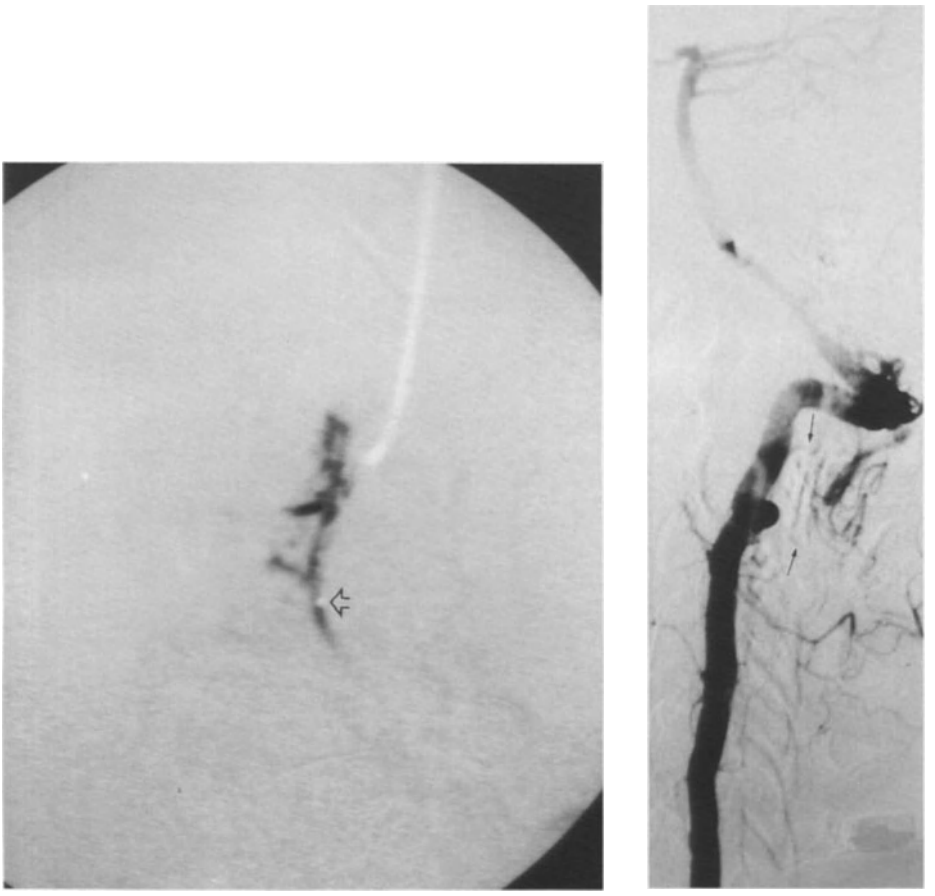
rience with 25 cervical and 24 thoracolumbar high-flow AVMs, complete obliteration was possible in more than 75% of cervical lesions. Only one patient became worse after treatment. Among the thoracolumbar AVMs, 60% were completely obliterated; two patients became worse after treatment.

A second group of patients are those with extensive metameric lesions in which the spinal cord is only part of the involvement. In these cases the



A

Figure 8.14. (**A**) Lateral vertebral artery angiogram of an intramedullary cervical spinal cord AVM (same patient as in Figure 8.9) demonstrating areas of ectasia (arrows) within the high-cervical nidus. (**B**) Superselective embolization of the anterior spinal artery showing the glue cast. Punctate artifact (open arrow) represents the prior position of the microcatheter tip; an artifact from the larger coaxial catheter is also seen. (**C**) Postembolization control angiogram shows occlusion of the intramedullary nidus. Arrows point to the glue artifact. (Reprinted with permission of Berenstein and Lasjaunias. Surgical Neuroangiography, Vol. 5.)



B C

Figure 8.14 (*continued*)

vascular malformation may involve the spinal cord, dura, bone, muscle, subcutaneous tissues, and even skin. These patients have a significantly more complex problem, and treatment is directed toward the symptomatic area, which usually relates to the spinal cord (SAH) or to nerve root compression by large veins.

The third group consists of the slow-flow dural spinal AVMs, which usually present during the fifth or sixth decade of life with progressive myelopathy. They probably are acquired and are similar to dural malformations in other locations. Angiographically, the feeding pedicle is usually single, it is not hypertrophied, and the circulation time is slow. The angiomatous network consists of 300- to 500-μm vessels and is outside the spinal cord. The venous drainage of these lesions is into medullary veins, which can be

followed for long segments, even up to the intracranial dural sinuses and can explain the neurological symptoms. Treatment of these dural slow-flow malformations is best achieved by IBCA or NBCA embolization. In cases where the feeding pedicle to the lesion also gives rise to a spinomedullary artery (ASA) or when embolization fails, surgery, consisting of a duraplasty, can achieve similar results and is greatly facilitated by prior angiographic localization.

Reconstruction

Arteriovenous Fistulas

Arteriovenous fistulas usually represent open communication between an artery and a vein with blood passing through an abnormal AV shunt at arterial pressure. A significant quantity of blood is diverted from normal tissue beyond the fistula to the venous circulation (region of lower resistance). It may result in elevated venous pressure and significantly decreased regional tissue perfusion. Complications of the abnormal hemodynamic state resulting from the fistula include congestive heart failure related to high output in infants or debilitated older patients, cerebral ischemia, and venous hypertension. The latter may result in communicating hydrocephalus or can produce aneurysmal dilatation of veins. It results in adjacent compression symptoms and the effects of chronic venous outflow obstruction.

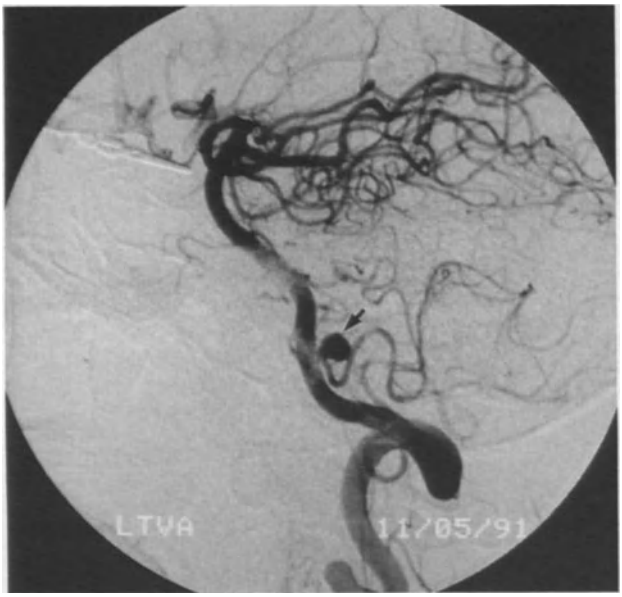
Although large single-hole fistulas may occur anywhere, they are commonly seen between the internal carotid artery and the cavernous sinus, producing a carotid–cavernous fistula (CCF) (Fig. 8.12). Another frequent site of AV fistulas is in the cervical vertebral artery. In this instance, there may be a communication with the paravertebral venous plexus. Fistulas may occur within the intracranial circulation but are less frequent there.

Arteriovenous fistulas of the head and neck and the base of the skull are usually posttraumatic in nature and consist of one or two large holes between the artery and the adjacent vein or sinus. These is little tendency toward spontaneous cure. Clinical signs and symptoms depend on the size of the shunt and the direction of outflow from the cavernous sinus, the paravertebral venous plexus, or intracranially from involved pial veins.

Surgical approaches to AV fistulas primarily in the cavernous or vertebral artery distributions are difficult. The approach is indirect and usually results in occlusion of the internal carotid artery by a trapping procedure. Embolization ideally involves selective placement of an appropriately sized balloon or combination of occluding coils directly into the fistula, thereby preserving flow in the parent vessel.

Aneurysms

Aneurysms represent one of the most exciting new frontiers where surgical neuroangiography may offer an alternative in management. At present,



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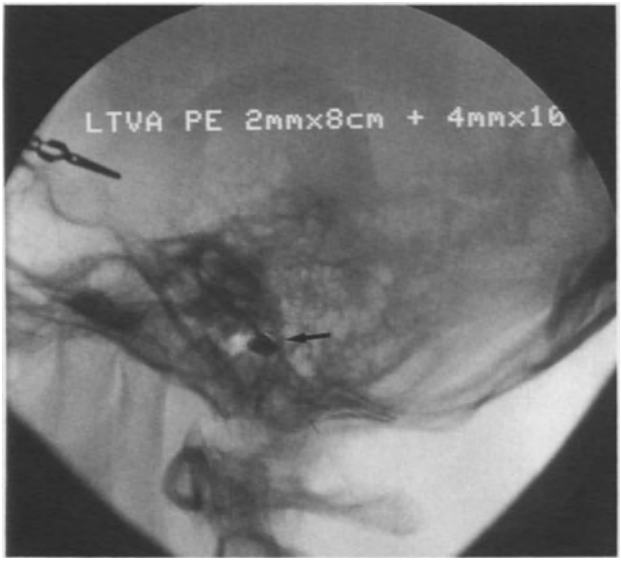
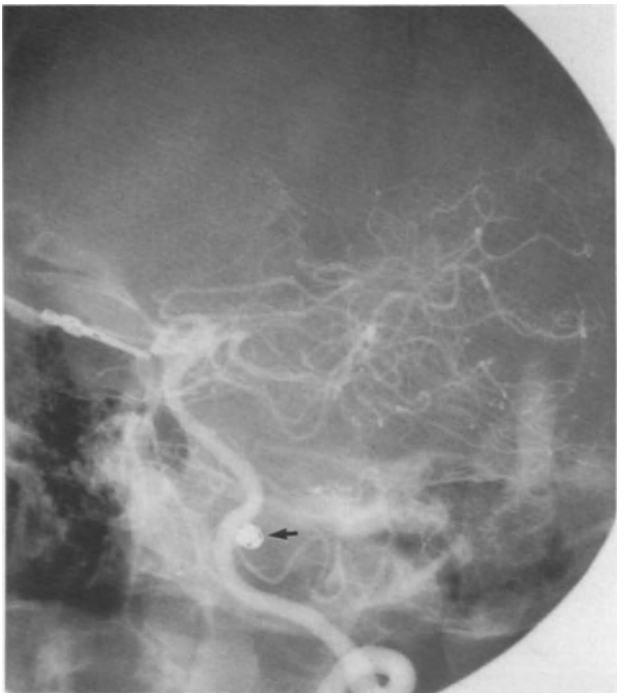


B

Figure 8.15. (**A**) Preembolization left vertebral DSA in a patient with a left posterior inferior cerebellar artery (PICA) aneurysm (arrow). There had been prior clipping of a right posterior communicating artery aneurysm. (**B**) Postembolization lateral skull radiograph demonstrating the GDC complex (arrow). (**C**) Postembolization left vertebral angiogram demonstrating occlusion of the aneurysm with preservation of the parent vessel. Arrow indicates the GDC coil.



C

Figure 8.15 (*continued*)

neuroangiograply is especially valuable in instances where contemporary microsurgical techniques are unavailable or, if available, carry significant risks.

At present, the treatment of aneurysms by embolization may be divided into two approaches: (1) for cases in which the parent vessel can be sacrificed; and (2) for more selective procedures where the aneurysm itself may be occluded with preservation of flow in the parent vessel. An example where parent vessel occlusion is appropriate is balloon trapping of the internal carotid artery in a patient with a symptomatic cavernous carotid aneurysm, a patent circle of Willis, and collateral flow supporting ipsilateral hemispheric functioning.

Techniques have been developed that allow selective access to, and obliteration of, intracranial aneurysms with preservation of the parent vessels. Romodanov and Scheglov from the Soviet Union in 1982 published an impressive report of the intravascular occlusion of saccular aneurysms of the cerebral arteries by means of detachable balloons. In their report, 119 patients with developmental aneurysms were treated in this manner. In 93 patients (78%) they were able to occlude the aneurysms with patency of the

parent artery. They called this technique their "reconstructive operation." In 15 patients (12.6%), they occluded the aneurysms but sacrificed the parent artery, procedures referred to as "deconstructive operations." In 11 cases (9.2%), the authors failed to occlude the aneurysm by the endovascular route.

Since 1991 a device called the Guglielmi Detachable Coil (Target Therapeutics), or GDC, has been undergoing clinical trials for use in aneurysm occlusion. These fine platinum coils are soldered to a stainless steel stem wire, which may be detached electrolytically once satisfactory placement has been achieved (Fig. 8.15). This device has now been employed in more than 200 cases (primarily giant or otherwise nonsurgical aneurysms) with impressive results; wider use of this technique is expected.

Risks and Complications of Embolization and Reconstruction

The risks and complications of surgical neuroangiographic techniques vary depending on the lesion treated. In experienced hands, for head and neck embolization, the procedure carries a morbidity of 1% and near 0% mortality. In the cerebral circulation, depending on the complexity of the problem, location, and extent, reported morbidity is less than 10% and mortality less than 5%. These figures include the risk of angiography and embolization.

Aberrant Embolization

When eloquent areas of the central nervous system are involved, aberrant embolization is the most serious complication. It occurs during intracerebral embolization or may occur with head and neck embolization where emboli are refluxed into the cerebral arteries or when antegrade embolization between anastomosis of the external carotid artery and the intracerebral circulation occurs (Table 8.4).

Embolization to the pulmonary circulation may occur through large AV shunt. Although usually it has produced no clinical manifestations in adult patients, we have seen two newborns early in our experience with vein of Galen malformations who died from pulmonary emboli. Aberrant embolization may also produce ischemic ulcerations in skin and mucous membranes.

Nerve Palsies

Aggressive embolization of various vascular territories occasionally results in selective cranial nerve deficits. For instance, liquid, alcohol, or small particle (< 100 μm) embolic ablation of the petrosal branch of the middle meningeal artery or stylomastoid artery may result in palsy of the VII cranial nerve and the maxillary division of the V cranial nerve. Embolization of the neuromeningeal branch of the ascending pharyngeal artery may damage the

IX, X, XI, and XII cranial nerves (Table 8.4). In the lumbosacral area, embolization of the hypogastric branches can produce palsy of the sciatic nerve and sacral plexus. Nerve damage and other nonneurological complications are more likely to occur when liquid embolic or cytotoxic agents are used. They are less likely to occur and are more transient when larger particulate embolic (>150 μm) are used.

Intracranial Hemorrhage

Rupture of a cerebral artery during microcatheter manipulation can result in intracerebral or subarachnoid hemorrhage. Immediate hemostasis can usually be obtained through the same microcatheter. In addition, some investigators believe that intracranial hemorrhage, associated with massive edema, may follow abrupt closure of a large cerebral AVM and may be analogous to the "perfusion-pressure breakthrough" phenomenon. Hemorrhage may also complicate embolizations in which the venous drainage is significantly occluded in the face of residual AVM nidus. This complication should be prevented by the use of polymerizing mixtures that allow more precise control in the deposition of the embolic agent and by staging the procedures, allowing hemodynamic accommodation to the altered postembolization.

Necrosis

Ischemia to normal tissues may produce necrosis, primarily if the collateral circulation is compromised. Critical territories include the tip of the tongue and pinna of the ear. In addition, when multiple ligations have constrained circulation, embolization through small collaterals may produce skin necrosis. Poor wound healing and necrosis have been reported following significant reduction of scalp vessels. Fever, pain, and local swelling can be observed and usually reflect ischemic changes in normal tissue. The association of muscle pain and trismus also results from occlusion of normal branches of the masticator muscles.

Tissue Swelling

Local tissue swelling due to inflammatory changes may follow embolization. It is of particular concern for those lesions located in or near the upper respiratory tract and for certain intracranial lesions in which postembolization swelling may result in a sudden increase in intracranial pressure or local mass effect. The potential complications may be ameliorated in part by the use of diuretics and corticosteroids. In some cases of paratracheal lesions, prophylactic intubation or tracheostomy may be indicated.

Lymphadenopathy due to inflammatory reaction to emboli has been re-

ported in the scalp and skin and is usually transient. Atrophy of muscles, such as the facial muscles, has also been reported.

Bradycardia

At times, bradycardia is seen during injection of the internal maxillary or ascending pharyngeal arteries. It usually resolves spontaneously, and atropine is administered only if necessary.

Catheter Adherence

With the use of liquid polymerizing material (cyanoacrylates), catheters may adhere to vessel walls. This problem occurred more frequently in the past when calibrated-leak balloon microcatheters and IBCA were in common usage. Clinically, no adverse effects have been observed or reported from this technical complication (10 times in our experience).

Complications of CCF Closure

Complications associated with CCF closure include cranial nerve palsy related to neural compression by the inflated balloon within the cavernous sinus; it is usually transient. Varying degrees of extrinsic compression of the carotid lumen may occur. The main risks of the procedure are thromboembolic episodes or premature balloon detachment (highly unusual) that may require immediate balloon embolectomy. False aneurysm or pouch-like formation within the cavernous sinus may result from too-rapid balloon deflation, although the patient is usually asymptomatic. Several cases have been reported where pain or persistent nerve palsy secondary to the pseudoaneurysm occurred. A second procedure may be needed that could require occlusion of the carotid artery. Serious complications occur in fewer than 1% of cases, and mortality is rare. If catheterization of the fistula is not accomplished, trapping of the fistula with distal and proximal balloon occlusion in the internal carotid artery may be carried out in patients previously shown to tolerate carotid occlusion.

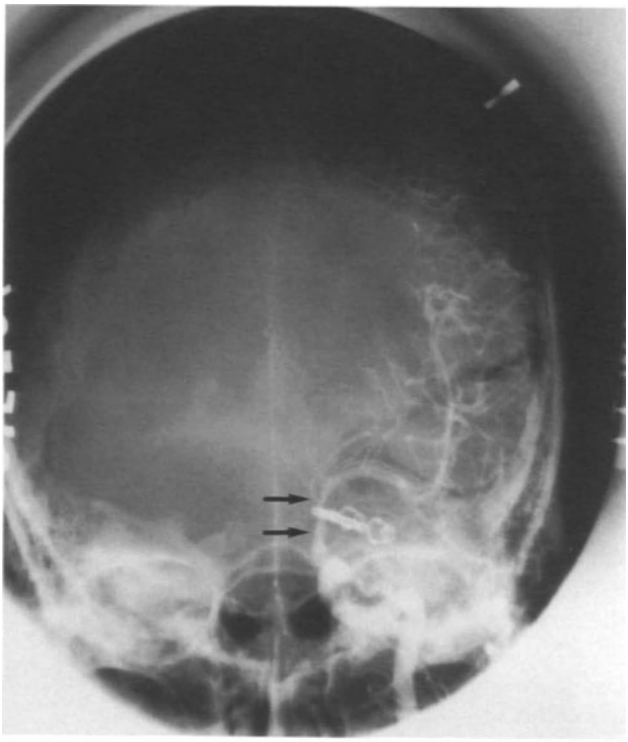
Revascularization

Revascularization may be accomplished by angioplasty or thrombolytic therapy, depending on the suspected cause of the vascular occlusion.

Angioplasty

Angioplasty of cerebrovascular arteries is not widely performed despite its extensive use in the coronary, peripheral, and renal circulations. In the carotid and vertebral territories, the fear of distal cerebral embolization has

inhibited the use of angioplasty in atherosclerotic lesions. Several successful dilatations of brachiocephalic arteries, without complications, have been reported. With atherosclerotic lesions, the best indications for angioplasty at present are to relieve subclavian steal syndrome or to dilate the external carotid artery in preparation for bypass surgery. It can be done retrogradely or antegradely at the origin of the common carotid artery where direct surgery is more difficult. Indications, however, await clear definition of risks and comparative efficacy in relation to alternative surgical and medical approaches. Balloon angioplasty in stenotic lesions such as fibromuscular dysplasia has been successfully performed in brachiocephalic vessels and has produced results comparable to or better than those of surgical dilatations. The balloons can easily reach multiple and more distal segments of narrowing compared with surgical dilators. The procedure is done percuta-



A

Figure 8.16. After a left posterior communicating artery aneurysm was clipped, this patient developed right-sided weakness and paresthesias postoperatively. (**A**) AP left internal carotid artery angiogram. Arrows indicate stenotic segments proximal and distal to the aneurysm clip. (**B**) Postballoon angioplasty angiogram clearly demonstrates dilatation of these segments (arrows). Patient improved clinically following the procedure.

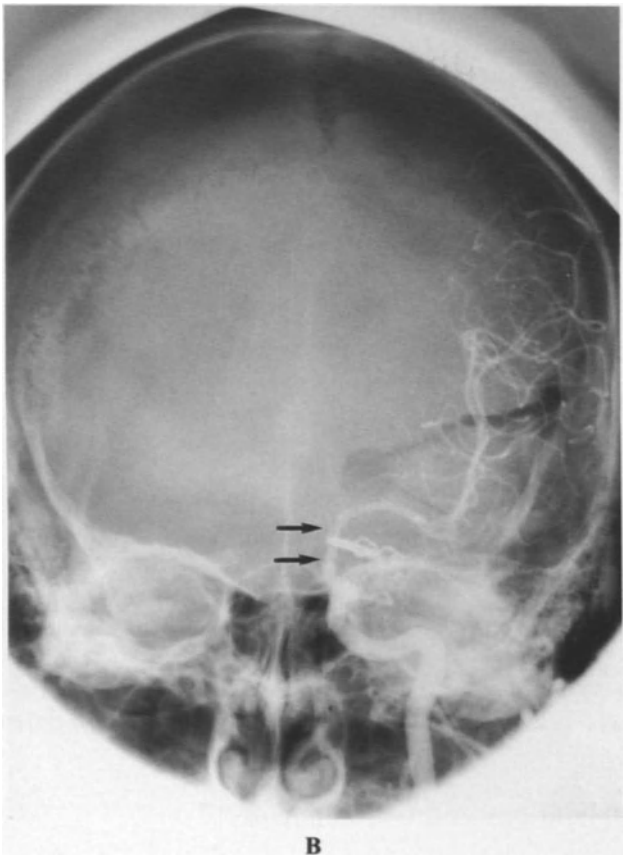


Figure 8.16 (*continued*)

neously under fluoroscopic control while the patient is awake. Postoperative angiography can be done at the same catheterization.

Angioplasty of intracranial arteries is also recommended for the treatment of vasospasm complicating subarachnoid hemorrhage. Both the evaluation [e.g., transcranial Doppler (TCD) monitoring, single photon emission computed tomography (SPECT)] and treatment (rheological, intraarterial papaverine, or angioplasty) of this condition is actively evolving. Results of angioplasty have been shown to be dramatic and long-lasting when patients are properly selected (Fig. 8.16).

Thrombolytic Therapy

Recanalization of acutely occluded cerebral arteries using fibrinolytic drugs such as streptokinase and urokinase was tried during the early 1960s with

poor and sometimes catastrophic results. In cardiology, fibrinolytic therapy has stimulated a renewed interest in this therapy. A newer approach of delivering the fibrinolytic drug close to or within the clot itself has been successful in selected cases of vertebrobasilar and middle cerebral artery thrombosis. Zeumer demonstrated the feasibility of recanalizing an occluded cerebral artery when done emergently without hemorrhagic complications. We have also used intraarterial thrombolytic agents to treat acute thromboembolic phenomena complicating neurointerventional procedures with good results. Again, this area is actively evolving, and the best "recipe" for clot dissolution has not yet been determined.

Intraarterial Infusions

Intraarterial infusions of cytotoxic agents have been used for the treatment of malignant tumors without major benefits. Our technological expertise allows selective delivery of these agents, but it appears to offer no advantage over systemic administration of currently available chemotherapeutic agents.

We have used 95% ethyl alcohol injected intraarterially for palliative treatment of selected malignant or aggressive tumors of the base of the skull, orbit (Fig. 8.17), or spine with encouraging results. The infusion of hormones such as estrogens has been used for dural AVMs and meningiomas and may play a role in treating some tumors with the appropriate receptors.

Future Applications and Developments

As endovascular therapeutic procedures are evolving, important developments and advancements are being made that point to an exciting future. The growth of this new frontier is accelerating. As the body of knowledge increases, new dimensions are being reached that permit the innovative application of these technologies to clinical practice.

The search for better, more reliable delivery systems and embolic agents is continuing. Major advancements in the future development of delivery systems include hydrophylic-coated catheters and wires, allowing greater ease of use and even better selectivity.

There is significant interest in the development of intravascular stents or percutaneously placed arterial grafts made of nitonil wire coils (a temperature-dependent flexible metal) or other materials, such as stainless steel multifilament, self-expanding, macrocompound stents. These stents can then recoat the inner surface of an artery harboring an aneurysm or an ulcerated atheromatous plaque without occluding the artery or its side branches.

The use of fibrinolytic agents has demonstrated that it is possible to achieve functionally significant revascularization of occluded cerebral arteries under certain time constraints without significant risk of producing

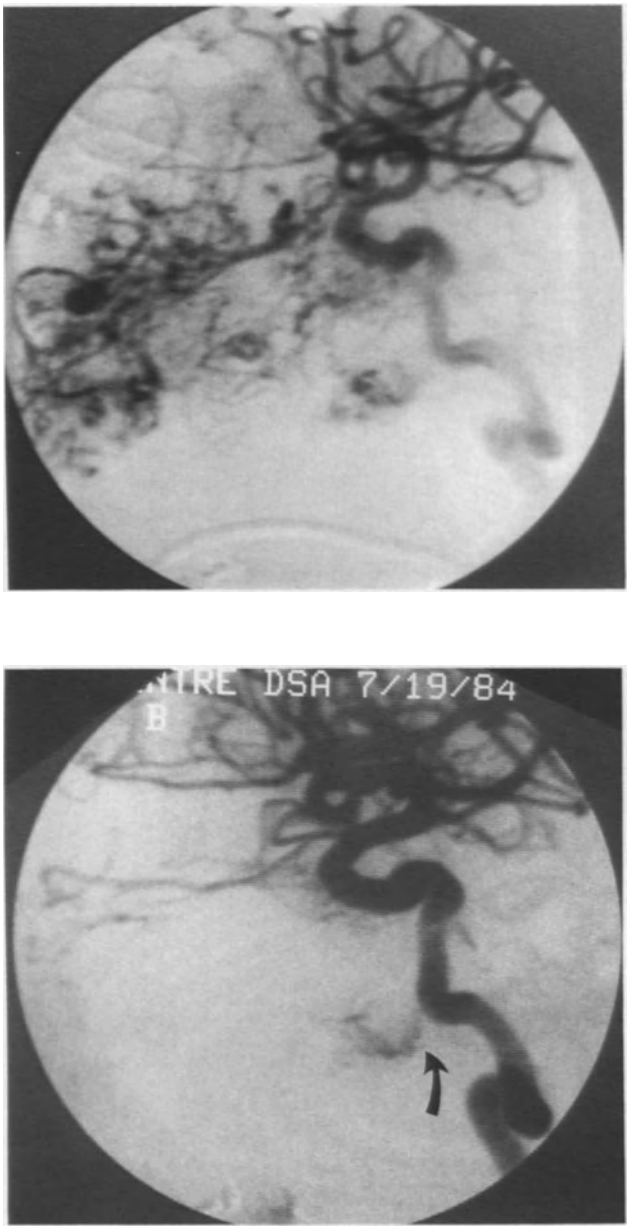


Figure 8.17. Aggressive esthesioneuroblastoma involving the orbit. (**A**) Lateral DSA of the right internal carotid artery demonstrates a hypervascular tumor. (**B**) One month follow-up after 95% ethanol was infused in the ophthalmic artery, middle meningeal artery, accessory meningeal artery, and artery of the foramen rotundum (not shown). Note the reduction in tumor vascularity and diameter of the ophthalmic artery. A supply from the noninfused mandibular artery remains (curved arrow). (Reprinted with permission of Berenstein and Lasjaunias. Surgical Neuroangiography, Vol. 2.)

disabling or fatal hemorrhage. Further experience with these techniques is necessary and should permit thrombolytic therapy in a wider selection of patients, including acute stroke victims.

Advancement in embolic agents requires the discovery of a combination of synthetic materials and biologically derived products. The ideal embolic agent is one that, when injected into a pathological territory, is biocompatible and nonreabsorbable—but at the same time, if injected into a normal area it can be dissolved or retrieved.

The ability to use time-released microcapsules or to tag embolic agents with chemotherapeutic agents or radioisotopes may permit us to treat malignant lesions more effectively with the appropriate receptors (e.g., estrogens, progesterones). The use of radiosensitizers placed within the interstices of a lesion may be used to maximize the effects of external irradiation.

At present, provocative testing with intraarterial Amytal injection may permit mapping of specific anatomical locations of neurological functions. Interventional neuroradiology is rapidly evolving in numerous areas. Physicians interested in pursuing this exciting frontier in medicine will have to become involved in the various areas of research and clinical applications of endovascular therapy on a full-time basis. The methods used for endovascular surgery require a great deal of technical skill in addition to an understanding of the anatomy and pathophysiology of the blood supply of the central and peripheral nervous systems. Physicians must understand the clinical presentation, natural history, and alternative modes of treatment in relation to each disease state. Physicians involved in this field must take responsibility for the performance of these specific operations, as well as take part in the decision-making process of combined therapies. The new medical field of surgical neuroangiography is now established, and participants in this endeavor must attain expertise in all aspects of patients' care, going far beyond the technical requirements of the associated procedures.

Suggested Reading

Surgical Neuroangiography series, Springer-Verlag, Pierre Lasjaunias, series editors.

Vol. 1: *Functional Anatomy of Craniofacial Arteries*, 1987
Vol. 2: *Endovascular Treatment of Craniofacial Lesions*, 1987
Vol. 3: *Functional Vascular Anatomy of Brain, Spinal Cord and Spine*, 1990
Vol. 4: *Endovascular Treatment of Cerebral Lesions*, 1992
Vol. 5: *Endovascular Treatment of Spine and Spinal Cord Lesions*, 1992

For further reading on selected topics, please refer to references within these volumes.

Discussion

Neuropsychological Evaluations

Dr. Eliava: If pre- and postoperative neuropsychological investigations are performed, are the data always taken into consideration relative to the results of surgery?

Dr. Berenstein: For the last 160 to 170 patients they have been performed by the same individual, and they are considered pertinent to the surgical outcomes.

Percentage of Total Occlusion of AVMs

Dr. Berenstein: The percentage of total AVM occlusions in my full series is about 16% to 17%, or about one-sixth. However, when you take into consideration a holohemispheric AVM, where the entire hemisphere is involved, in no case has there been total obliteration. On the other hand, when we have one or two pedicles we obtained complete obliteration of the lesion in approximately 90% of cases.

Dr. Eliava: Therefore with different types of AVM you can achieve different percentages of total occlusion?

Dr. Berenstein: We now have a number of patients in the process of being treated. That means they have been in treatment for 3 to 4 years. We can accomplish results today that we could not accomplish 4 to 5 years ago. We have a number of patients who are undergoing embolization followed by radiotherapy for the remainder of the lesion. In those cases I do not have exact figures as to how many were completely obliterated. One can argue (and I have heard this argument many times), "You only close 15% of the lesions. That is not too good a result." Present me with a frontopolar or an occipital single-pedicle AVM and I can get good results. However, with most of the patients we treated from the beginning this was not the case. They had large AVMs, and I cannot cure holohemispheric AVM.

AVMs of the Brainstem

Dr. Eliava: What can be done with AVMs located in the brainstem? Can you operate on these patients using endovascular methodologies? Such patients are a real challenge for surgeons using a direct approach. I personally do not conform to one method of treatment or the other. I do, however, believe that an important solution to the problem is to combine the techniques of direct surgical intervention and endovascular intervention.

Dr. Berenstein: We palliate them. We can partially decrease their flow. Is that a benefit? I do not know. Will it prevent recurrent hemorrhage? I do not know. We have had approximately 11 patients with brainstem lesions—patients with the worst deficits including the locked-in syndrome and others with severe paresis whose condition improved following embolization of a brainstem AVM.

Dr. Moret: We consider brainstem localization to be a contraindication because we believe that treating the AVM completely could subject the patient to a high risk of a major stroke. For this reason we do not touch lesions of the brainstem. That caveat does not include AVMs of the cerebellum.

Dr. Eliava: When I referred to the brainstem it excluded the thalamus. Dr. Moret stressed that the thalamus was a relatively safe area for endovascular approaches.

Air Embolization During AVM Embolization

Dr. Taveras: What was the percentage of patients suffering air embolus following endovascular interventional procedures?

Dr. Berenstein: Very few, perhaps 5% to 10%.

Selection of Patients Suitable for Endovascular Therapy

Dr. Apuzzo: How do you select patients for treatment?

Dr. Berenstein: We select them in a joint manner. I believe that no single physician can cover all the aspects of these patients. The procedure is similar to what Dr. Viñuela has described. The patient's films are sent to either the neurosurgeon or directly to us with a detailed history. The case is presented in a conference. Four services are involved: the neuropsychologist, the neurologist, the neurosurgeon, and ourselves. The location and nature of the AVM is discussed and then a plan of management is devised. Not all cases engender agreement as to the given plan for management. There are often conflicting opinions, but once we come to an agreement a recommendation is made.

Dr. Apuzzo: Forgive me for pressing this point, but I would like to have an idea of whether the capability for managing AVMs in New York in any way transcends what is the "party line" from the standpoint of surgical intervention. We have new arrows in our quiver in terms of the endovascular approach and in terms of radiosurgery. Does this information in fact change the approach we take toward an individual who comes in with a headache, has a scan, and is discovered to have an AVM? Obviously, if the patient has had a hemorrhage, more vigorous thought is given given to treating them in some fashion. If an individual has seizures that are intractable or if there is evidence of a "steal phenomenon" we know we may have to treat that patient. But what about the incidental finding of an AVM in the frontal lobe of a patient who presents with headache?

Dr. Berenstein: I would say that today we would recommend treatment for a 25-year-old woman with only one seizure who is neurologically intact and has a dominant hemisphere lesion. Yes, we would treat her today—probably recommending surgery.

Dr. Apuzzo: Basically what you are saying is that the patients who are operable will be operated on?

Dr. Berenstein: Correct. If we are performing a preoperative embolization in a patient who is an operable candidate and we close the entire malformation, we do not necessarily operate because we can always operate as a follow-up procedure should repeat angiography demonstrate reopening the AVM. I say to myself: What I would like to do if I had this problem in *my* head? Take the case of the posterior fossa inferior vermian AVM. Even though it is surgically accessible, if it can be occluded endovascularly and at follow-up 1 year later it is still occluded, why operate?

Dr. Emily Friedman: The decision to operate in such cases was based on the experience with less than successful embolizations in the past. The reasons given were that postembolization surgery where the AVMs appeared to be occluded demonstrated persisting flow and clear evidence that the AVM was going to reform.

Dr. Berenstein: The technique I described is not last year's work; it represents the evolution of a technology over 10 to 11 years. When I was in Japan in 1982 Professor Handa said to me: "Dr. Berenstein, all your malformations are on the left side and are huge. What do you do with the small ones?" I answered, "I never see them." Now

I am starting to see and treat malformations that before were seen exclusively by the neurosurgeons. For example, a lesion that involves almost the entire occipital lobe is not a small malformation. Here try embolization first because we believe there is at least a 70% chance of preserving visual function. We are proceeding with the aim of trying to cure a surgically accessible lesion in which the neurosurgeon with whom I work tells me there is an 80% chance of the patient having a homonymous hemianopia after surgery. In that case I believe I am justified in trying to preserve visual function. A hemianopia is not a minor complication.

Previously we would not accept a frontopolar AVM for endovascular treatment, but now I do. Most patients we treat had had "impossible lesions." At the present time we have a number of patients "in transit"; that is, they have had radiosurgery, and it will take 2 years to determine their status. Some respond to radiosurgery, and some do not.

Dr. Leeds: As I understand you, when a patient returns to you he or she is considered a new patient. You know the problem, but it must be reevaluated for either recurrent symptoms or for a radiological appearance. Is that a correct assessment?

Dr. Berenstein: When the patient comes back he or she is evaluated for anatomical changes that have occurred since the initial treatment for the designated lesion. How can I argue if one can obliterate a lesion by any method? What I believe will be the answer in the future is that partial embolization of certain lesions that cannot be cured by any other method will result in some improvement in the natural history of the lesion. Partial embolization is not comparable to partial surgery.

Dr. Viñuela: One thing that must be considered is the dynamics in the decision-making process; a primary decision can change afterward. The other thing is that AVMs are different in each person. One AVM in a frontal lobe can change one person's way of life, whereas it may be tolerated by another. Given the statistics, the patient may say, "I want to keep the AVM. I have had it my entire life and nothing has happened. Why should I take a 2% risk with anything?" The dynamics of the decision-making process thus evolves in different ways for different patients.

One also works within a team. Our team chooses a course of action that entails making the most radical decision that has the least number of complications. Our basic aim is to eliminate the lesion.

Dr. Berenstein: What do you do with a 25-year-old woman who had a single seizure and a Broca's area AVM. She is neurologically intact. We physicians must admit that we can sway patients in the decision-making process. In this case you could play statistics, telling her that she has a 2% risk of morbidity following embolization. On the other hand, should you wait until the AVM ruptures and she becomes aphasic?

Dr. Viñuela: What of the reverse? Suppose the procedure produces the neurological deficit. Perhaps the patient will bleed 20 years from now or tomorrow and die. You can go either way.

Dr. Berenstein: That is what I am saying. Patients must participate in the decision-making. I know that 5 years ago I would not have recommended intervention in a 25-year-old with a Broca's area AVM. I would not touch it. Today it is different because I have abilities and techniques that I did not have previously.

Dr. Debrun: We have reached a difficult point in decision-making. We need guidelines. Let us take the Spetzler classification, which I consider useful for evaluating the risk of any treatment for a brain AVM.

Dr. Berenstein: Do you think that the Spetzler classification applies to endovascular intervention or surgical intervention?

Dr. Debrun: To classify the AVM according to the Spetzler classification, we con-

sider the age of the patient and the clinical presentation. Then we add the risk of any treatment: surgical resection, embolization, or embolization as a prelude to surgical resection. Our goal is to reach a complete cure of the AVM whenever possible; and to reach this goal, in a few patients we start with embolization. If we achieve a 100% cure that is fine. If we do not, we consider subsequent surgical resection. Finally, if we are not successful, we consider radiosurgery on the remnant of the AVM. Our decisions are based on a team decision, balancing the risk of any aggressive treatment. There are patients we do not treat and those we do. Most of the patients who undergo embolization had subsequent surgical resection. If I show you the statistics of the AVMs, you would see that they are not very different from those of your AVMs—and we have many more than 5% of AVMs that are operated upon after embolization. I think your statistics are based on AVMs that are surgically resectable —AVMs that could be resected and the patient cured forever.

Dr. Berenstein: Do you not think that after complete obliteration they are cured?

Dr. Debrun: You have very few in that category. In the best hands there are only about 18%.

Dr. Berenstein: Do you or your neurosurgeons take a holohemispheric AVM and cure it by surgery, embolization, and radiation?

Dr. Eliava: Do you achieve 70% of total occlusion in a widespread AVM?

Dr. Berenstein: No. I do not disagree that if the AVM is surgically accessible and we have not completely obliterated the lesion the patient should go to surgery. However, if the AVM can be completely obliterated and at the 2-year follow-up it remains so, I see no reason to operate.

Dr. Debrun: That is not my point. My point is that if only 18% of the patients are completely cured, it is not enough. I am sure you can do better with surgery after embolization.

Dr. Berenstein: For most of my patients I did not object to surgery; but if the surgeon does not wish to operate, should I say Dr. Debrun says you have to operate? The AVMs were monumental. They were so large nobody wanted to operate on them.

Dr. Moret: I want to relate my experience with brain AVMs. We have treated 303 patients using the same technique: glue and flow control. Flow control does not mean that we are always using the balloon, it means that when we are dealing with small vessels the size of the catheter is enough to control the flow. In most cases we are using a calibrated l-cc balloon. We approach the brain AVM in a completely different way. There are two factors. The first is to make a decision regarding treatment. This decision has always involved embolization first. The goal is to treat the AVM completely by embolization. Then if we do not reach our designated endpoint, we consider submitting the patient to either surgery or radiation surgery.

Dr. Berenstein: This is essentially the same approach as ours.

Dr. Moret: It is not the same because you are not treating the small brain AVM in the frontal area by endovascular means.

Dr. Viñuela: Our approach is different. It has evolved. In our institution endovascular therapy is available, and every AVM is embolized before surgery. The morbidity of the procedure is now so low that neurosurgeons have come to believe that having a partial embolization is valuable.

Dr. Moret: That was not my understanding. Do you agree that all brain AVMs in the frontal areas in the United States should be embolized first instead of having surgery?

Dr. Viñuela: Yes. The neurosurgeon allows me to embolize them.

AVMs and Their Pedicles

Dr. Moret: It does not matter how many pedicles there are. If one pedicle gives you the best approach to the nidus and you can place, with one attempt, 4 cc of glue inside the nidus, the other pedicles are irrelevant. One pedicle, two pedicles, ten pedicles—it does not matter. The only thing that is important is to reach the nidus, and the best way to catch the nidus involves proper selection of the pedicle.

Dr. Viñuela: The dynamics of the glue are different in a ten-pedicle AVM than in a one-pedicle AVM. You see the wash-in and the wash-out. You can do whatever you like in a one-pedicle AVM, but in a ten-pedicle AVM you cannot control the rest of the pedicles; you can inject as much as 10 cc, and wash-in controls where it goes. It relates to the pressures in the other pedicles.

Dr. Moret: This approach is purely theoretical. What pushes the glue in multiple pedicle angiomas is completely different. The way the glue enters the nidus and the way the glue polymerizes does not depend on the mixing. It depends only on the timing and on the surface between the blood and the mixture. There is a kind of layer deposition inside the nidus. The number of pedicles is unimportant. In a multiple-pedicle angioma it is possible to push 4 cc in one pedicle to reach the nidus without it seeping through the vein.

Dr. Berenstein: What has happened to the other pedicles?

Dr. Moret: The nidus is filled with glue.

Dr. Berenstein: You do not need to embolize the other pedicle?

Dr. Moret: We do not need to embolize the other pedicles. I am not saying that that is the case 100% of the time, but I am saying that for a ten-pedicle AVM if you embolize two or three pedicles it is possible to get the whole nidus.

Assessment of Surgery and Embolization

Dr. Alan Fox: What Dr. Berenstein has done during the past year to analyze his series has been an important contribution. He has examined details, and he is opening his records for us. Most of what Dr. Berenstein has said applies to our own case material, although there are some major differences. We have had the chance to embolize about 150 cases over the past 10 years, and the percent that were surgically resected after embolization is about 45% to 50%. If we consider just the past 3 years, about 90% to 95% of cases underwent resection after embolization.

After listening to this discussion I have arrived at the conclusion we must have different classifications. One category includes small or medium-sized AVMs. Dr. Stein told us he could remove these lesions safely from just about anywhere in the brain and that is the same with our surgeons if the lesions are small. They can even be removed from the most eloquent areas of the brain and safely in most instances. Dr. Moret has a growing experience of treating these lesions purely by embolization, and I think our results show some similarity with his aneurysm results. The cases that would be the best candidates for the lowest risk and the most successful embolizations are the ones (both AVMs and aneurysms) that could be treated by either microneurosurgery or endovascular surgery. I think we are all in general agreement on that.

At our institution I am probably the one with the least experience with those AVMs because I do not get the opportunity to treat them by embolization. There is no question in my mind that those would be the best cases. At the other extreme are the ones that are so large or in such inaccessible areas that there is no way, as Dr.

Berenstein has said, that one could ever completely obliterate them by embolization and there is no way one could ever remove them.

It becomes an important issue whether we should do anything with them. We have had cases where we blocked off 90% to 95% of the AVM, and the patient was intact afterward. Six months later there was no recanalization angiographically, but at 1 year, with no change in the remaining 10% of the AVM, a hemorrhage occurred and the patient died. What did we do for that patient? I am not sure. We cannot know that by blocking the remaining 10% we would have helped the patient.

There is a group of surgically difficult AVMs with the potential—with a great deal of luck—of being resected, and I think we can offer major help to these patients. It is mostly these patients we are preparing for the surgeon. We can stage the AVM using the endovascular approach. We can convert these AVMs which are at high risk of producing morbidity and mortality, by surgical resection into AVMs that can be more readily resected.

When I hear that only 5% of cases go on to surgery, I wonder how many of those have been incompletely embolized and have been denied cure. It is not your fault: It is the system. You say that they should undergo resection, but the surgeons does not think so, and thus these patients are being denied the cure you have enabled. Perhaps this rather large group of patients should go to a different surgeon who could handle the lesion. We should not be competing so much as working together. What the long term entails is the decision of whether the easy cases should be treated by the endovascular route or the surgical route. For both aneurysms and AVMs it becomes a philosophical, ethical, medical, and legal discussion, as well as a financial consideration. It is an enormous problem.

Dr. Sadek Hilal: We also have some data from preoperative embolization done in our institution. We had an opportunity to investigate the total obliteration of the nidus. There was much streaming of the embolization material. There is necrosis or partial thrombosis of channels, and one corner of that channel is filled as a completely normal vessel.

We use Dr. Viñuela's cocktail or something similar to that; we do not use bucrylate, the alcohol cocktail. We inject large amounts of these solutions. Once the material gets into the nidus, one cannot predict how much streaming will occur and how this material will mix with the blood.

The question remains whether a negative postembolization angiogram is sufficient for patient management. There will always be a surgeon who finds microscopically a small ipsilateral feeder coming to the nidus where perhaps a small amount was not filled with glue, alcohol, or whatever you were using.

The question then remains: Can we have a prospective study where some of the angiographically completely obliterated malformations can be followed for a long time, with some of them undergoing operation?

Dr. Berenstein: Is the surgeon then correct?

Dr. Hilal: The question is what is biologically significant to the patient.

Dr. Berenstein: How do you interpret an angiogram showing no AVM 2 years after initial embolization?

Dr. Hilal: You cannot tell me that the patient is definitely not going to rebleed. We simply do not have the statistics to support such a statement. What I am suggesting here is important because it affects not only patient management but the financial income to some of our colleagues in accordance with the system that exists in the United States. We need to perform a good controlled study to see what is best for this

type of patient. The study could be constructed from patients with postembolization negative angiograms, comparing nonsurgical and surgical outcomes.

Dr. Solomon: Who would operate on a patient with a negative angiogram?

Dr. Berenstein: I consulted with a neurosurgeon, who pointed out that no matter how skillful your neurosurgical technique there is a volume of brain that you cannot get away with removing without creating a deficit. If proper neuropsychiatric testing is done, the patients may have recognizable deficits, despite their outward appearance of physical integrity, which render them not the same human being.

Dr. Viñuela: We do not disagree. What I am saying is that the percentage of operations should not determine the final decision. The other important point relates to angiography. I believe we must be strict when interpreting angiograms. For the past 20 to 30 years the final evaluation was left in the hands of neurosurgeons. Today I must emphasize that the final evaluation regarding complete or incomplete resection of an AVM should be an angiographic evaluation. The point is that angiography 1 week postoperatively is not the same as angiography performed 3 months later. Early postoperative angiography (7–10 days) after surgery is important only to see the gross changes. A negative angiogram 10 days later means nothing. On the other hand, an angiogram 3 months later may be significant.

Dr. Fox: It is the same for postresection evaluation. Our surgeons do not reevaluate the results until 6 months later.

Dr. Viñuela: For cerebral angiography we have a parameter that has been "holy" for more than 30 years. No neurosurgeon has brought a patient back for angiography at 6 months after a negative study.

Dr. Berenstein: It is demanded of us.

Dr. Viñuela: I remember instances in which recurrent AVMs were found long after negative angiograms, and patients were hospitalized with a cerebral hemorrhage. Retrospective analysis of the angiogram done during the immediate postoperative period was "negative" for residual AVM, showing only some "mass effect" and a small hematoma. Three years later the patient returned with recurrence of the malformation.

Dr. Fox: "Regrown."

Dr. Viñuela: Regrown is probably incorrect terminology because the regrowth was what Dr. Berenstein showed; namely, leptomeningeal collaterals open and lead to the re-formation of the same nidus in the same location with the same draining vein.

Dr. Berenstein: They have not proliferated from a cellular point of view.

Dr. Viñuela: The point is that we must be realistic and admit that a negative angiogram 10 days after surgical excision of an AVM is not necessarily a negative angiogram. We must review the angiograms after 3 months, 6 months, and even 1 year.

Dr. Hilal: Dr. Viñuela, if the angiogram is negative, do you let the surgeon intervene? From my standpoint the surgeon is allowed to touch it if the angiogram is not negative 10 days or a month later.

Dr. Debrun: I would even reinforce what you said. When you are using the PVA/alcohol cocktail you may have a negative angiogram at the end of embolization; yet after 30 minutes, injecting the same pedicle reveals the nidus again. This picture is virtually proof of a temporary spasm, a temporary apparent occlusion of the nidus but not an actual occlusion.

Dr. Hilal: That is why we do not use only alcohol.

Dr. Viñuela: I think that is true, but the explanation is not valid. The reason is that

when you use the cocktail, or "liquid mixture," the first portion collects in the pedicle and then flows slowly into the AVM. Therefore it is wise to wait. I wait sometimes an hour and on many occasions I have performed 6, 7, 8, 10, and even 15 injections. If I use one pedicle and do not inject more than 10 syringesful, I am concerned. I wait until I know the result conclusively. An AVM is three-dimensional; if it has a volume of 5 to 6 cc and we inject only 1 cc, what should we condude?

Dr. Hilal: Absolutely right. How many of you have injected 10 cc of Bucrylate into a vascular malformation?

Dr. Viñuela: The results are good, even spectacular.

Dr. Hilal: The question is how much of the AVM's volume do we fill? But that question is not really important. The important point is that we have a negative angiogram at the end of the embolization.

Dr. Viñuela: And one year later.

Dr. Hilal: We should repeat the angiogram in about a month. If it is still negative, we can wait.

Dr. Berenstein: That is what we are doing with our patients and what Dr. Moret is doing with his patients. Dr. Debrun, if you have a completely negative angiogram after the embolization do you still operate?

Dr. Debrun: No, of course not.

Steal Phenomenon

Dr. Pile-Spellman: The size of an AVM is relevant to the total steal that can take place from a carotid system. The holohemispheric AVM is a shunt with multiple other potential shunts that can open up. If there are no other shunts, the actual functional cross-sectional area of a large AVM would be the resistance decrease that would be equal to the total steal. Depending on how many pieces you slice, resistance into the cross-sectional area increases. Therefore in order to occlude an AVM you may have to inject 10 cc of glue, but theoretically it must be composed of hundreds or thousands of fistulas. The real question may have to address not the volume but the cross-sectional area. The major achievement will be to find the fistula across which the pressure drops.

Classification of AVMs

Dr. Eliava: I want to comment on the different points of view in different clinics. It is a good situation because each of us develops our separate approaches to the surgical treatment of these patients. In the future, it will be possible simply to discuss the results of each method of treatment and maybe finally arrive at the best way to treat these cases.

I would like to return to the important question of classification. I am of the opinion that we can create an ideal classification that is acceptable to both neurosurgeons dealing with direct surgical approaches and neuroradiologists dealing with endovascular approaches. It would be advantageous to work out, at least in some preliminary fashion, a format for classifying AVMs so there might be improved understanding when we read each others' articles and when we compare our experiences. For example, classifying AVMs according to the feeding artery is a system that may be more important for the endovascular surgeon than for the neurosurgeon. For direct surgical approaches the important points are the site and size of the AVM.

Dr. Moret: Why do we need a classification system from the endovascular point of view? The goal is to reach the nidus, occlude the nidus, and avoid injury to the surrounding brain tissue.

Dr. Berenstein: The goal is to cure the patient.

Dr. Eliava: How then are you going to compare your observations with the observations of other surgeons?

Dr. Moret: By simply observing the results of treatment.

Dr. Eliava: But what about the site and size of the AVM?

Dr. Moret: Yes, but that is not a true classification. A classification system is a kind of scale that provides information for the purpose of making a decision. If you look at the angiogram from the endovascular point of view, there is no way to obtain this type of information. It can be obtained only when you are actually in the nidus.

Dr. Eliava: If you are going to compare your results of treatment using the endovascular method with those obtained by direct surgical intervention you must take into consideration the site of the lesion and its size, and perhaps the type of angioarchitecture, namely, the feeding arteries and the draining veins. The last point is an important one for endovascular surgeons but not as important for the neurosurgeon. Maybe there exists a way to find a common solution, to have a common language, so we can understand each other.

Dr. Holtzman: I think the point is well taken. I believe classifications are walls to which one takes a battering ram. The serve as a challenge to determine the truth at a given time. It is not unreasonable to propose that a classification system be developed independently by interventionalists and neurosurgeons to see if there are common denominators that allow for common understanding of each lesion and the subsequent revision of the scheme.

Dr. Taveras: A classification system would be an important framework and at least a basis for future evaluation of our results. A second consideration is the philosophical question regarding AVM treatment. Is the treatment aimed at total elimination of the malformation, which can be accomplished only by direct surgical intervention; or are we to be satisfied with angiographic elimination of the malformation, as it is the only method by which we can evaluate the AVM in vivo prior to surgery. If we are going to accept elimination of the lesion by angiography, when can we accept that angiographic elimination is equivalent to full treatment of the malformation? Is it 3 months later or 6 months later? Or should we wait even longer to be certain? These questions are important and need to be answered.

HEMA and Balloon Integrity

Dr. Fox: In the case where HEMA destroyed the balloon and you had a complication, I am not certain I understand the mechanism. About 2 years ago we bought a liter of HEMA and half a liter of PEGDM. Our pharmacy divided it into aliquots and placed the solutions in plastic syringes in the refrigerator. Whenever I want to use one I warm it beforehand. I have used many different types of balloon—Debrun balloons and others—and never in a warm waterbath or in air have I noticed the latex to dissolve in the presence of HEMA. We have now used it in more than 30 balloons and we have never had a balloon burst in the acute state.

Dr. Berenstein: Perhaps you were lucky.

Dr. Fox: Is it possible that it has something to do with the way the HEMA is packaged or the way our pharmacy has it sitting in a closed container in the refrigera-

tor? Has the ether somehow dissipated? I have no idea, but I do know that I have no problem with the material that I am using.

Dr. Berenstein: Perhaps the mixture of HEMA is different. We have also tried it with different mixtures. The ruptures occurred acutely, within 30 to 40 minutes of injection. Obviously it is a problem of the HEMA. Dr. Moret told us that he also had an experience with balloon rupture.

Dr. Moret: The problem with the HEMA occurred because of premature degradation of the latex. We took the HEMA and sent it to a chemist. After the analysis the chemist said that some bottles the HEMA we received had at least 10% ether. Ether, as you know, can degrade latex. That is the reason we have searched for a HEMA that has no ether. I would strongly recommend that if you are going to use a latex balloon to make sure that the ether evaporates before it is used.

Test Inflation of the Balloons

Dr. Kachkov: Do you inflate the balloons before the operation? Several times to determine maximal tolerance?

Dr. Moret: Yes, but we do not preinflate them with HEMA. We inflate them many times, overinflate them, and deflate them.

Dr. Eliava: How many times?

Dr. Berenstein: Five to ten times. What is important is not only the stretching and inflation but also the symmetry of the balloon after it is inflated. As you know, latex may change color, and you many get a latex that is dark yellow or pale. The palest ones seem to pop more easily when subjected to pressure. We test them several times.

Dr. Scheglov: Are you sure that the ruptures are not the fault of the balloon itself, rather than the HEMA.

Dr. Moret: Dr. Debrun reported a magnificent experiment that demonstrated every balloon into which he placed one batch of HEMA popped, whereas all the balloons that had the other HEMA did not burst, and two had cracks.

Dr. Debrun: The latex balloons we use are from India, and you can inflate them 100 times with iodine without bursting them. Therefore I believe that it would be the absolutely exceptional case in which the rupture was due to the latex itself.

Dr. Fox: I agree. They are standard size balloons made from a mold. The No.9 balloon, for example, can take 2.5 or 3.0 ml in the laboratory. I would never use more than 1 ml in a patient—0.8 or 1.0 ml, but never 2.5 ml. This figure amounts to 40% of the capacity of the standard size.

Dr. Scheglov: It is impossible to inflate the balloon maximally in the aneurysmal cavity without risk of rupturing the aneurysm.

CHAPTER 9

Interventional Neuroradiology: The Massachusetts General Hospital Experience

John Pile-Spellman

During 1987 and 1988 nearly 350 interventional neuroradiological procedures were performed in slightly more than 200 patients at the Massachusetts General Hospital. The diseases treated included bleeding, tumors, craniofacial arteriovenous malformations (AVMs), aneurysms, vasospasm, and stenotic cerebral vascular disease, with most of these patients having brain AVMs. During this period there has been a shift from treating for heroic and palliative indications to giving adjuvant and definitive treatment.

The development of a team approach to these problems has been rewarding. An integrated approach to the patients with cerebrovascular disease has allowed the rapid development and deployment of these methods. Increased awareness of the problems and possibilities of the endovascular approach has enhanced the selection process for patients undergoing endovascular treatment.

Advancements in materials, methods, and our understanding of the disease has increased the possibility of: (1) focally localizing the pathological process; (2) identifying the normal; and (3) effectively ablating the abnormal. The first has been done with the help of more selective catheterization using variable-stiffness microcatheters and greater use of more direct vascular access, such as the transcarotid or direct percutaneous approach. Additionally, greater understanding of the nature, findings, and effect of secondary high-flow angiopathy has allowed us to focus on the underlying disease. Selective temporary tolerance testing using Amytal, lidlocaine, or temporary occlusion with closely tailored neurological examination or electrophysiological monitoring of the patient is performed prior to permanent occlusion of vessels. This technique has allowed greater confidence when occluding a noncritical vessel, has allowed us to occlude a vessel that otherwise would have possibly created a deficit, and has stayed one's hand when a presumably noncritical vessel could have led to a significant transient deficit. Additionally, it has given important physiological information to the surgeon in those cases where the occlusion or ablation is to be done surgically. Safe and effective ablation of the vessel has been made possible with the help of new tissue adhesives, including *n*-butylcyanoacrylate and cryoprecipitate-thrombin mixture.

Disease-Specific Results

Head and Neck Disease

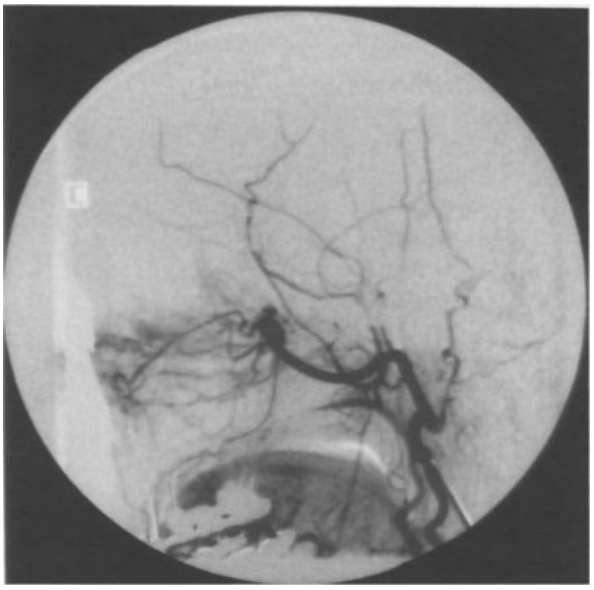
Endovascular occlusion of bleeding vessels has developed into a highly effective and attractive method of treatment.[1] In our experience with more than 25 medically and surgically intractable patients with epistaxis, endovascular occlusion was effective in more than 90%, without significant complications. Embolization for epistaxis at our institution is considered when nasal packing has failed (Fig. 9.1). Endovascular occlusion was equally efficacious in approximately 15 patients with bleeding related to head and neck tumors, irradiation, and sinus formation. These patients present with a sentinel bleed prior to the dreaded "carotid blowout." Surgery can be a particularly unappealing alternative in these patients, who have undergone extensive surgery and irradiation. Usually endovascular occlusion of the bleeding site entails occlusion of a branch of the external carotid artery. It can be done with a small risk. Embolization for highly vascular head and neck tumors continues to be useful.[2]

Arteriovenous Malformations

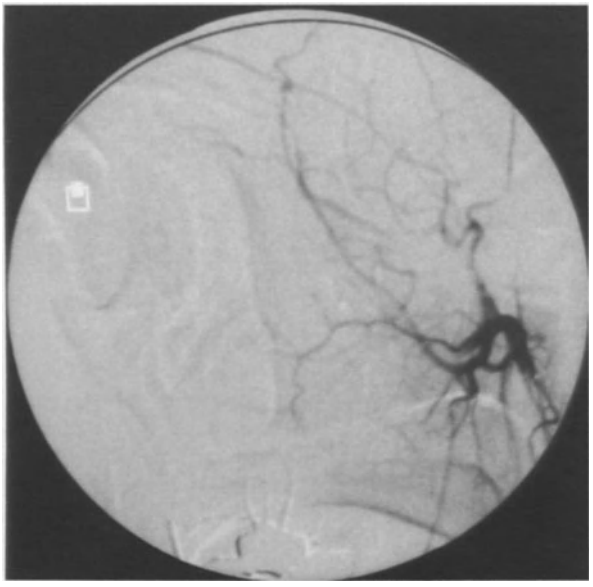
The indications for treating nearly 50 brain AVMs have included palliative as well as adjuvant and definitive treatment. Endovascular occlusion of an AVM nidus with a permanent liquid agent such as acrylate is highly effective for palliation in patients with progressive neurological deficit.[3] Permanent obliteration of the nidus, sparing the feeding arteries and draining veins, is essential for lasting results. Proximal or distal occlusion is particularly harmful, as it may lead to untreatable steal or venous hypertension, thereby exacerbating the neurological deterioration after an initial hiatus. For this reason great care must be taken to identify and selectively embolize only the nidus.

Most of the patients undergo treatment as an adjuvant for surgery. Large AVMs with deep multiple feeders are excellent candidates for embolization. The feeders from the posterior (PCA) and anterior (ACA) cerebral arteries can be particularly bothersome if the venous drainage from the AVM is superficial and overlies the feeders. In these patients embolization is often useful. It can allow a safer, quicker operation. Additionally, patients with troublesome deep feeders can be treated with adjuvant embolization, as in Figure 9.2. There appears to be some benefit as well from this "staging" of the AVM obliteration by allowing the brain to adjust to the altered hemodynamics.

A small number of patients with brain AVMs have undergone definitive endovascular obliteration of the entire AVM. Permanent occlusion of the AVM nidus with a permanent agent is also needed here, as in the cases of palliative treatment. Additionally, these cases demonstrate that it is possible to totally obliterate the AVM from a neurologically critical area using endo-



A

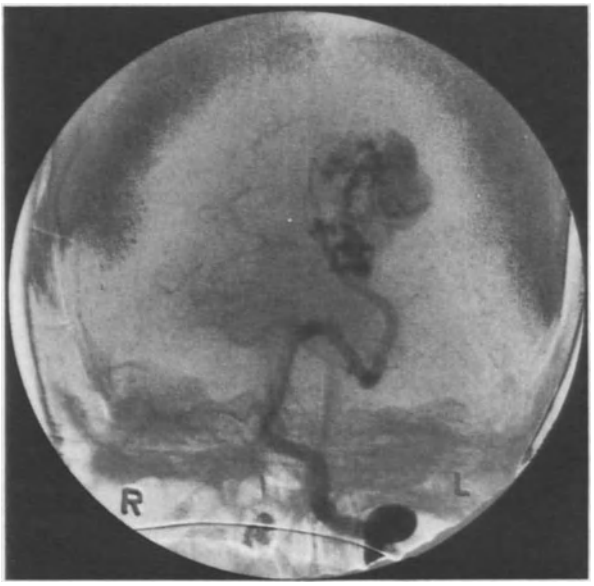


B

Figure 9.1. A 52-year-old woman suffered recurrent epistaxis. (**A**) Lateral view of the left external carotid artery showing typical hypervascular nasal mucosa with cork-screw vessels seen in patients with idiopathic epistaxis. (**B**) Left external carotid artery after embolization with PVA, Gelfoam, and silk threads.

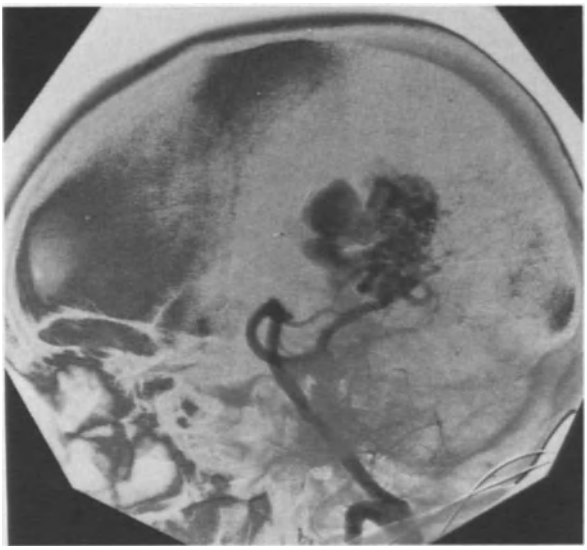
vascular techniques. For example, one patient with an AVM on the motor strip underwent embolization without neurological deficit or even electroencephalographic (EEG) changes.

Dural AVMs are increasingly being treated primarily by endovascular occlusion.[4] For more than 40 dural AVMs, transarterial embolization with acrylate has been highly effective as definitive treatment. Our indications for treating them include progressive neurological impairment (e.g., failing vision, progressive paraparesis) or cortical venous drainage. Again the need for a permanent agent with penetration into the microfistulas is required—a liquid agent such as acrylate.



A

Figure 9.2. A 61-year-old woman had a large left parietooccipital AVM fed by the ACA and PCAs with venous thrombosis. Venous ectasia caused venous hypertension. (**A**) AP view of the left vertebral artery injection showing a 3.5 × 3.5 × 4.0 cm left medial parietooccipital high-flow AVM. The parietal branch of the PCA is seen to feed the AVM via a macrofistula into the calcified medial atrial vein. (**B**) Lateral view of the left vertebral artery injection showing a 3.5 × 3.5 × 4.0 cm left medial parietooccipital high-flow AVM. (**C**) Lateral view of the left internal carotid artery injection showing a 3.5 × 3.5 × 4.0 cm left medial parietooccipital high-flow AVM fed by the distal pericallosal and internal parietal branches of the ACA. (**D**) Lateral view of superselective ACA injection revealing superior and inferior parietal and pericallosal feeders. (**E**) AP view after embolization of left vertebral injection showing subtotal obliteration of the AVM. (**F**) Lateral view after embolization of left vertebral injection showing subtotal obliteration of the AVM. (**G**) Lateral view after embolization of left internal carotid injection showing subtotal obliteration of the AVM.



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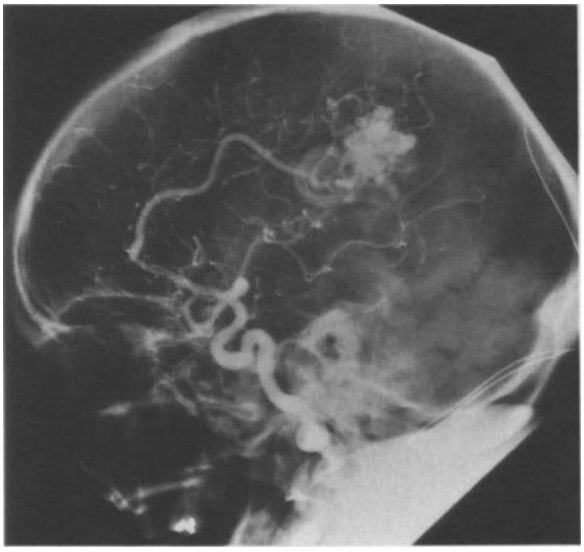

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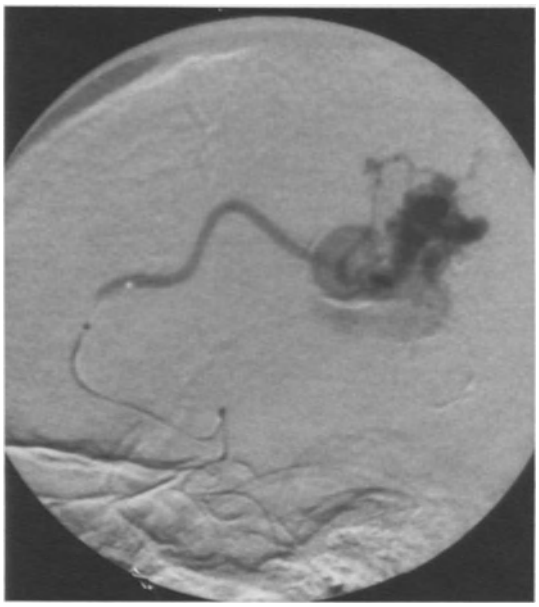
Figure 9.2 (*continued*)



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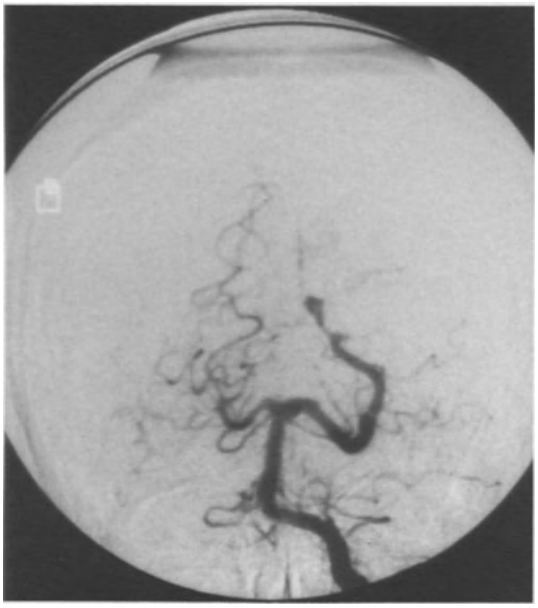

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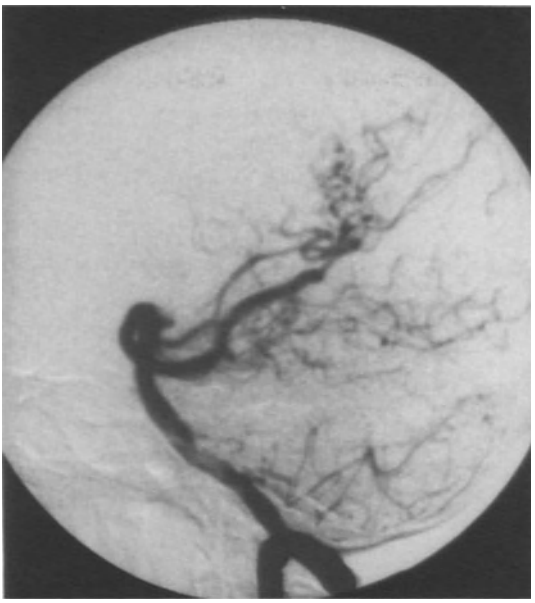
Figure 9.2 (*continued*)



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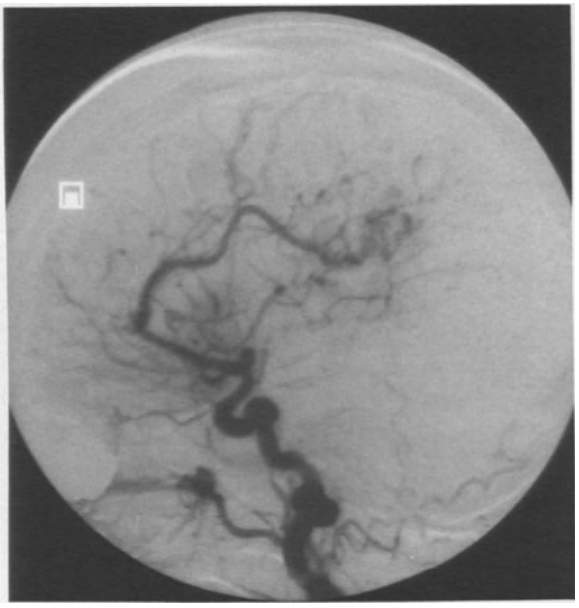

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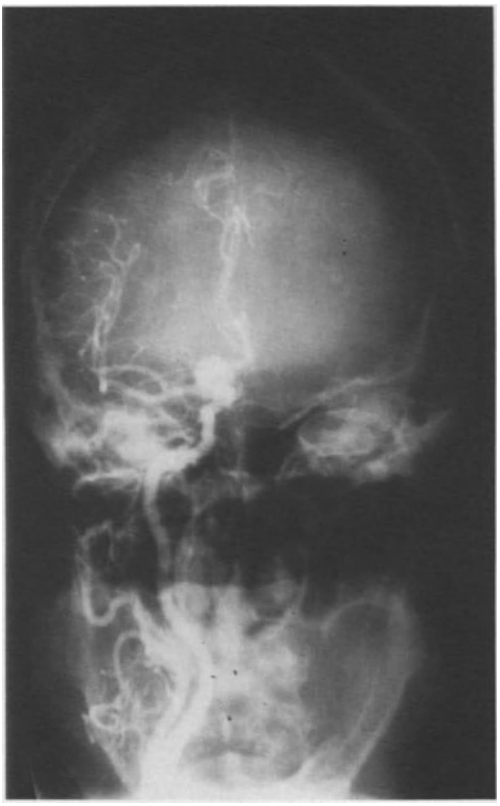
Figure 9.2 (*continued*)

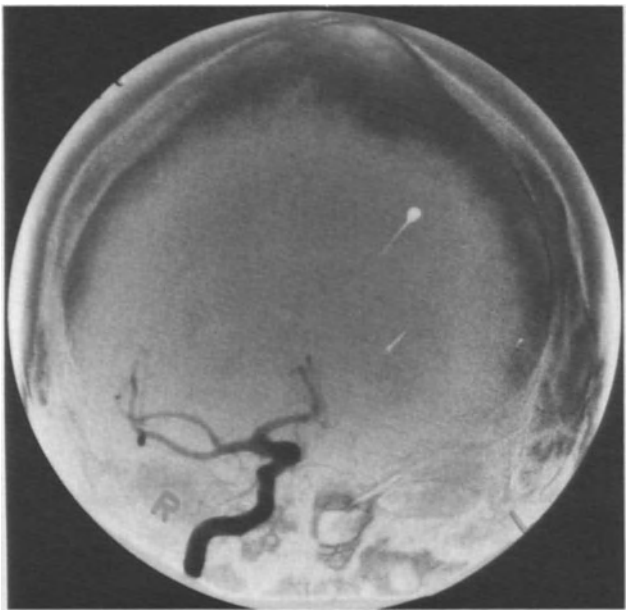
Although a variety of agents can be used, the advantages of a permanent liquid agent such as glue is clear. One advantage that occurs not infrequently is the opportunity to delay the decision of whether the patient is to be treated by an adjuvant or a definitive method until after the initial embolization. Highly successful "adjuvant embolization" can be definitive. Likewise, highly successful "palliative embolization" can turn into adjuvant treatment for surgery.

Our initial experience with *n*-butylcyanoacrylate (Avacryl) in 28 patients has been encouraging. Technically, the material has many of the beneficial properties of isobutylcyanoacrylate (IBCA), such as low viscosity and permanence of occlusion. However, Avacryl is significantly safer to use because it does not have the dangerous properties of IBCA. It has high tensile strength, which allows greater flexibility in the way the material is delivered.



A

Figure 9.3. A 62-year-old female patient complained of headaches. (**A**) AP view of a right internal carotid injection showing a right ICA bifurcation 10 × 8 mm aneurysm pointing superiorly. (**B**) Six-month follow-up angiogram after balloon obliteration using the Scheglov technique.



B

Figure 9.3 (*continued*)

Aneurysms

Initial experience with aneurysms has been encouraging.[5–8] We have treated only patients in whom surgery was considered impossible or exceedingly dangerous, or by whom surgery was refused. Most of the patients had cavernous or parasellar aneurysms. All aneurysms have been effectively treated. Four patients had parent-vessel-sparing procedures (Fig. 9.3). The remainder had a deconstructive (parent-vessel-occluding) procedure. One patient had an intraoperative rupture; although he had a stormy course, he suffered only lost vision in the ipsilateral eye to this caroticoophthalmic aneurysm. Saving this man from a near-fatal event was attributed to the immediate occlusion of the parent vessel with trapping of the aneurysm coupled with vigorous medical treatment.

Our experience with vessel occlusion has led us to explore the way to predict who will and will not tolerate occlusion. Matas, as early as the turn of this century, tried to determine who would tolerate surgical ligation of the carotid artery. Manual compression of the internal carotid artery (ICA) was performed while neurologically monitoring the patient. Patients who developed neurological deficit from this maneuver were highly likely to develop ischemic complications from carotid occlusion. Advancements in ways of

attempting carotid occlusion include monitoring the EEG, stump pressure, and cerebral blood flow (CBF) during test occlusion.

A provocative Matas test was utilized in more than 40 patients considered for cerebral vessel occlusion. After angiography, a balloon catheter was placed in the vessel to be tested for temporary occlusion under full heparinization for routine test occlusion. If the patient tolerated 15 minutes of this temporary occlusion, the blood pressure in this patient was lowered to the patient's low normal physiological range for an additional 5 minutes. This provocative measure culls out an additional group who would tolerate ICA occlusion at a high pressure but would not tolerate it at the low end of their blood pressure. This information has been found to be specific and sensitive to the effects of vessel occlusion. Additionally, it provides clinical blood pressure parameters that can be used when managing these patients during the occlusion period.

Other Areas of Investigation

Embolic agents could be made safer in a variety of ways. Our laboratory is evaluating modified blood products for use as embolic agents. Cryoprecipitate-thrombin mixtures offer a biologically compatible and easily manageable embolic agent. Our initial laboratory studies showed that (1) the coagulation time and clot density could be controlled with the amount of thrombin added; (20 nonionic contrast agents increased clotting time, and ionic agents decreased clotting time; and (3) relatively low concentrations of thrombin could be used that avoided the problems of thrombin excess. We have used this agent in 12 patients primarily via direct puncture but also transarterially and transvenously. It is well tolerated by the tissues despite the fact that it causes thrombosis and fibrosis. Direct injection of this material into the vascular lesion can be useful as both a palliative and an adjuvant procedure. The occlusion does not appear to be nearly as dense and permanent as with the acrylates. The high viscosity of the material is a disadvantage in that it cannot be used through present calibrated leak systems. The risk of giving blood products can be alleviated or mitigated by autologous or designated-donor procedures. We lack sufficient follow-up to know this agent's role in endovascular treatment but are encouraged, particularly regarding its use for facial AVMs.

Lastly, angioplasty of cerebral vessels for vasospasm may be useful for treating vasospasm.[9] Our laboratory work in the cerebral vessels of dogs suggests that the highly muscular arteries are paralyzed and the endothelium defunctionalized after angioplasty. It also suggests that the highly muscular and relatively nonelastic cerebral vessels do not tolerate overdistension as well as the highly elastic systemic vessels, which have the added protection of a thick adventitia.

Conclusion

Our initial and limited experience suggests that endovascular treatment of cerebral and head and neck disease can be beneficial. Advances in our understanding of the diseases, as well as in methods and materials, will no doubt bring this young field forward.[10]

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Discussion

Dr. Kachkov: How many patients with saccular aneurysms were treated by your methods, and how many complications have you had?

Dr. Pile-Spellman: We have treated about 15 saccular aneurysms primarily with deconstructive techniques over the past 2 years and six with reconstructive procedures. We have had one major complication of bleeding that was similar to the case already reported. He subsequently recovered and is back at work.

CHAPTER 10

Principles of Endovascular Neurosurgery at the N.N. Burdenko Neurosurgical Institute

Alexander N. Konovalov, Fedor A. Serbinenko, Anatoliy G. Lysatchev, Valeriy A. Lazarev, Nikolai A. Smirnov, Igor V. Koval, and Teodor P. Tyssen

Endovascular methods play an increasingly important role in the treatment of various vascular illnesses of the central nervous system (CNS). Dr. Charles Drake, in the presidential address at the annual meeting of the American Surgical Association 1987, said, "Whereas now the endovascular surgery techniques are presently used by only a few skilled physicians and radiologists, the future potential volume of this work is enormous."

In Moscow at the N.N. Burdenko Institute of Neurosurgery we began to use endovascular methods in 1964, when Serbinenko developed the balloon catheter technique. This method immediately became one of the most important techniques for treating a variety of CNS vascular lesions not only at the Burdenko Institute but also in other clinics of the Soviet Union as well. The endovascular method is frequently used together with the classic intracranial microsurgical method. Both methods have their advantages and indications, and in some cases the best results are achieved when these techniques supplement each other.

In the beginning endovascular procedures were performed by neurosurgeons in the vascular section of a neurosurgical department. Currently at the Burdenko Institute we have a special department devoted solely to patients who require treatment utilizing endovascular techniques. All endovascular procedures are carried out by neurosurgeons who have specialized training in endovascular surgery. It must be noted that some endovascular procedures such as superselective catheterization, and free embolization are also performed in the Radiology Department of the Burdenko Institute, but in this review we have not taken those results into consideration.

For the treatment of patients with vascular lesions we use the following methods: (1) intracranial microsurgery, (2) endovascular techniques, 93) proton beam irradiation, and (4) a combination of these methods.

It is evident that the indications for endovascular surgery are widening. The relative importance of microsurgical and endovascular methods for management of arteriovenous malformations (AVMs), carotid-cavernous fistulas (CCFs), and arterial aneurysms is illustrated in Table 10.1. One can

Table 10.1. Place of endovascular surgery (indicated by white pie slice) in the treatment of vascular deseases

Years	CCFs	AVMs	AAs
1960–1969	199	76	227
1970–1979	270	593	420
1980–1989	373	533	1291

Source: The numbers accompanying each figure represent the number of lesions.

see that at the present time practically all patients with CCF are treated by endovascular methods. There is almost equal use of endovascular and microsurgical methods for treatment of AVMs, and endovascular procedures have become common for treating arterial aneurysms, especially giant aneurysms in difficult sites.

Variants of Endovascular Surgery

There are several ways to accomplish the endovascular occlusion of pathological vessels (Table 10.2): (1) balloon occlusion, (2) induced thrombosis via the balloon catheter technique, and (3) directed and free embolization. These methods can be used independently or in combination.

The most important tool for endovascular surgery is the balloon catheter. There are many modifications (which we have employed) made of the techniques, used according to the character of the illness, exemplified by using detachable and nondetachable balloon catheters of different sizes and forms. According to the clinical situation, a one- or two-balloon catheter method may be used. The two-balloon technique permits direct occlusion by one balloon in the necessary direction and in some cases it facilitates the detachment and removal of the second occluding balloon.

Pathological vessels can be occluded by balloons filled with special hardening material or by empty balloons. Balloon catheter techniques also may be

Table 10.2. Types of endovascular surgical procedures

Balloon occlusion (AVM Feeders, CCF, AA)
Induced thrombosis with help of balloon catheters (temporal balloon occlusion, MK6 or MK7 injection)
Directed embolization (with temporary balloon occlusion of important arteries)
Free embolization (e.g., with empty balloons, Gelfoam, plastic balls)
Combined method (endovascular occlusion, intracranial surgery, proton beam therapy)

Table 10.3. Diagnostic tests

Test	Functional tests[a]
CT + MRI	
Neurological investigation	Compression of the carotid artery on the neck
AG (total artery selective)	Functional occlusion of feeding artery with a balloon
EEG	
Transcranial Doppler	
rCBF (^{133}Xe)	

[a]These tests are performed in conjunction with the neurological investigation

Table 10.4. Endovascular surgery performed at the N.N. Burdenko Institute, 1970–1989

Pathology	No. of operated patients
Carotid–cavernous fistulas	630
Other arterial–sinus and AV fistulas	348
AVMs	318
Arterial aneurysms	267
Others	126
Total	1689

utilized for inducing thrombosis of an AVM or arterial aneurysms with the help of, for example, fast-hardening cyanoacrylic compounds.

Because endovascular methods always interfere with the cerebral blood circulation, it is important to check the circulation before, during, and after surgery. For this purpose we use a number of methods that help us investigate cerebral blood flow (CBF) changes and thereby predict some complications of endovascular interference (Table 10.3).

Over a 25-year period we accumulated a sizable experience regarding management of vascular brain lesions. The main findings in the endovascular surgical patients are summarized in Table 10.4. As one can see, endovascular surgery is the main method for managing CCFs and other arterial-sinus fistulas. Only in occasional cases was it supplemented with intracranial inter-

vention, mostly to occlude additional sources of the fistula vascularization. Among this group of patients, endovascular operations are much more effective and less dangerous than the surgical methods used previously. The endovasal method is also effective for treating large, deep-seated AVMs, giant aneurysms, and some arterial aneurysms in difficult intracranial sites.

The effectiveness of endovascular surgery for the above-mentioned groups is discussed elsewhere. Here we direct our attention to the complications of endovascular intervention.

Complications

The complication and mortality rates for our patients are summarized in Table 10.5. The highest mortality occurred in the group with arterial aneurysms. It can be explained in part by the selection of patients for surgery, since that group consisted mostly of giant aneurysms and those that were accessible only with great difficulty.

The most important and most common complications were cerebrovascular insufficiency, embolization of cerebral arteries by inadvertently displaced balloons or blood clots, and rupture of an arterial aneurysm or AVM feeders with intracerebral hemorrhage (Table 10.6). Some (if not all) complications can be prevented by improving our surgical techniques and by the use of

Table 10.5. Complications of endovascular surgery, 1970–1989

	No. of patients		
Pathology	Operated	Disabled	Died
CCFs	630	21 (3.3%)	5 (0.8%)
Other arterial–sinus and AV fistulas	348	17 (4.7%)	17 (4.7%)
AVMs	318	21 (6.6%)	7 (2.2%)
Arterial aneurysms	267	14 (5.2%)	20 (7.4%)
Others	126	9 (7.1%)	2 (1.6%)
Total	1689	92 (5.4%)	45 (2.7%)

Table 10.6. Main complications of endovascular surgery (1689 patients)

Complication	No. of patients	%
Circulatory insufficiency	82	4.8
Thromboemboli	13	0.7
Balloon emboli	35	2.0
Rupture of vessels	11	0.6

better equipment. A thorough investigation of the cerebral circulation is also of great importance.

In some cases the serious consequences of cerebral embolism and intracranial hemorrhage can be diminished or even prevented by immediate intracranial intervention. (Displaced balloons were surgically removed in three patients; in three cases intracerebral clots resulting from the rupture of an AVM were removed, with improvement in all cases.) We believe that such surgical interventions should be used more often if such a complication occurs. We agree with Drake, who said, "One can foresee too that vascular surgeons and neurosurgeons and their operating rooms would have to remain on standby to deal with the complications." Our results of endovascular surgery and the rapid development of this method has led us to believe in its future.

Previous experience has convinced us that the Stonwin Medical Conference is an effective forum for discussing and solving some of these serious problems. Important issues to be addressed at this conference include the following:

1. Comparative analysis of the various endovascular methods
2. Equipment for endovascular surgery and ways to improve it (e.g., balloon catheters, thrombogenic substances, radiographic imaging)
3. Role of endovascular techniques for managing different vascular lesions
4. Complications of endovascular surgery and their prevention
5. Monitoring during endovascular procedures
6. Education of upcoming interventional neuroradiologists
7. Organization of endovascular services

Treatment of Diseases

Carotid-Cavernous Fistulas

Traumatic arteriovenous (AV) fistulas, particularly CCFs, are formed by direct communication between the internal carotid artery (ICA) and the cavernous sinus. Balloons can repair the ICA wall, filling its defect when they are positioned in the venous portion of such fistulas. We have treated 630

Table 10.7. CCF: operations performed, 1970–1988

Operation	No. of cases	%
ICA reconstruction	478	75.8
ICA deconstruction	141	22.6
ICA deconstruction + intracranial clipping	11	1.6
Total	630	100.0

Table 10.8. CCF: steal of the flow

Steal	No. of cases	Reconstruction	Deconstruction
Complete	221 (35%)	134 (60.6%)	87 (39.4%)
Partial	409 (65%)	344 (84.2%)	65 (15.8%)
Total	630 (100%)	478 (75.8%)	152 (24.2%)

patients with traumatic CCFs by the intravascular balloon catheter method (Table 10.7).

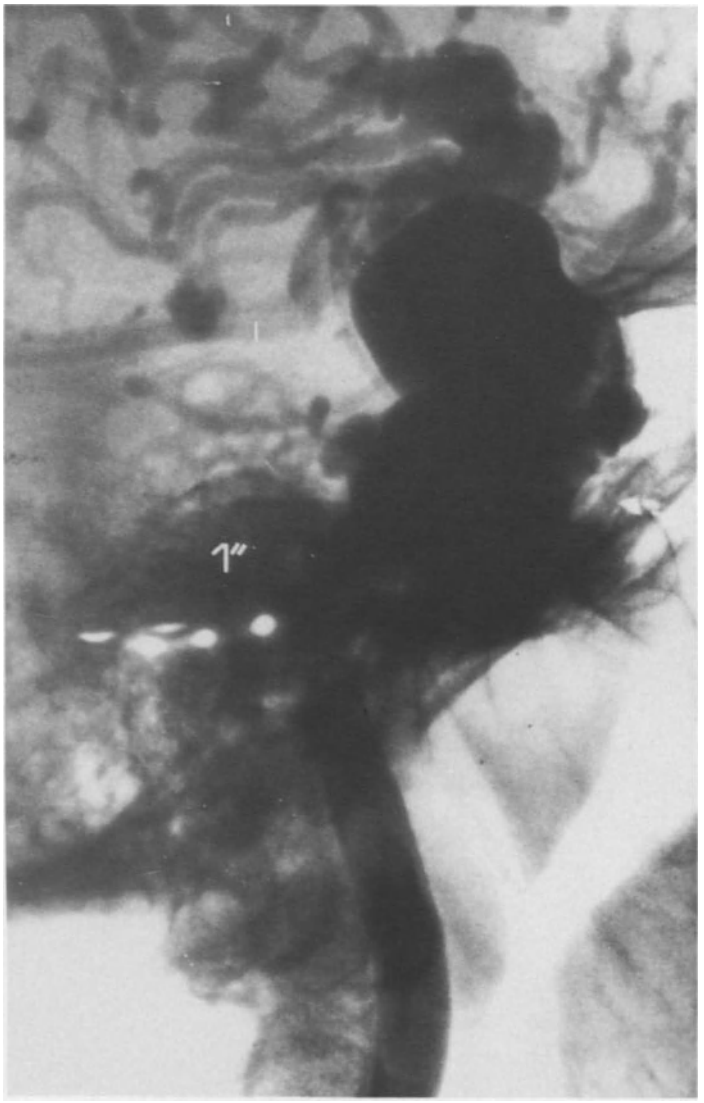
Reconstruction of the ICA was performed in 76% of patients. It must be noted that 50% (40 patients) of the reconstructive operations were performed before 1975. Reconstruction of the ICA wall is done when there is total or partial drainage of the ICA into the cavernous sinus (Table 10.8). We performed reconstructive operations in 60.5% of patients with total drainage (35% of all patients) and in 84.2% of those with partial drainage (Fig. 10.1).

It is often very difficult to accomplish ICA reconstruction with varying degrees of shunting occurring from small defects in the arterial wall (e.g., stab wounds) to complete ICA rupture within the cavernous sinus. Most often the ICA defect is located at the site of its entry or exit from the cavernous sinus, where it is fixed by dura mater.

Occlusion of the ICA at the site of the fistula (deconstructive operation) was performed in 22.4% of cases. In only 10 patients (1.6%) was additional intracranial ICA clipping required owing to incomplete balloon occlusion of the fistula. It is of note that in the group of patients with deconstructive operations we also achieved temporary ICA reconstruction in 33% during balloon manipulations in the cavernous sinus. We believe that with most deconstructive operations it is possible to perform ICA reconstruction as well by staged endovascular operations. This theory was confirmed by the cases where we used as many as 17 balloons and could still reconstruct the ICA.

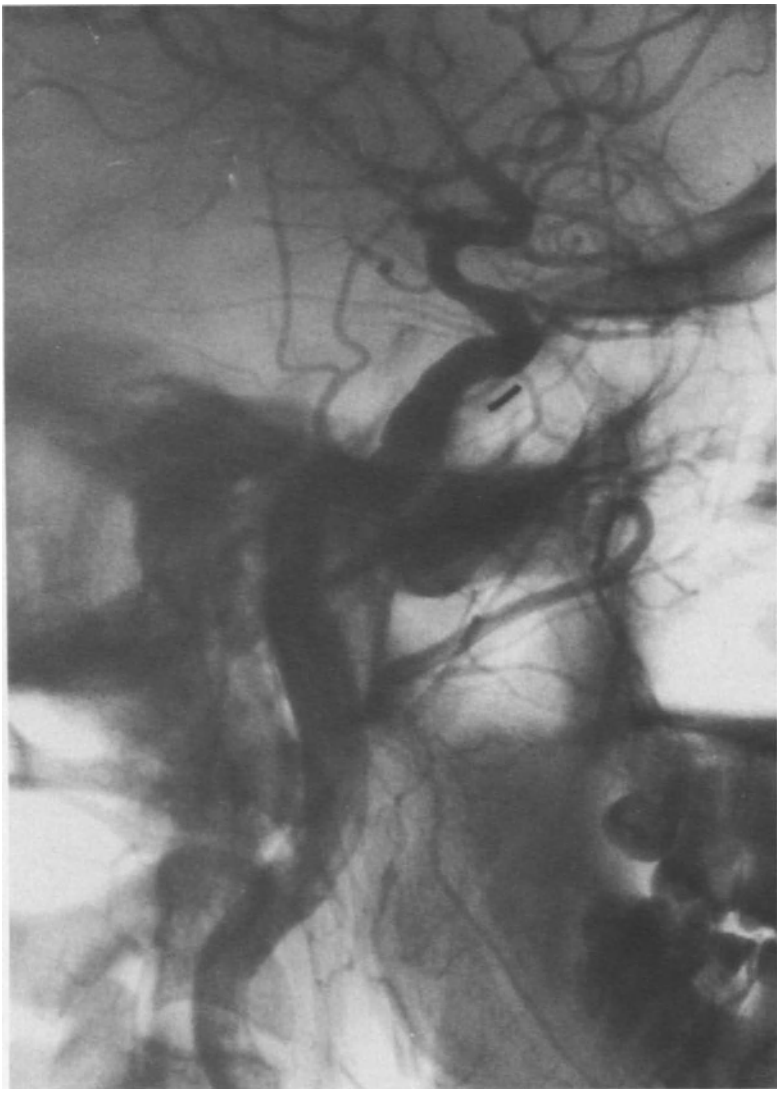
In some cases the endovascular method helps to eliminate a fistula after a number of unsuccessful direct operations, for example, after ICA ligation or trapping. In 11 patients CCFs still functioned after ICA ligation and in one patient after trapping. In each of these cases the ICA had not been thrombosed. We occluded the fistula by introducing a balloon catheter into the artery above the ligature. In two patients the fistula was occluded using the transjugular approach, and in one patient with ICA thrombosis the fistula was obliterated through the posterior communicating artery using the transfemoral approach.

Surgery of traumatic CCFs is rarely associated with mortality (Table 10.9). Five patients died (0.8%). In two cases death resulted from septic inflammation of the cavernous sinus, which was difficult to diagnose. In



A

Figure 10.1. Traumatic CCF. (**A**) Carotid angiography before operation. Note the full shunting of ICA flow through the fistula. (**B**) Postoperative carotid angiography. The fistula is occluded, and ICA blood flow is restored.



B

Figure 10.1 (*continued*)

one patient who underwent ICA reconstruction, death was due to laryngospasm caused by manual compression of the ICA. One patient died from circulatory insufficiency during balloon embolization of the ICA and middle cerebral artery (MCA) bifurcation. One patient died from systemic complications not associated with the operation.

Twelve patients with vertebrovenous fistulas were operated. In 2 of the 12 vertebral artery patency was restored.

Table 10.9. CCF mortality

Cause of death	No. of cases
Cavernous sinus septic inflammation	2
Laryngospasm	1
Cerebral ischemia after MCA balloon embolus	1
Systemic complications	1
Total	5 (0.8%)

Table 10.10. Cavernous dural AV fistulas: treatment 1970–1988

Operation	No. of cases
Superselective free embolization of ECA branches	101
Intravascular thrombosis with glue composition (MK-6, MK-7)	5
Stereotaxic proton radiosurgery	9
Superselective embolization + proton radiosurgery	5
No surgery	80
Total	200

Table 10.11. Occipital dural AV fistulas: treatment, 1970–1988

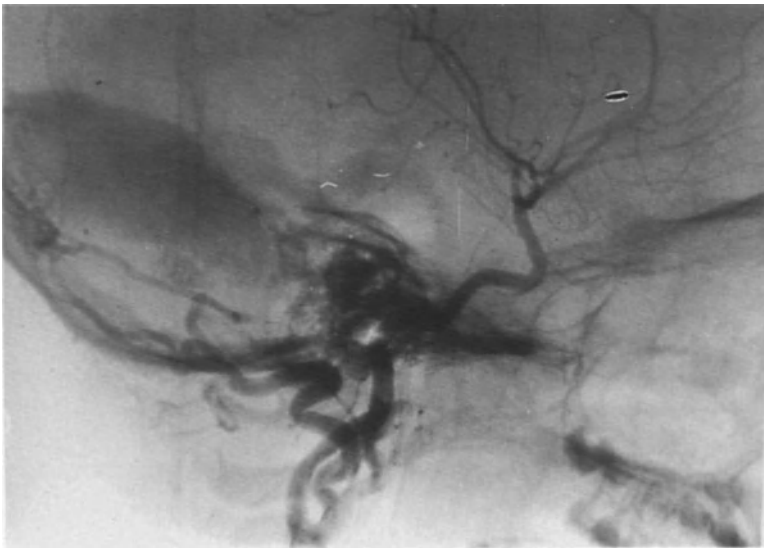
Operation	No. of cases
ECA ligation, scalping of squamous portion of occipital bone, trephination of the bone over the sinus	44
Superselective embolization of ECA branches	106
Intravascular thrombosis of ECA branches	20
No surgery	10
Total	180

Cavernous and Occipital Dural AV Fistulas

Treatment of numerous spontaneous fistulas in the cavernous and transverse sinuses is difficult. We have treated 200 patients with dural AV fistulas in the cavernous sinus and 180 patients with fistulas involving the transverse sinus. Numerous anastomoses between dura mater vessels from the external carotid artery (ECA) and the ICA account for the difficulty of surgical treatment.

Morphological studies of cavernous and occipital dural AV fistulas have demonstrated varied abnormalities of the vessels and sinuses. In cross section, the sinus resembles a sponge, and clots in different stages of organization are found within its lumen.

Sixty percent of the patients with cavernous and occipital dural AV fistulas were operated on using free embolization (Tables 10.10 and 10.11). In 25



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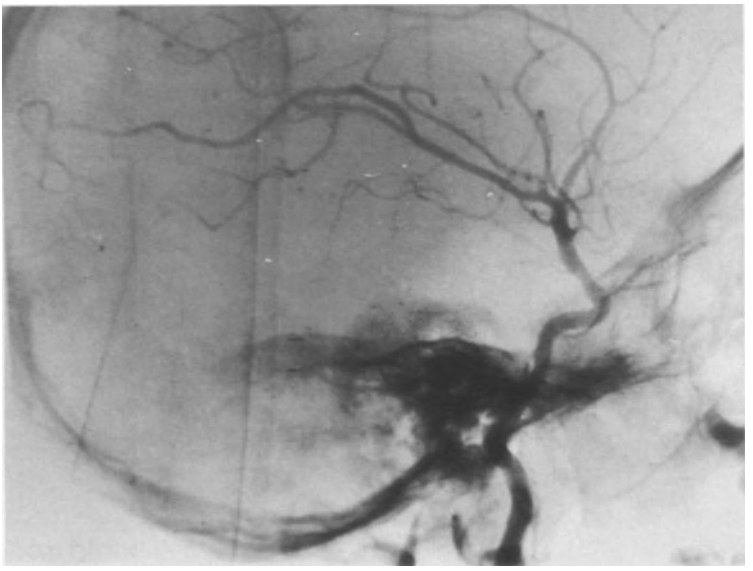


B

Figure 10.2. Occipital dural AV fistulas. (**A**) Carotid angiography before operation. Large ECA branches and wide transverse sinus are opacified. (**B**) Carotid angiography after intravascular thrombosis of ECA branches. Transverse sinus is not opacified.

patients intravascular thrombosis of afferent vessels was performed using glue (Fig. 10.2).

Most recently we used proton beam irradiation for cavernous and occipital dural AV fistulas. In cases of low flow shunting, proton beam therapy was used as the first stage. It was performed in 15 patients, 13 of whom recovered clinically and angiographically. When shunting is high flow, proton beam therapy is used after free embolization.

Angiography rarely demonstrates total elimination of the fistula. Treatment of cavernous and occipital dural AV fistulas requires study and the development of new methods.

Arteriovenous Malformations

The AVMs present the most difficult problem in endovascular surgery. We treated only inoperable malformations, taking into consideration their size, their site, and the neurological status of the patient (Table 10.12). Two techniques are used: balloon occlusion of AVM afferent vessels (208 patients) and intravascular thrombosis with glue composition (110 patients). Free embolization of ECA branches and proton beam therapy have also been used.

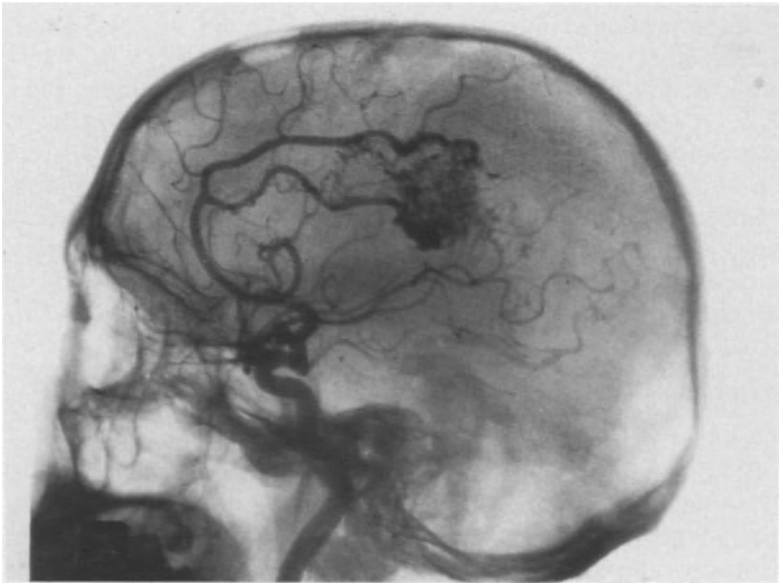
Balloon occlusion of an AVMs afferent vessels decreases shunting of the blood flow, but it is difficult to exclude the AVM totally (Figs. 10.3 and 10.4). Intravascular thrombosis ensures exclusion of part of AVM from the circulation. Total AVM thrombosis, achieved in 12.7% of patients, was possible depending on the site in instances of compact AVMs (Figs. 10.5, 10.6, and 10.7). Partial AVM exclusion was achieved in 20% of patients; in this group the AVM volume decreased by 70% or 5 cm^3 in residual malformations of up to 2 cm in diameter. The residual AVM in these cases was treated by proton beam irradiation. (Some may be eradicated using the direct approach.) Surgical mortality and complications are summarized in Table 10.13.

It is important to evaluate the results of endovascular treatment of AVMs in a follow-up study, comparing these patients with the group of nonoperated patients. Such a study was performed in 397 of our patients (Table 10.14), with the average follow-up period 6 to 10 years.

Intracerebral hemorrhage was the main manifestation of the malformations in all groups of patients. In the nonoperated patients, recurrent hemor-

Table 10.12. AVM: treatment, 1970–1988

Operation	No. of cases	%
Intracranial excision	533	34.3
Endovascular operation	318	20.5
No surgery	703	45.2
Total	1554	100.0



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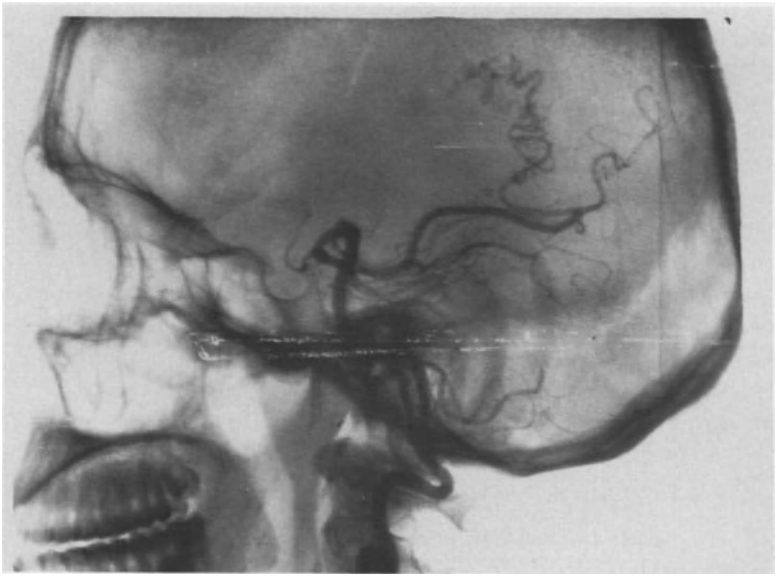
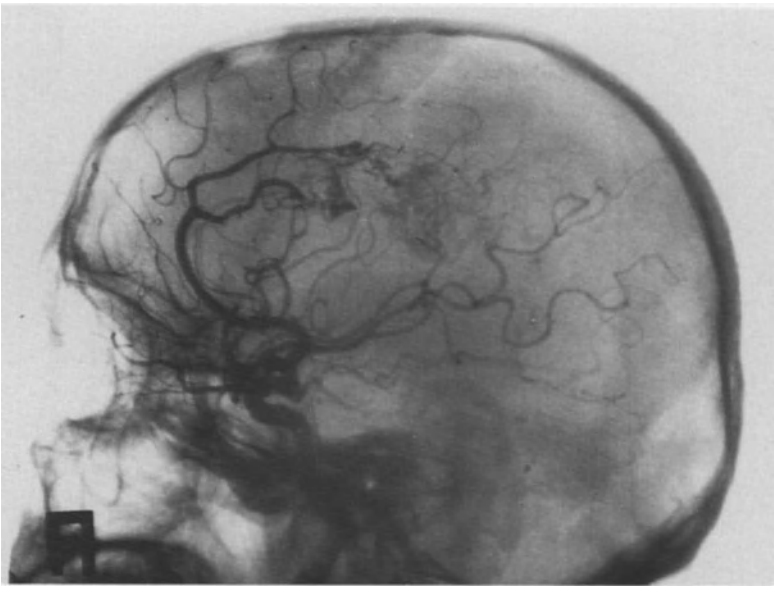


B

Figure 10.3. AVM of the corpus callosum and gyrus cinguli. (**A**) Carotid angiography before operation. (**B**) Vertebral angiography before operation. (**C**) Carotid angiography 1 year after balloon occlusion of AVM afferent vessels. Balloon markers are visualized. (**D**) Vertebral angiography 1 year after operation.



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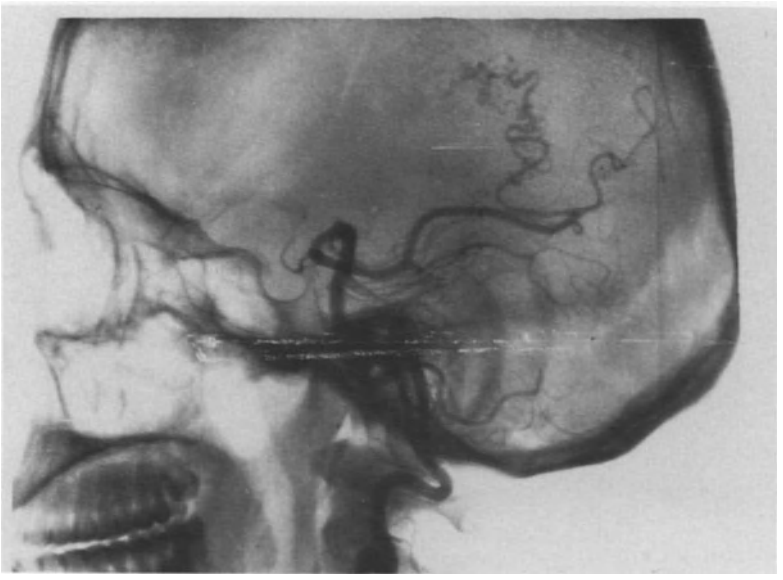

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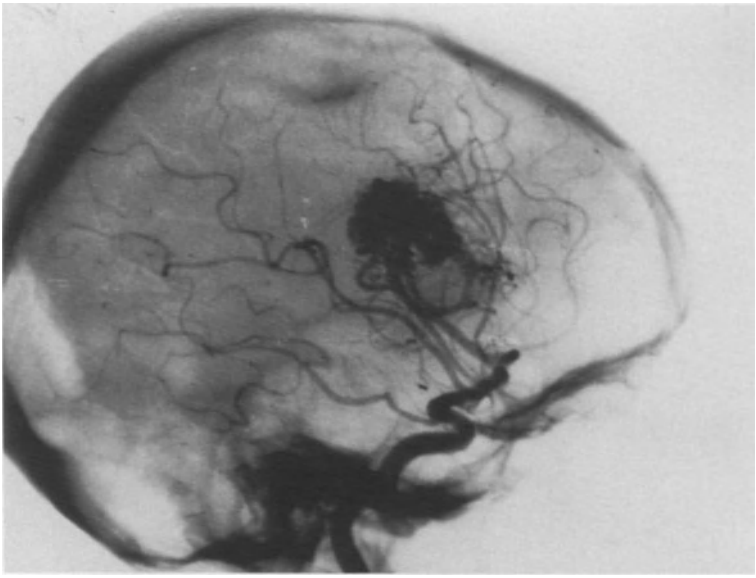
Figure 10.3 (*continued*)



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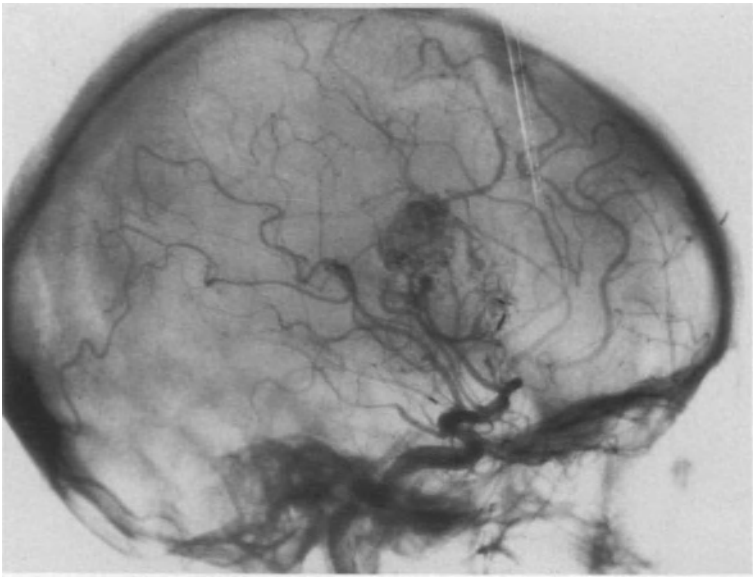
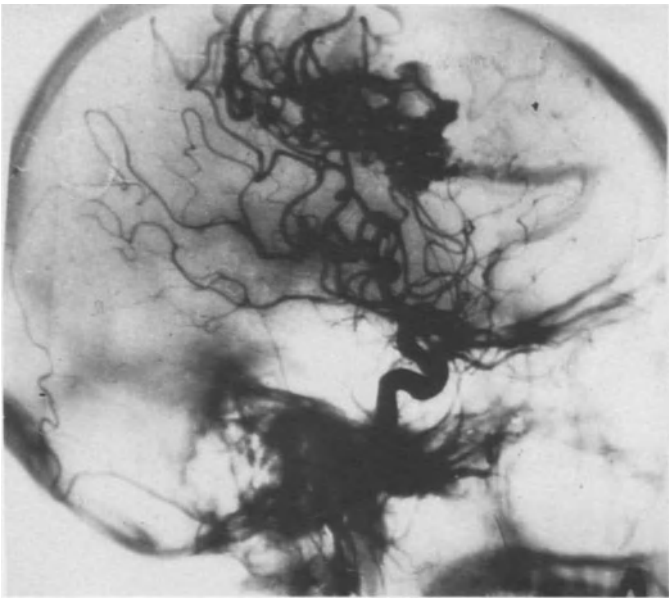


B

Figure 10.4. AVM of the speech-motor area. (**A**) Carotid angiography before operation. (**B**) Carotid angiography after balloon occlusion of afferent vessels.



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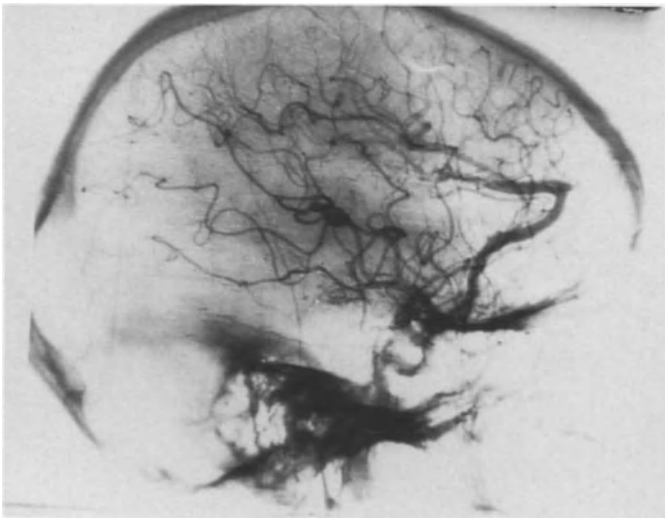
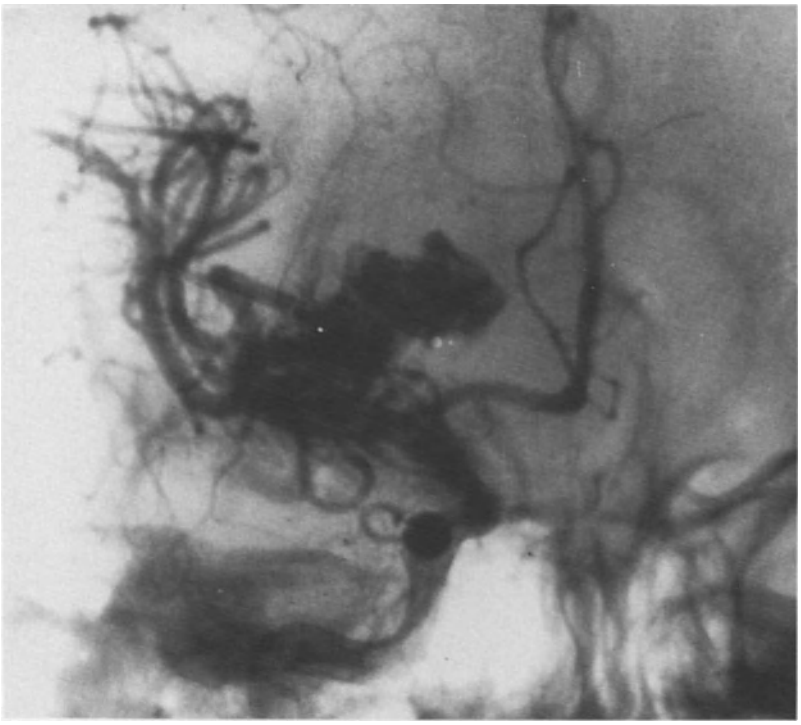


B

Figure 10.5. AVM of corpus callosum and gyrus cinguli. (**A**) Carotid angiography before operation. (**B**) Carotid angiography after intravascular thrombosis of AVM.



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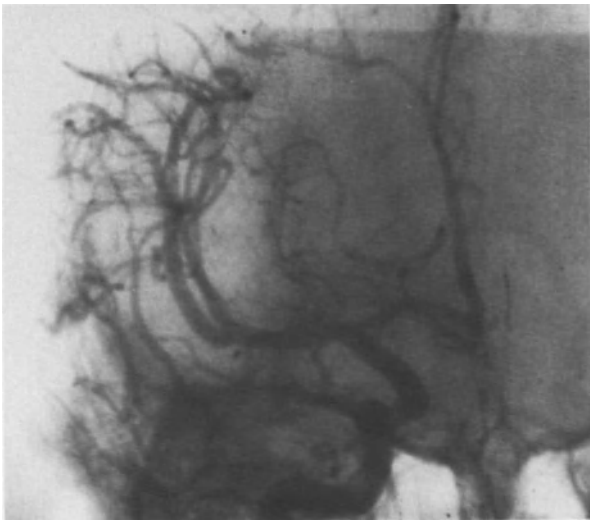

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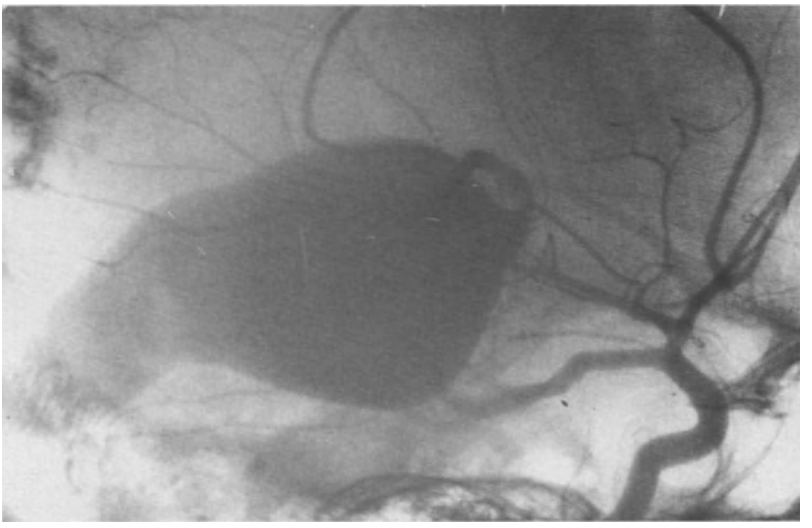
Figure 10.6. AVM of subcortical ganglia. (**A**) Carotid angiography before operation. (**B**) Carotid angiography 1 year after intravascular thrombosis of AVM.



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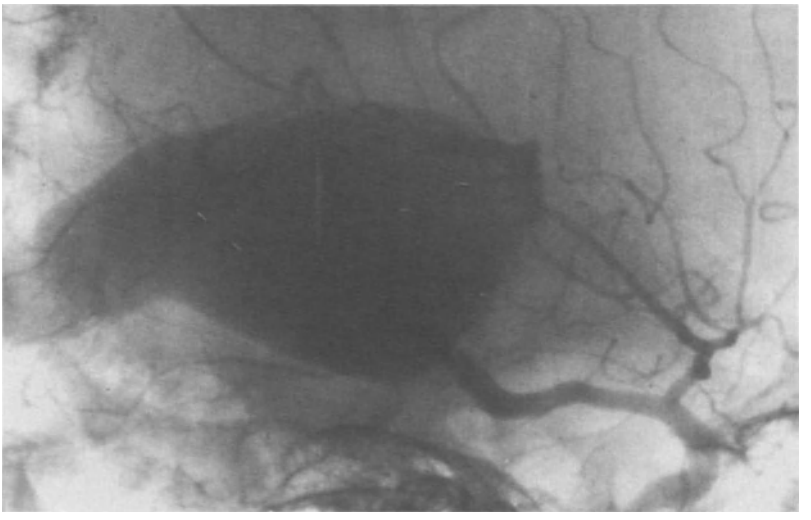
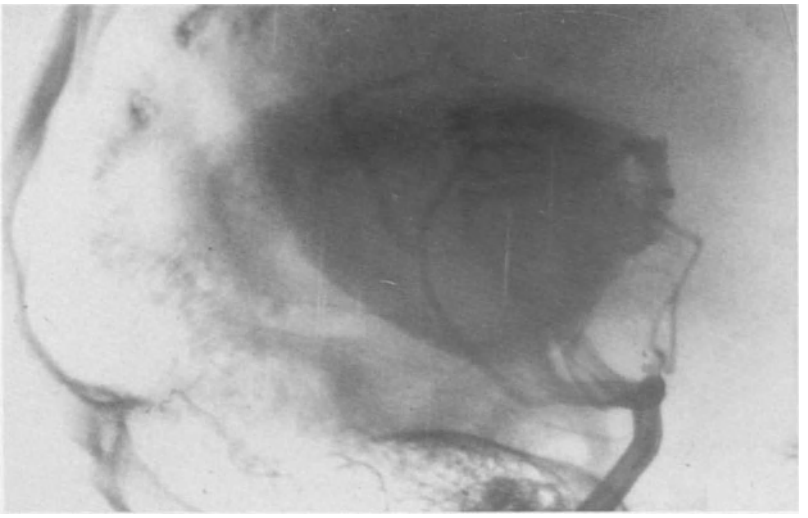


B

Figure 10.7. AVM of the vein of Galen. (**A**) Left carotid angiography before operation. (**B**) Right carotid angiography before operation. (**C**) Vertebral angiography before oepration. (**D**) Left carotid angiography 2 years after intravascular thrombosis of the AVM. (**E**) Right angiography 2 years later. (**F**) Vertebral angiography 2 years later.



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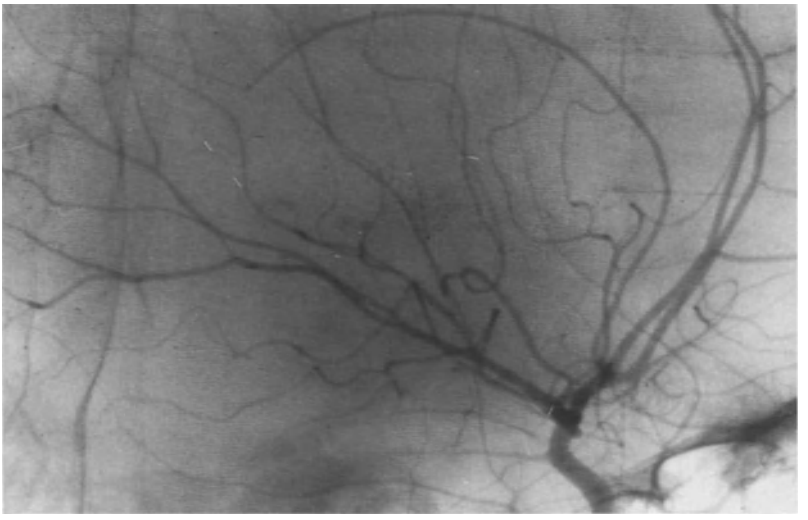

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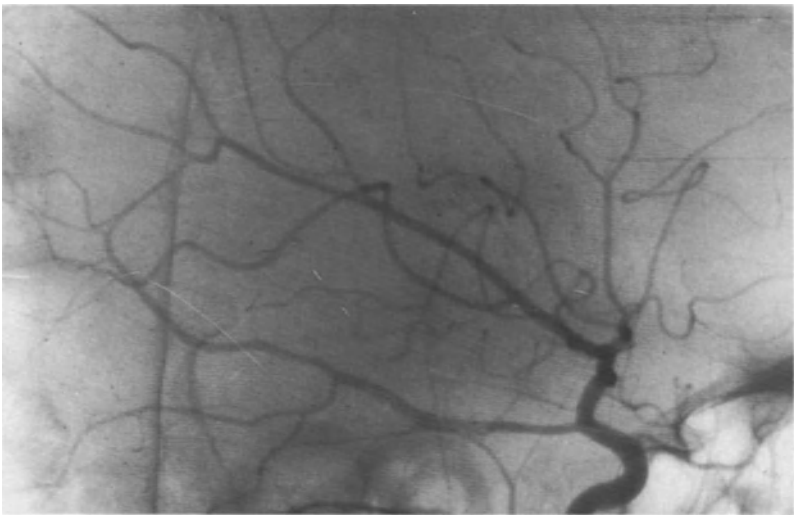
Figure 10.7 (*continued*)



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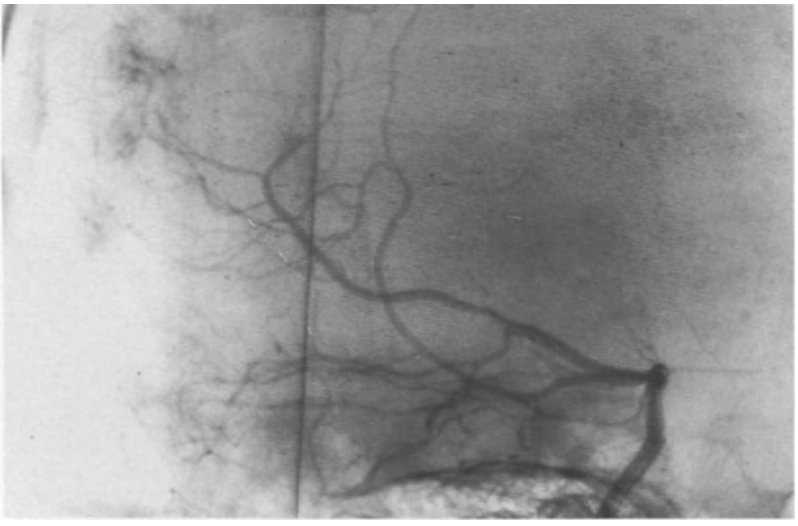

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Figure 10.7 (*continued*)

Table 10.13. Complications of AVM endovascular treatment, 1970–1988 ($n = 318$)

Operation	Hemorrhage during operation	Morbidity	Mortality
Balloon occlusion	7 (3.4%)	11 (5.2%)	3 (1.4%)
Intravascular thrombosis	2 (1.8%)	10 (9.1%)	4 (3.6%)
Total	9 (2.8%)	21 (6.6%)	7 (2.2%)

Table 10.14. Comparative analysis of patients with AVMs, by treatment (follow-up study)

Treatment group	No. of cases
No surgery	180
Balloon occlusion	115
Intravascular thrombosis	102
Total	397

Table 10.15. Results in patients with intracranial hemorrhages (follow-up study)

Treatment group	No. with hemorrhage in history	No. with recurrent hemorrhages	Mortality due to recurrent hemorrhage
No surgery ($n = 180$)	133 (73.9%)	48 (26.7%)	28 (15.6%)
Balloon occlusion ($n = 115$)	86 (74.8%)	21 (18.3%)	9 (7.8%)
Intravascular thrombosis ($n = 102$)	67 (65.7%)	4 (3.9%)	2 (2.0%)

Table 10.16. Effect of treatment on epilepsy (follow-up study)

Groups of patients	No. of patients with epilepsy	Improvement	Worse	No change
No surgery	55 (30.6%)	16 (29.1%)	19 (24.5%)	30 (54.5%)
Balloon occlusion	49 (42.6%)	27 (55.1%)	5 (10.4%)	20 (40.8%)
Intravascular thrombosis	35 (34.3%)	24 (68.8%)	—	11 (31.4%)

rhages occurred in approximately one-third of the patients who had had hemorrhages in the past. Balloon occlusion of afferent vessels and intravascular thrombosis decreased the risk of recurrent hemorrhage (Table 10.15). Afferent vessel balloon occlusion had a positive effect in 55.1% of those with epileptic syndrome. Intravascular thrombosis was helpful in regulating anticonvulsant treatment (Table 10.16) in 68.6% of patients.

Arterial Aneurysms

The first endovasal occlusion of an arterial aneurysm (AA) was performed in 1964 by Luessenhop. At the Burdenko Institute we began to use this method of arterial aneurysm occlusion in 1970. Since then we have treated 267 patients endovascularly (14% of all patients with arterial aneurysms operated during this period) (Table 10.17).

The number of endovascular occlusions of arterial aneurysms has increased, and the shape and sites of the aneurysms treated by the endovascular method has become more variable. Concomitantly, our experience with this treatment has been increasing rapidly, and the results attained by the endovasal method compare favorably with those achieved by intracranial aneurysm surgery. The advantage of this method becomes even more

Table 10.17. Summary of endovascular surgery for arterial aneurysms, 1970–1989, N.N. Burdenko Neurosurgical Institute

Group	No.	%
All surgically treated patients	1939	100.0
Intracranial approach	1672	86.2
Endovascular occlusion	267	13.8
Combined operations	37	1.9

Table 10.18. Site and size of 267 arterial aneurysms treated by endovascular surgery, 1970–1989

	No. of aneurysms				
Site of aneurysm	Small and medium (<1 cm)	Large (1.0–2.5 cm)	Giant (>2.5 cm)	Total	%
Carotid artery					
Cervical	—	2	4	6	2.2
Petrosal	—	1	1	2	0.8
Cavernous					
True aneurysm	—	6	41	47	34.0
False aneurysm	—	—	44	44	
Carotid ophthalmic	15	25	30	70	26.2
Supraclinoid	4	19	17	40	15.0
Bifurcation	1	4	4	9	3.4
Middle cerebral artery	1	8	4	13	5.0
Anterior cerebral artery	5	6	5	16	6.0
Vertebrobasilar	2	6	12	20	7.4
Total no.	28	77	162	267	
Percent	10.5	28.9	60.6		100.0

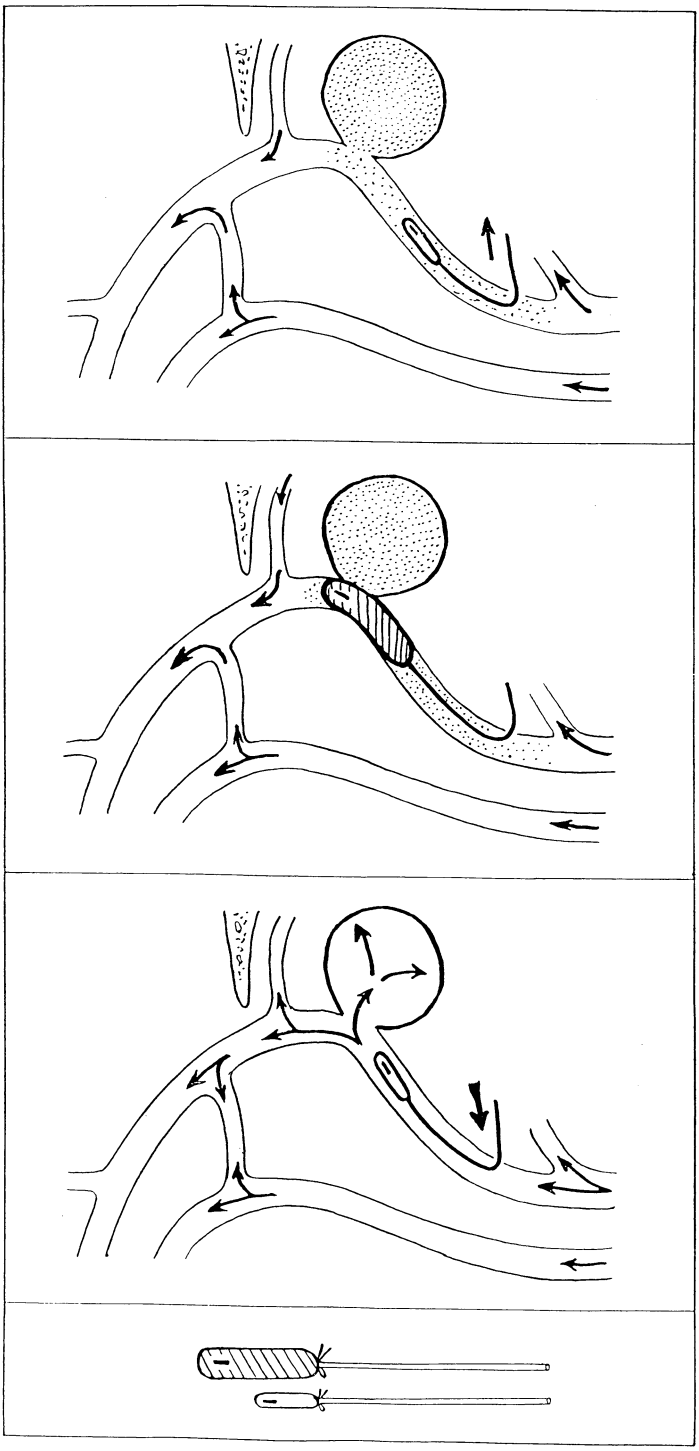

Figure 10.8. Temporary occlusion of the parent artery at the level of an aneurysm by means of a balloon catheter.

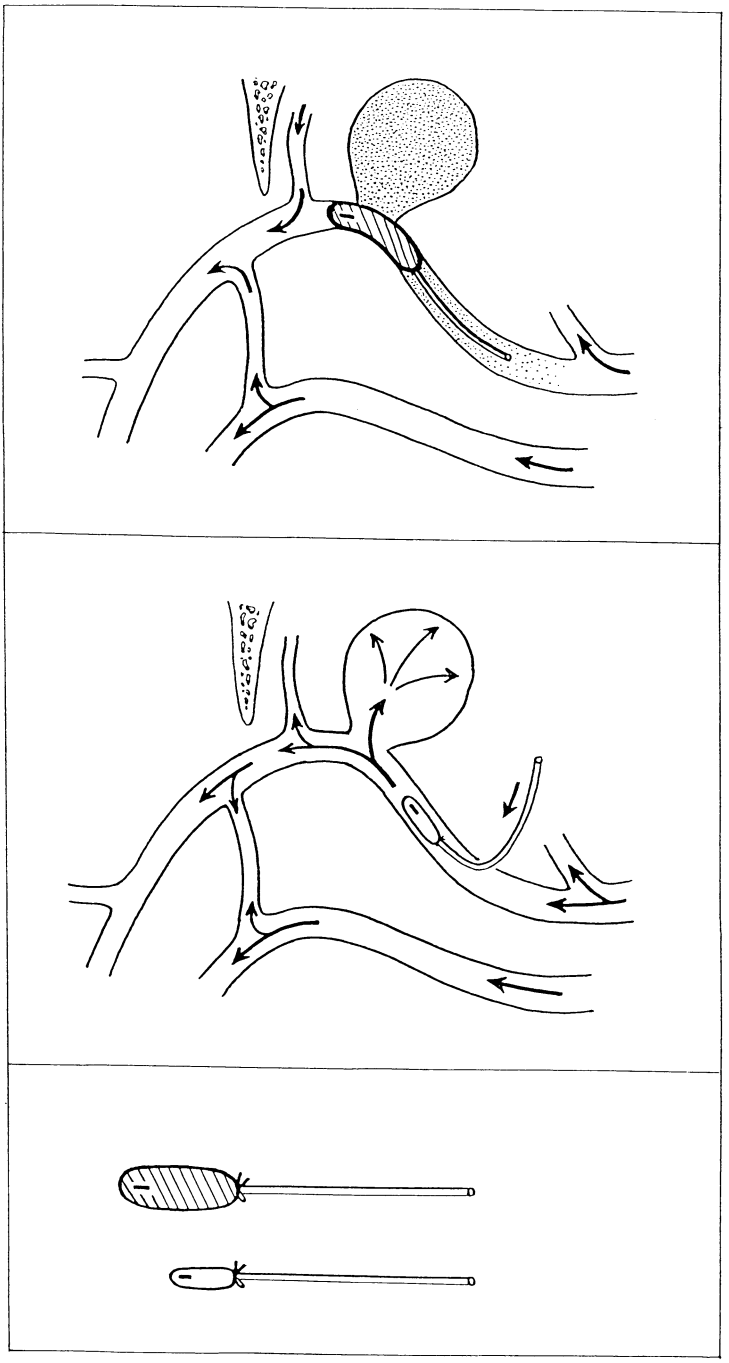

Figure 10.9. Permanent occlusion of parent artery at the level of the aneurysm with a nondetachable balloon catheter.

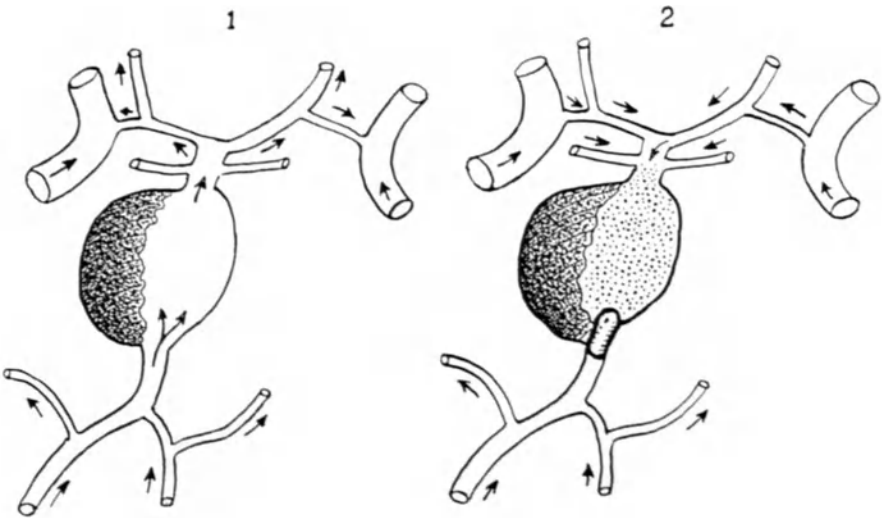

Figure 10.10. Occlusion of a feeding artery and an aneurysm of the basilar artery (transfemoral approach).

apparent when we combine our data of the Moscow N. N. Burdenko Institute with those from the Kiev Neurosurgical Institute, where the sole intent was to operate upon all arterial aneurysms using only the endovasal method, in contrast with our use of the endovascular method, which occurred mostly when intracranial surgery was deemed technically difficult or even impossible. At first, we operated only on patients with giant and carotid infraclinoid aneurysms. With acquired experience, we began to use the technique for aneurysms of other sizes and in other sites. The location and size of aneurysms treated by the endovascular method are presented in Table 10.18.

There are various ways by which to approach balloon occlusion of a parent artery (deconstructive surgery), including proximal occlusion and occlusion of an artery at the aneurysms (Figs. 10.8, 10.9, and 10.10). In some cases and aneurysm can be trapped using the balloon catheter technique.

Primary Proprial Occlusion of an Aneurysm (Reconstructive Surgery)

Various methods can be used to separate an aneurysm from its blood circulation. For example, an aneurysmal cavity can be occluded with the help of detachable balloons (Figs. 10.11 and 10.12). In some cases it is necessary to use two-balloon catheters to occlude an aneurysm. Here temporary occlusion of one of the two arterial branches allows us to direct the balloon into the aneurysmal cavity. In the case of an anterior communicating aneurysm, temporary balloon occlusion of the middle cerebral artery followed by com-

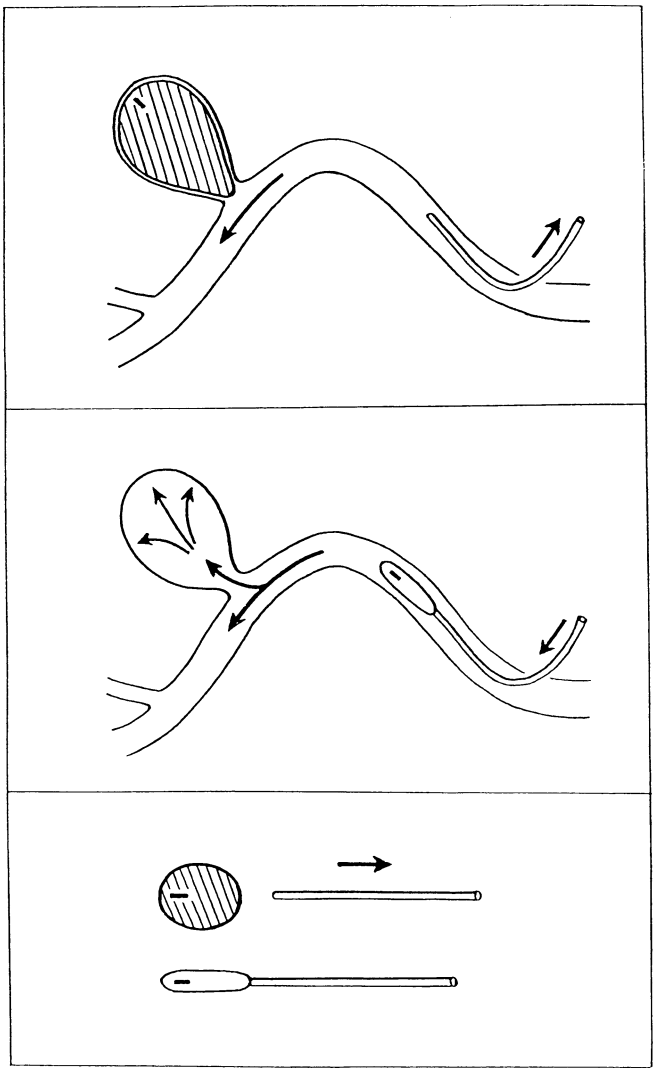

Figure 10.11. Occlusion of an aneurysm cavity with a detachable balloon.

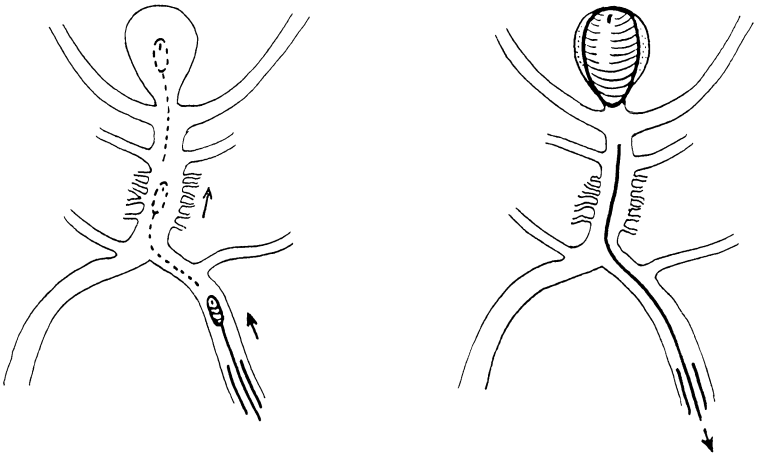

Figure 10.12. Occlusion of a basilar bifurcation aneurysm with a detachable balloon catheter (transfemoral approach).

pression of the contralateral carotid artery helps move a balloon catheter into the aneurysm cavity (Fig. 10.13).

Two-balloon catheter technique also allows us to withdraw a catheter more easily and prevents dislocation of an occluding balloon (Fig. 10.14). In cases of large and giant aneurysms two balloons are sometimes necessary to produce complete occlusion of the aneurysm (Fig. 10.15). The balloon catheter method can also be utilized to achieve thrombosis of an aneurysm by temporary occlusion of the aneurysm neck using a nondetachable balloon catheter (Fig. 10.16). The balloon catheter method also permits injection of a polymerizing substance into an aneurysm cavity (Fig. 10.17).

Planning the Operation According to the Size and Site of the Aneurysm

Most of our patients had large or giant aneurysms that had a wide neck communicating with the parent artery. Separation of the aneurysm from its blood supply in two-thirds of patients was possible only via occlusion of the feeding artery. In 92 cases the aneurysms had a well-shaped neck or their size was relatively small; these aneurysms were occluded and the parent artery preserved.

Although it was possible in only 80% to predict preoperatively whether exclusion from the circulation could be accomplished with the parent artery remaining patent, it is always important to understand the efficacy of the collateral circulation and to evaluate the outcome of test occlusion of the feeding artery prior to the intervention. We use a number of clinical methods to assess this problem. We outline three grades of collateral circulation effi-

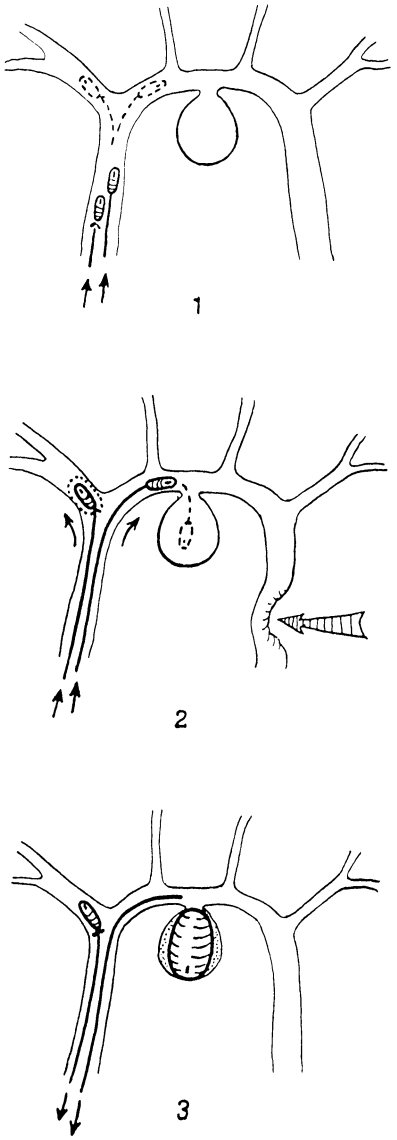

Figure 10.13. Endovasal occlusion of a communicating anterior aneurysm with the help of two-balloon catheters.

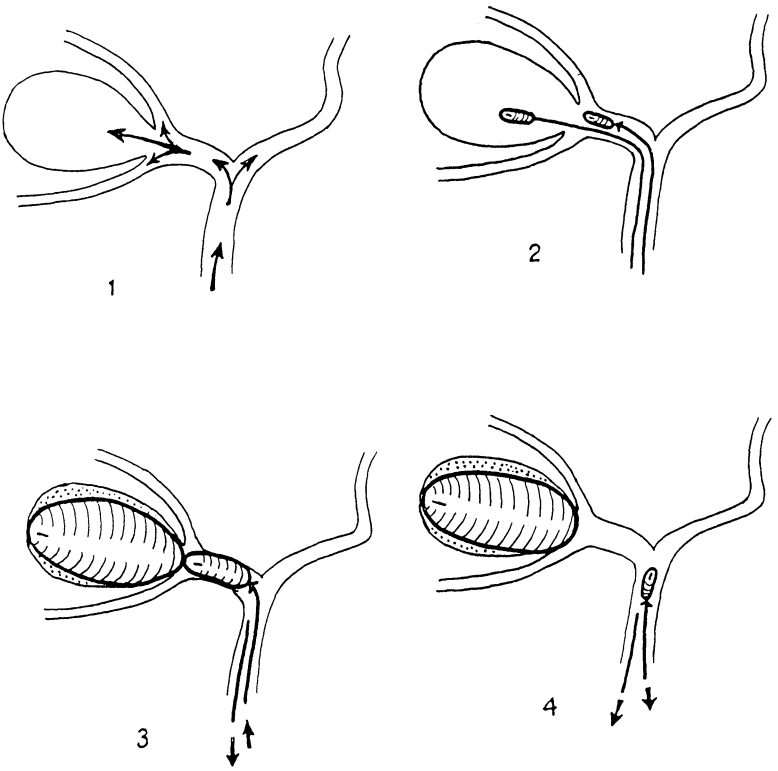

Figure 10.14. Endovasal occlusion of a middle cerebral aneurysm with the help of two-balloon catheters.

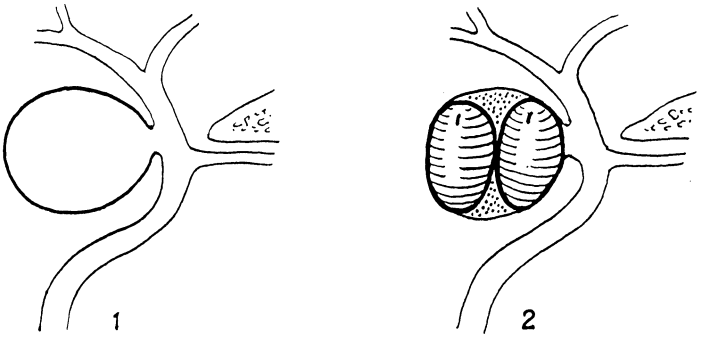

Figure 10.15. Occlusion of an aneurysm by two balloons.

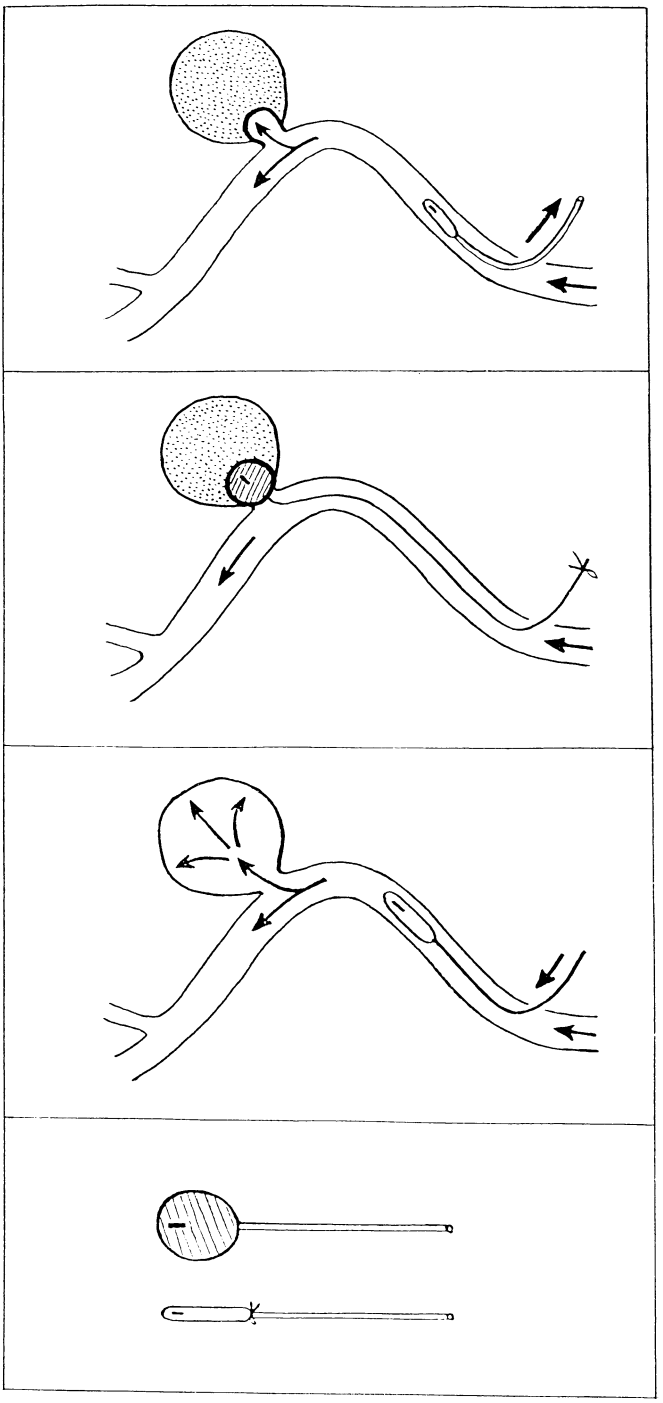

Figure 10.16. Stage I: Induced thrombosis of an aneurysm cavity via temporal occlusion of the aneurysm neck using a nondetachable balloon catheter. Stage II: Resection of the aneurysm.

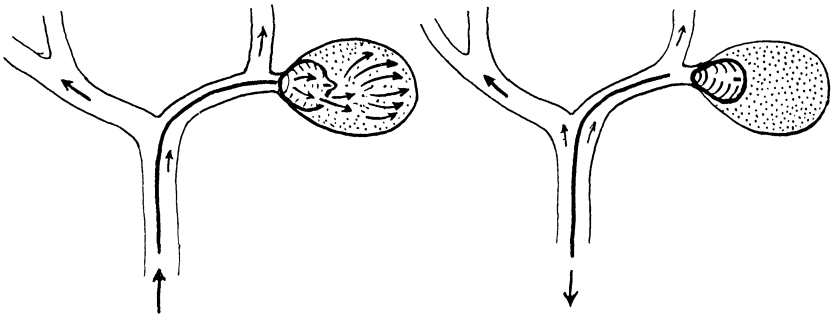

Figure 10.17. Injection of a polymerizing substance into an aneurysm cavity via a detachable balloon catheter.

Table 10.19. Criteria for compensated collateral circulation

Site	Pathological changes
Circle of Willis	None
Functional artery occlusion	No clinical reaction No EEG changes Normal hemispheric and regional cerebral blood flow (rCBF)

Table 10.20. Criteria for subcompensated collateral circulation

Site	Pathological changes
Circle of Willis	Hypoplasia of communicating arteries Compression of communicating arteries by a giant aneurysm
Functional artery occlusion	Aggravation of general and focal EEG signs Decreased rCBF (to subnormal levels)

cacy; compensated, subcompensated, and decompensated (Tables 10.19, 10.20, and 10.21; Fig. 10.18).

If there are signs of cross-circulation insufficiency, we consider the feasibility of aneurysm occlusion by endovascular intervention or intracranial clipping; alternatively, we consider the use of bypass surgery.

Patient's Condition at Surgery

All but two of our patients were operated at a "cold" stage. It is important to mention that among our 267 patients, 185 (69%) had signs of an aneurysm rupture. Rated according to the severity of their clinical signs, most of our

Table 10.21. Criteria for decompensated collateral circulation

Site	Pathological changes
Circle of Willis	Disconnected
Functional artery occlusion	EEG changes Decreased rCBF (to below normal levels)

patients belonged to groups I and II of the Hunt-Hess classification. Twelve patients (4.5%) were in bad or poor conditions (grades III and IV) when they were operated on.

Surgical Techniques According to Aneurysm Location and Size

The endovasal procedures utilized, according to the location of an aneurysm, are summarized in Tables 10.22 and 10.23. It is obvious that occlusion of a parent artery was more common in cases of infraclinoid carotid aneurysms and vice versa; reconstructive surgery with preservation of a parent artery predominated when treating aneurysms of the supraclinoid portion of the carotid artery and its branches.

Occlusion of an artery was the most common way of treating giant aneurysms. Fewer than 20% of these aneurysms could be occluded with the preservation of the circulation along the parent artery. On the other hand, reconstructive surgery was the most common treatment for other groups of aneurysms.

Combined Surgery

In 37 cases two-stage combined surgery was performed (Table 10.24). In these patients the aneurysm and a feeding artery were occluded and bypass surgery was performed. In cases where an arterial anastomosis was constructed before or simultaneously with the occlusion, there were no clinical signs of collateral insufficiency.

In two patients with giant aneurysms we resected part of the aneurysm to diminish brain and cranial nerve compression. The clinical effect was marked. In cases where organized thrombosis in the aneurysm cavity is soft, the size the aneurysm may be markedly reduced without additional intervention (Fig. 10.19).

Traumatic False Aneurysms

The common clinical manifestation of traumatic false aneurysms is profuse, life-threatening hemorrhage (epistaxis). The endovascular method is highly effective for treating profuse nasal hemorrhage due to false aneurysms in the sphenoid sinus. Special anatomical studies have shown that with this abnormality the osseus plate in the sphenoid bone and the ICA in the carotid

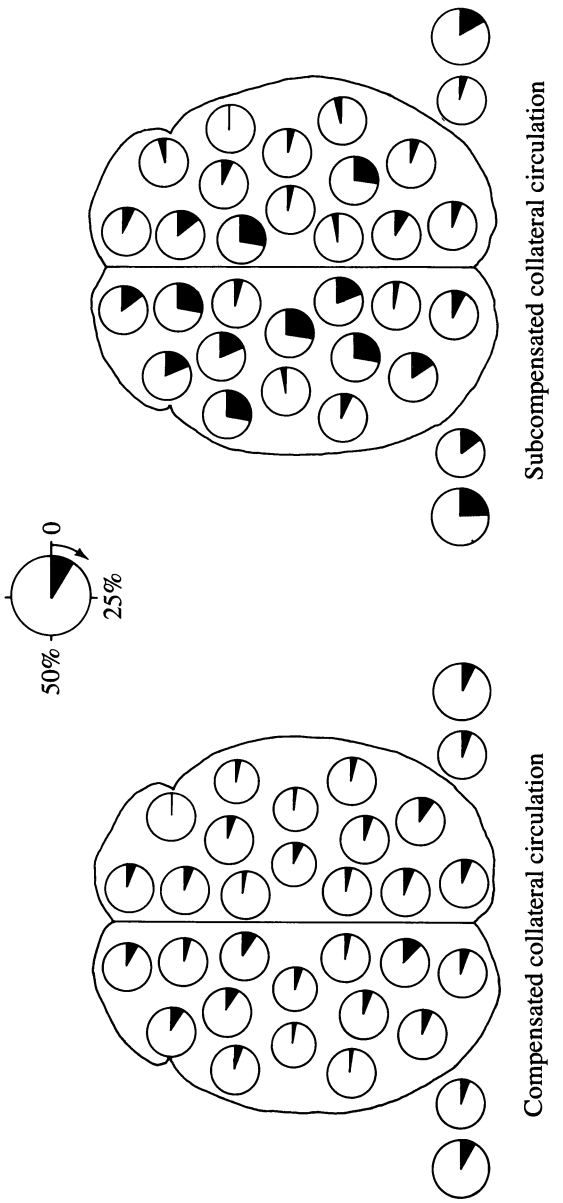

Figure 10.18. RCBF reactivity to functional artery occlusion (^{133}Xe method).

Table 10.22. Endovascular surgery performed, according to the size of the aneurysm, 1970–1989

	No. of cases					
	Deconstructive surgery		Reconstructure surgery			
Aneurysm size	Proximal occlusion of parent artery	Artery occlusion at aneurysm level	Aneurysm cavity occlusion	Induced thrombosis of aneurysm cavity	Total no.	Mortality (no.)
Giant (>2.5 cm)	70 (20)	65 (7)	24 (5)	3 (1)	162 (33)	15
Large (1.0–2.5 cm)	7 (2)	14 (2)	53	3	77 (4)	2
Small and medium (<1 cm)	1	11	15	1	28	3
Total	78 (22)	90 (9)	92 (5)	7 (1)	267 (37)	20

Numbers in parentheses indicate the number of patients who had a combined operation.

Table 10.23. Type of surgery performed, according to the site of the aneurysm, 1970–1989

	Type of surgery						
	Deconstructive surgery		Reconstructive surgery				
Aneurysm site	Proximal occlusion of parent artery	Parent artery occlusion aneurysmal level	Occlusion aneurysmal cavity	Induced thrombosis, aneurysmal cavity	Total no.	Mortality No.	Mortality %
Carotid artery							
Cervical	6	—	—	—	6	—	—
Petrous cavernous	—	2	—	—	2	—	—
True	42	—	4	1	47	1	2.1
False	—	41	2	1	44	—	—
Carotid-ophthalmic	13	34	22	1	70	2	2.9
Supraclinoid	11	8	20	1	40	2	5.0
Bifurcation	1	—	8	—	9	2	22.2
Middle cerebral artery	2	—	10	1	13	2	15.4
ACA–anterior comm. a.	—	4	10	2	16	1	6.3
Vertebrobasilar system	3	1	16	—	20	10	50.0
Total	78	90	92	7	267	20	7.5
%	29.2	33.7	34.5	2.6	100.0		

Table 10.24. Combined surgery for arterial aneurysms

Aneurysm type	Surgery
Type A	
Stage I	Bypass
Stage II	Balloon occlusion of aneurysm and feeding artery
Type B	
Stage I	Balloon occlusion of aneurysm and feeding artery
Stage II	Bypass
Type C	
Stage I	Balloon occlusion of aneurysm
Stage II	Resection of aneurysm

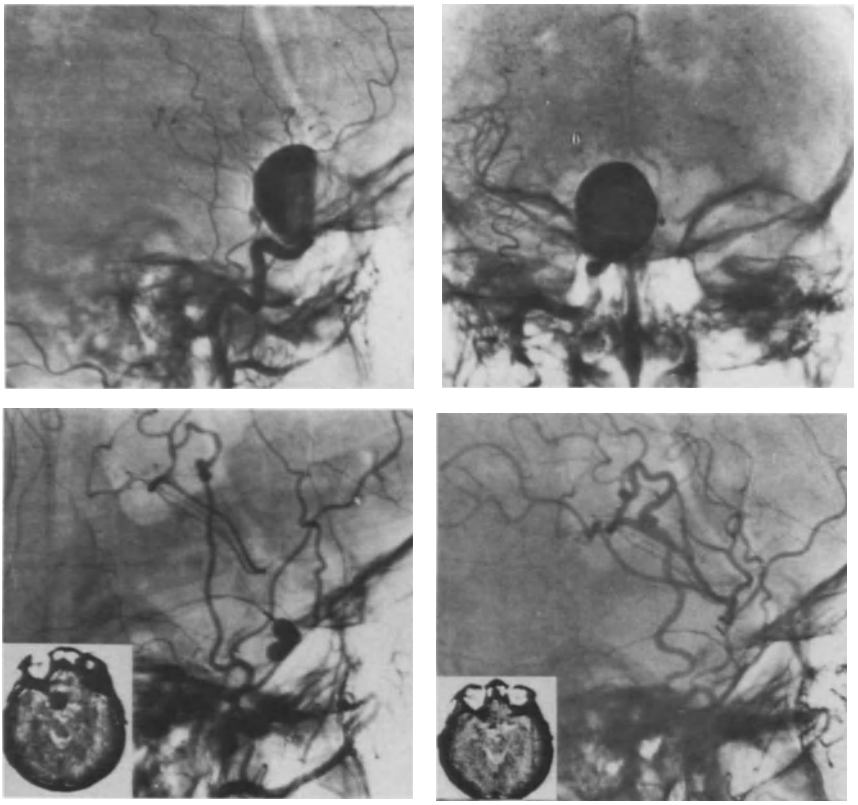

Figure 10.19. Combined surgery for arterial aneurysms. (**Top**, right and left) Carotid-ophthalmic giant aneurysm before operation. Bypass was performed, and the ICA was occluded by balloon. (**Bottom**) Angiography after operation (left) and 1 year later (right).

Table 10.25. ICA false traumatic aneurysms with epistaxis

Lesion	No. of cases
Sphenoid sinus false aneurysm	36
False petrous carotid aneurysms	2
False sphenoid sinus aneurysm + CCF	6
Total	44

canal are injured most often. In almost all cases good and satisfactory results were achieved by preventing recurrent external bleeding.

Among our 267 patients, 44 had false traumatic aneurysms at the level of the cavernous portion of the carotid artery (Table 10.25). In six patients false aneurysms were associated with a CCF and in two, false aneurysms of the petrous ICA manifested as hemorrhage from the ear. In this group we occluded the ICA at the site of its rupture in 36 patients and performed trapping in 10. One patient died. In all cases the collateral circulation was adequate. The principles of occlusion of false aneurysms are practically the same as for true arterial aneurysms. A difference consisted only in that many patients with traumatic aneurysms must be treated in the presence of profound anemia and unstable hemodynamic parameters.

Follow-up studies revealed no recurrent hemorrhage. Further development of the endovascular method for this lesion is associated with techniques of artery reconstruction. Prospective methods include thrombosis of a false aneurysm in the sphenoid sinus by transarterial or transphenoidal approaches.

Results

Some of the results of our study are summarized in Tables 10.26 through 10.29. Complete occlusion of an aneurysm was achieved in about 91% of our cases and partial occlusion in 9%.

Surgical mortality was 7.5%. The highest mortality rate was in a group of

Table 10.26. Degree of arterial occlusion prior to endovascular surgery for arterial aneurysms, 1970–1989

Degree of occlusion achieved	No.	%
Complete	243	91
Partial	24	9
Total	267	100

Table 10.27. Results of endovascular surgery for 267 arterial aneurysms, 1970–1989

Result	No.	%
Good	216	80.9
Temporary complications	10	3.7
Permanent complications	21	7.9
Death	20	7.5

Table 10.28. Results of endovascular treatment for giant aneurysms ($n = 162$)

Result	No.	%
Good	122	75.3
Temporary neurological signs	12	7.4
Disabled	13	8.0
Death	15	9.3

Table 10.29. Mortality according to aneurysm size after endovascular surgery for 267 arterial aneurysms, 1970–1989

Aneurysm	Mortality
Giant (>2.5 cm)	9.3
Large (1.0–2.5 cm)	2.6
Small and medium (<1 cm)	10.7

patients with aneurysms of the vertebrobasilar system (50%), carotid bifurcation (22%), and middle cerebral artery (15%). Surgical mortality was high—higher than the average mortality associated with intracranial surgery of arterial aneurysms. It would be a mistake, however, to jump to the conclusion that endovascular aneurysmal surgery is more dangerous and less effective than the intracranial procedure because among our treated aneurysms there were large numbers of giant aneurysms and large aneurysms along with aneurysms in difficult surgical sites.

The mortality rate for the group of patients with giant aneurysms was 9.3% (Tables 10.28 and 10.29). For the purpose of comparison, we examined

Table 10.30. Main publications on surgical treatment of giant aneurysms

Author	Year	No. of cases	Mortality (%)
Hosobuchi	1979	40	15.0
Sund et al.	1979	80	8.0
Symon et al.	1984	35	8.0
Vinuela	1984	312	9.3
French Neurosurgical Society	1984	309	18.0
Drake	1985	170	8.0
Paqualin	1987	201	18.0

the data in the literature concerning intracranial surgery of giant aneurysms (Table 10.30).

Complications

Analysis of complications warrants special attention because it permits us to predict some of them and to improve the surgical results. As one can see from Table 10.31, the most common complication is circulatory insufficiency as a result of balloon dislocation and embolization of cerebral arteries with empty balloons, blood clots, and the polymerizing substance to fill the balloon. In two cases there was rupture of an aneurysm because of distention of the aneurysm wall. We hope that some of these complications can be avoided by improving the surgical technique, that is, modification of balloon catheters, and special techniques for balloon fixation in the arterial and aneurysmal lumen. It seems important also to widen the indications for prophylactic bypass surgery.

Table 10.31. Results of 267 aneurysms treated by endovascular surgery, 1970–1989: complications (38 patients)

	Neurological deficit		
Complication	Temporary	Permanent	Death
Thromboemboli of cerebral vessels	1	5	3
Blood flow insufficiency	1	5	4
Embolism with balloon	5	3	1
Embolism with balloon contents	—	1	1
Dislocation of balloon	2	5	2
Aneurysm rupture	—	2	2
Rupture of filled balloon	1	—	1
Total	10	21	14
%	3.7	7.9	5.2

Summary

After examining our results we conclude that the endovascular method is effective for treating giant aneurysms, aneurysms that are difficult to reach by direct surgical approach, false (traumatic) aneurysms, and some others. Widening the indications for endovascular treatment of arterial aneurysms may allow further improvement using the endovasal method. (New modifications include occluding balloons, balloon intraluminal fixation, improvement of the balloon filling substance, and so on.)

The achievements of endovascular treatment of vascular diseases are obvious. However, thorough ongoing analyses of these results are required for the evolution and development of new methods for treating these types of cerebrovascular diseases.

Discussion

Dr. Fox: I have a question concerning the training of young physicians in endovascular therapy in your institution. Are those individuals who are fully trained in endovascular interventional neuroradiology equal to other neurosurgery trainees, or do they have a separate training route and are required to take a different course of study?

Dr. Konovalov: In our country we have no special examination for endovascular surgery, so we have no so-called endovascular surgeons. For example, Serbinenko is a neurosurgeon. I presented the experience of Dr. Lazarov with his treatment of arterial aneurysms, and he too is a neurosurgeon. He performs intracranial approaches to arterial aneurysms as well as endovascular surgery.

Dr. Hilal: Do you have neuroradiologists?

Dr. Konovalov: Yes, we have radiologists, but I cannot speak of their experience. They use superselective catheterization as well. They may use thrombotic material, but not usually for the treatment of vascular lesions. They occlude tumors and the feeding vessels of tumors. Those young neurosurgeons interested in endovascular surgery spend time with Serbinenko and his assistants. After several months they understand what to do and may start to operate themselves.

Dr. Debrun: For aneurysms treated with bucrylate with the leaking balloon, how do you keep the bucrylate from escaping from the aneurysmal neck and embolizing?

Dr. Konovalov: There have only been a few such instances. I am unable to give the specific details, but as far as I know there were no complications. In the beginning there were some complications with arterial aneurysms. The catheter would stick to the wall of the aneurysm, making it dangerous to withdraw it. In those cases the catheter was left in the artery.

CHAPTER 11

Intravascular Embolization of Craniocerebral Vascular Diseases: Beijing Neurosurgical Institute

Chung-cheng Wang and Zhong-xue Wu

Embolization of craniocerebral vascular disorders has been performed in Europe and North America for more than 20 years and many advances in both knowledge and material have been achieved. Authors such as Leussenhop, Serbinenko, Romodanov, Debrun, Djindjian, and Berenstein have contributed to this field. We began to perform some work on embolization of craniocerebral vascular lesions in 1985. We made our own latex balloons, microcatheters, and isobutyl-2-cyanoacrylate (IBCA) since they were not available in our domestic market. We subsequently embolized more than 30 patients with cerebrovascular lesions using balloons and IBCA.

Materials

Latex Balloons

In 1982 Romodanov reported on his method of making latex balloons. In China, our balloons were prepared by dipping a cylindrical aluminum alloy or glass mold (0.6–1.6 mm in diameter and from 3 to 25 mm in length) into pure latex liquid. After the latex mass on the mold had been removed from the liquid and had dried for 10 minutes, it was coated with starch and allowed to dry at room temperature for 2 hours. The mass was then delicately slipped off the mold and became a balloon. The balloon was subsequently vulcanized to strengthen it.

Isobutyl-2-Cyanoacrylate

We produced IBCA in cooperation with the engineers of the Chemical Institute in Beijing. Several animal experiments with IBCA were performed and emboli showed little influence on animal growth (Table 11.1) or on tissues other than a chronic inflammatory reaction in the tunica media of the vessel wall. We also noted some of the side effects of using IBCA that had been previously reported. In view of the fact that there is no superior embolizing material for AVMs to date we have continued to use IBCA to embolize some of our AVMs.

Table 11.1. Influence of IBCA on growth of rabbits

Group	No. of animals	Mean body weight increase after embolization (g)			
		2 Weeks	4 Weeks	8 Weeks	12 Weeks
Control	10	136.0	230.0	540.0	712.0
Test	30	132.0	234.0	572.0	707.0

Table 11.2. Tissue reaction of rabbits to IBCA emboli

Postembolization interval (weeks)	Pathology	
	Inflammatory	Vascular
1	Leukocytic	Nil
2	Lymphocytic and plasma cells	Nil
4	FBGC, fibrosis	Partial destruction of intima
8	FBGC, fibrosis	Destruction of intima
12	FBGC, fibrosis	Intact elastica with loss of undulations

FBGC = foreign body giant cell.

In our experimental studies in 80 arteries of 40 rabbits, the main pathological findings were the presence of chronic foreign body giant cells and a mild fibroblastic inflammatory reaction with thrombus formation in the vessel lumina (Table 11.2).

The Treatment of Traumatic Carotid–Cavernous Fistulas with Detachable Balloons

The most frequent type of arteriovenous fistula (AVF) is the carotid–cavernous fistula (CCF). Among these the traumatic variety (TCCF) is the most common. Over a recent 2-year period we treated 18 patients with TCCF using detachable balloons. Fifteen of them were successfully embolized; the other three were not embolized because the balloon catheter would not enter the internal carotid artery. These three were treated by other methods.

There were 14 men and 4 women ranging in age from 21 to 52 years. Among the 18 patients, 10 had been injured in car accidents, 5 by blunt trauma, and 3 by falling. The interval from onset to admission was 10 to 180 days. In three cases there was no loss of consciousness initially. In the other 15 cases the initial loss of consciousness lasted 16 hours to 30 days and 13 of these patients complained of intracranial noises. The other two patients had aphasia or mental aberration. Exophthalmos existed for 4 to 60 days with a mean duration of 25 days.

Table 11.3. Initial traumatic lesions associated with TCCF

Trauma	No. of cases
Basal skull fracture	8
Vault skull fracture	1
Craniofacial fracture	3
Intracranial hematoma	2
Cerebral contusion	8
Cranial nerve injury	8
Optic nerve	2
III Nerve	3
VII Nerve	1
Multiple nerves	2
Other (including extremity fractures and visceral bleeding)	3

Table 11.4. Secondary lesions caused by TCCF

Symptoms and signs	No. of cases
Exophthalmos	18
Extraocular congestion	18
Restriction of eye movements	18
Bruit	18
Ipsilateral frontal	6
Bilateral frontal	8
Whole skull	4
Secondary hypopsia (caused by venous retinopathy and disc edema)	12
Secondary blindness (caused by secondary glaucoma and keratitis)	2
Hemispheric arterial insufficiency	3
Epistaxis	2

Initially, a number of other traumatic lesions accompany the TCCFs including fractures of the skull base, cerebral contusions, and cranial nerve palsies (Table 11.3). Secondary lesions resulted from increased intracavernous venous pressure and remote arterial "steal" phenomena (Table 11.4). Two patients developed delayed blindness, having had intervals of 132 and 180 days, respectively, from the time of injury to the time of admission.

Diagnostic Methods

Computed Tomographic (CT) Scanning

Of the 18 patients, 13 were examined by CT scanning, which demonstrated a markedly enhanced cavernous sinus and prominent ophthalmic vein (Fig. 11.1).

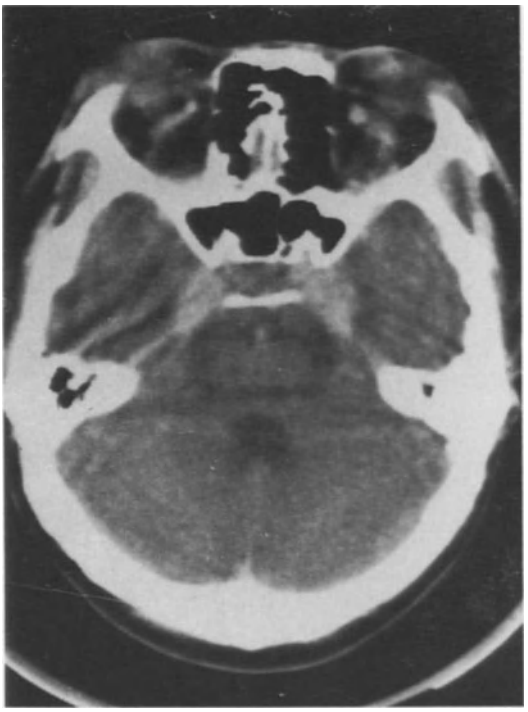

Figure 11.1. Axial CT scan with contrast medium showing abnormally high density in bilateral cavernous sinuses.

Cerebral Angiography

It is important to establish the location of the fistula, the features of the venous drainage, and the origin of the ophthalmic artery.

Many methods have been reported to be useful for establishing the site of the fistula. We commonly used lateral projection vertebral angiography with manual compression of the symptomatic internal carotid artery (Fig. 11.2) and angiography of the contralateral internal carotid artery in the frontal view with manual compression of the symptomatic internal carotid artery. Angiography of the 18 patients revealed five cases with the fistula located in the C3 segment, seven cases in the C4 segment, and five cases in the C3–C4 segments. One patient had bilateral TCCFs. The left fistula was in the C3–C4 segment and the right fistula in the C3 segment.

In terms of venous drainage, most patients had a mixed pattern of venous drainage.

Embolization Procedures

Local anesthesia was used in most cases, which permitted neurological monitoring throughout the procedure. If it lasted more than 1 hour, sedatives

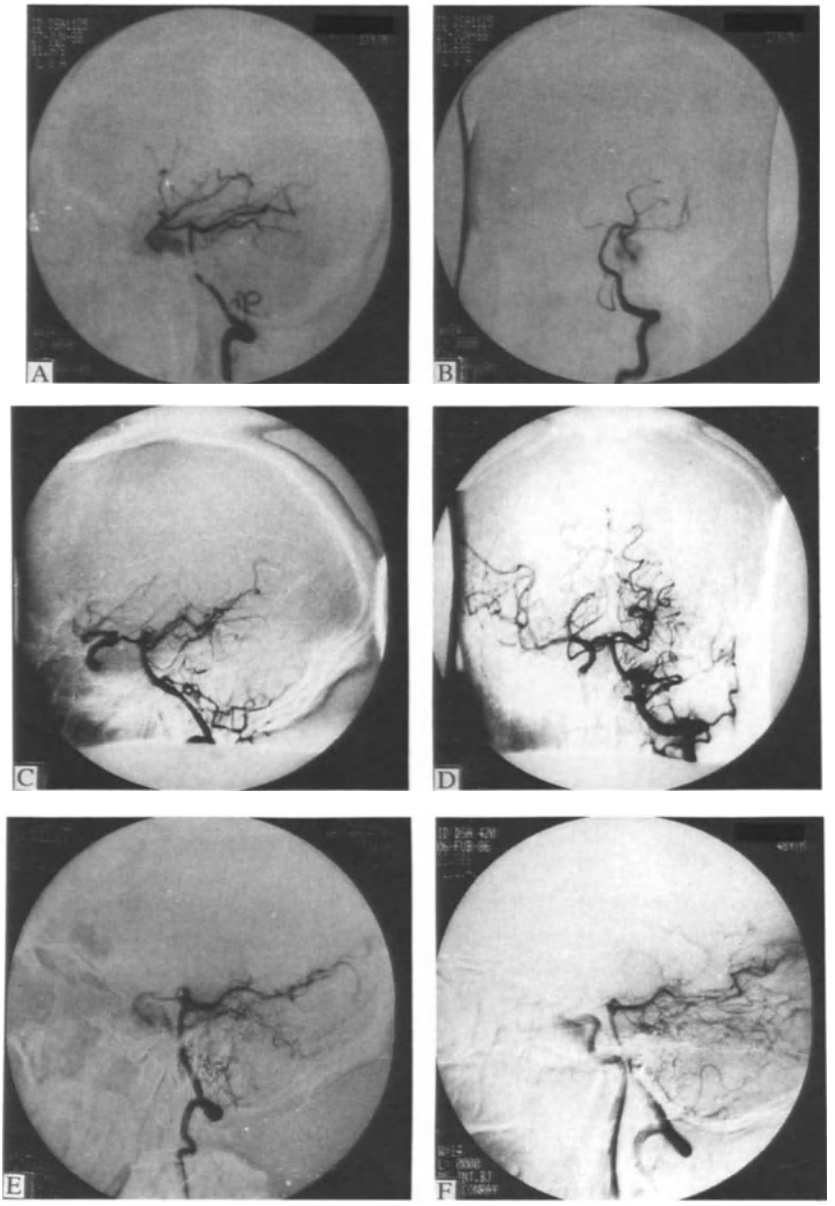

Figure 11.2. Six cases of TCCF. Preembolization angiograms of the vertebral artery with manual compression of the symptomatic carotid artery showing the location of the fistulas.

such as diazepam (Valium) 10 mg could be used so that the patient remained cooperative. Verbal contact is very important to determine if a satisfactory result has been achieved and to detect any complication immediately after occlusion of the ipsilateral internal carotid artery (ICA).

Slow intravenous administration of heparinized saline solution (total dose 15,000 units) was continued throughout the procedure as was interval injection of heparinized saline directly into the punctured artery. These two measures are useful to prevent the formation of clots in the vessels and catheter.

The conventional Seldinger technique was applied in all of our procedures, including both femoral and carotid approaches. The introduced sheath (5F or 6F sheath for carotid approaches and the 7F or 8F sheath for the femoral approach) was passed into the lumen of the punctured artery. The detachable latex balloon catheter was introduced through the sheath and a guiding catheter was placed into the ICA. Usually the latex balloon was coiled within a propelling chamber. To make the balloon radiopaque we placed stainless steel wire into the lumen of the balloon before operation. When saline was injected into the chamber, the balloon catheter was pushed through the guiding catheter inside the ICA into the fistula. The balloon inside the fistula was inflated carefully with contrast medium. When occlusion of the fistula was proved angiographically, the patient simultaneously noted the disappearance of the intracranial bruit.

We usually used 60% Conray to inflate the balloon. The volume of Conray injected into the balloon was determined according to the size and appearance of the balloon. If the inflated balloon showed an irregular configuration as it molded to the septations in the cavernous sinus, injection of Conray was discontinued to avoid the risk of rupturing the balloon. In our patients two or three balloons were needed to close the fistula in most cases. When the fistula was small and the balloon could not enter it, the first balloon was put at the fistula site and a second balloon proximal to the fistula. The carotid artery should be preserved as far as possible even though in most cases no complications occurred even after a TCCF trapping. If the ICA cannot be preserved, it is necessary to occlude it temporarily for more than 30 minutes and simultaneously carefully assess the patient's neurological function before the balloon is detached.

Balloons are detached by advancing the outer 3F polyethylene catheter and simultaneously retracting the balloon catheter until detachment occurs.

Postembolization Care

Each patient was kept at bed rest for 6 to 8 hours afterward. Within the 7- to 10-day period after embolization, any nausea, vomiting, serious cough, or constipation should be controlled. We suggest that any patient whose internal carotid artery had to be sacrificed should be kept at bed rest for at least 2 weeks to prevent balloon migration. When the patient has a headache, analgesics should be given. Intravenous administration of dexametha-

sone and dextran are continued for 3 days after embolization and systemic use of antibiotics is continued for 7 days after the procedure.

Results

Eighteen patients underwent a total of 21 embolization procedures. Complete occlusion of the fistula was achieved in 15 patients. Among these 15 the ICA was preserved in 9 (Figs. 11.3 and 11.4). In the other 6 patients the fistulas were occluded by trapping (Fig. 11.5).

Bruits disappeared immediately during the embolization procedures in 10 patients, after 1 week in 3, and after 2 weeks in 2. Exophthalmos and other symptoms of intraorbital hypertension (except double vision) disappeared gradually between 4 and 80 days after embolization in 15 cases. Among the other three patients whose fistulas were incompletely occluded, one lost the

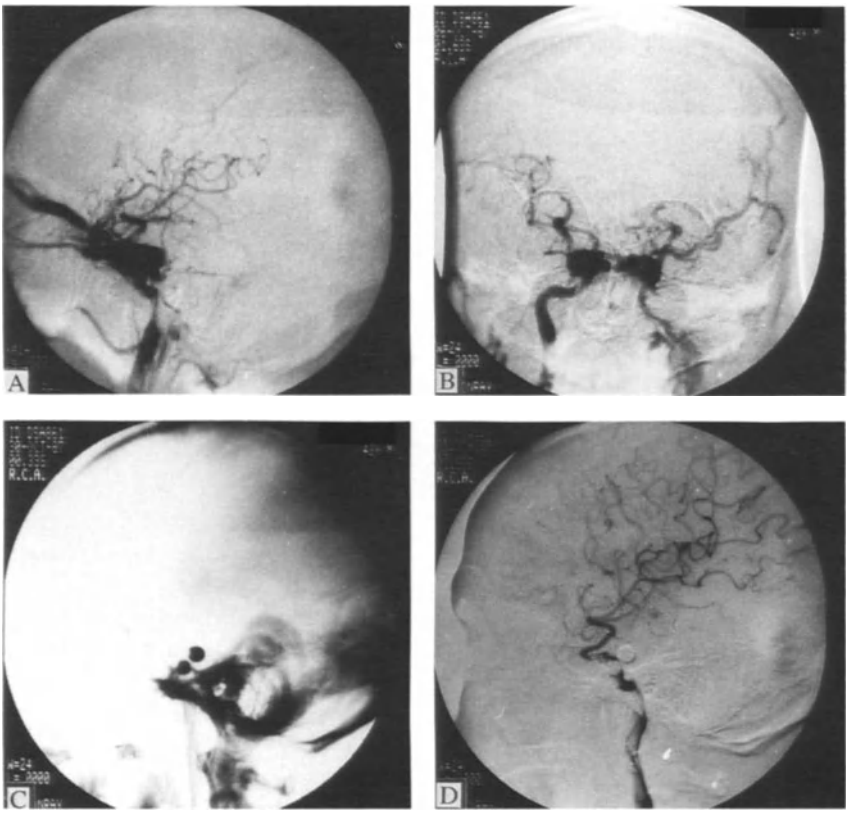

Figure 11.3. TCCF. **(A&B)** Preembolization angiograms showing mixed venous drainage. **(C)** Postembolization plain film showing two balloons placed in the cavernous sinus **(D)** Postembolization angiogram shows that the TCCF is no longer visualized and the ICA is preserved.

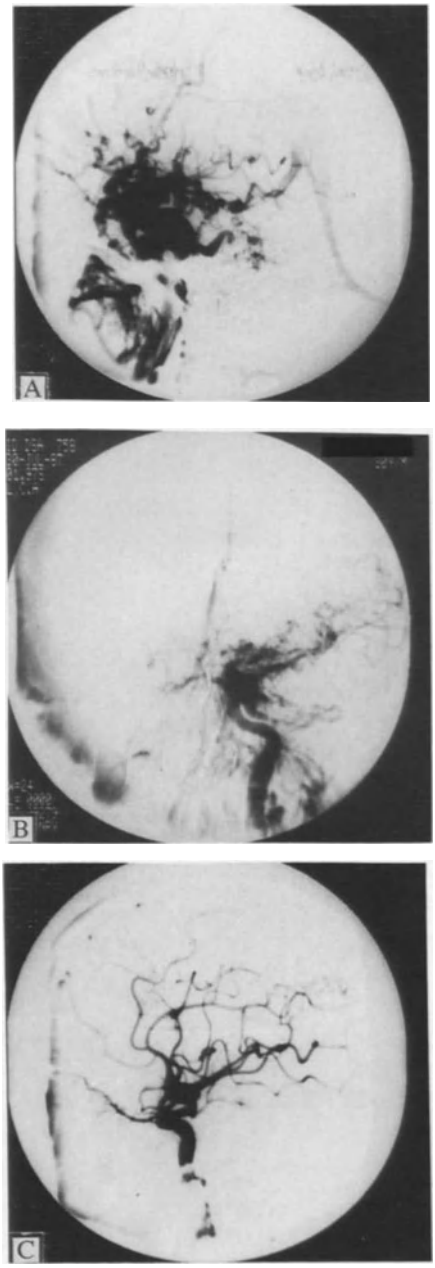

Figure 11.4. TCCF. In this case, a craniotomy had been done, with copper wire inserted into the cavernous sinus initially, but the patient had not improved. **(A&B)** Pre- and postcraniotomy angiograms showing that the fistula is still there. **(C)** Post-embolization angiogram shows that the fistula no longer exists and the ICA is preserved.

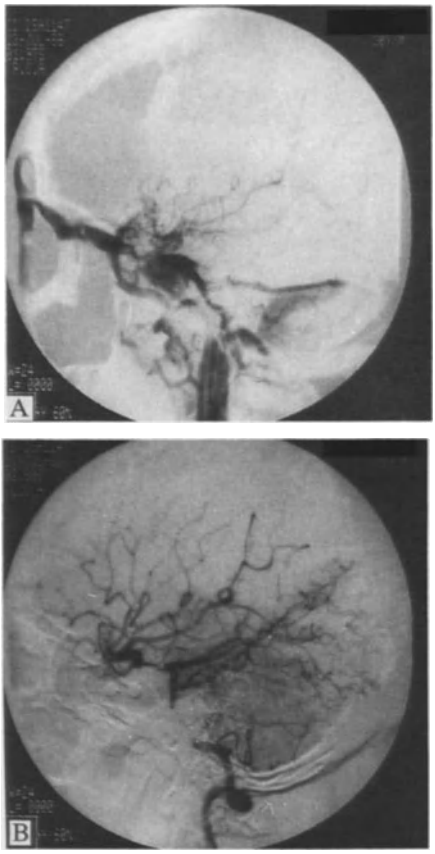

Figure 11.5. TCCF. **(A)** Preembolization angiogram. **(B)** Postembolization angiogram of the vertebral artery shows that two balloons block the ICA. The anterior cerebral circulation comes from the vertebrobasilar system.

bruit but his ocular symptoms remained, and two and persisting bruits but no exophthalmos or other ocular symptoms.

In one patient the inflated balloon embolized into the right pulmonary artery, but no adverse sequelae occurred. During five embolization procedures we found that the balloons inflated by Conray gradually deflated after detachment.

Discussion

The technique utilizing detachable balloon catheters is new. Serbinenko[1] introduced this technique in 1974 to treat not only TCCFs, but probably all AVFs throughout the body. Various reported series confirmed the efficacy and safety of this technique.[2–4] We believe that the detachable balloon catheter technique is the best available method for treating TCCFs. Compared

with other methods of treatment, the main benefit is that it not only occludes the pathological arteriovenous (AV) communication, but it also may preserve the blood flow of the internal carotid artery. Lasnjaunias and Berensteins[5] reviewed in their book the various methods of treating TCCFs. Using these techniques, balloon embolization has a cure rate varying between 85% and 98%. Preservation of the flow within the internal carotid artery ICA was attained in 60% to 70%.

In comparison ligation of the cervical internal or common carotid was successful in only 31% to 40%. Trapping of the CCF by a combination of intracranial ICA clipping and extracranial ICA ligation in the neck produces good results in 56.7%, but has a high associated mortality and morbidity. Although surgical approaches to a CCF have been shown to cure a TCCF and preserve the carotid flow, they are complex and major operations.[5]

We have used the balloon catheter technique for only a few years and we still have much work to do. In this group of patients we found that many balloons became deflated and detached themselves from their position in the fistula. There are two factors responsible for balloon deflation. In some cases the balloon was not fixed tightly enough to the catheter; this occurred in our earlier cases when we prepared the balloon catheters 2 to 3 days prior to the embolization procedure. Even balloons tightly fixed to the catheters with latex threads within 2 to 3 days prior to the embolization procedure had loosened by the time the procedure was performed. Hence, the balloon catheter is now prepared during the embolization procedure. The other factor was that we did not have available polymerizing (solidifying) agents that could be introduced into the latex balloons. Debrun et al.[4] advocated injecting vulcanizing silicone into the latex balloons and Taki et al.[6] suggested injecting 2-hydroxyethylmethacrylate (HEMA) into the balloons. Later Hieshima[7] modified the use of HEMA to facilitate a more reliable application. Such agents could have prevented the deflation of balloons in our patients.

In 1980 Charles et al.[8] reviewed bilateral CCFs in the English-language literature and found a total of 120 patients with bilateral TCCFs. We had one case of bilateral TCCFs in which the right-sided one was occluded with two balloons (Fig. 11.6) and the left TCCF was surgically treated because the patient could not tolerate intracarotid catheterization. His presenting clinical signs completely disappeared within 6 months after discharge from the hospital.

Embolization Treatment for Intracranial Arteriovenous Malformations with Isobutyl-2-Cyanoacrylate (IBCA)

Isobutyl-2-cyanoacrylate is a fast polymerizing liquid agent that rapidly solidifies in contact with an ionic fluid. Given this property it may enter and solidify with the core or nidus of an AVM. IBCA embolization of intracranial AVMs was performed in a series of 12 cases.

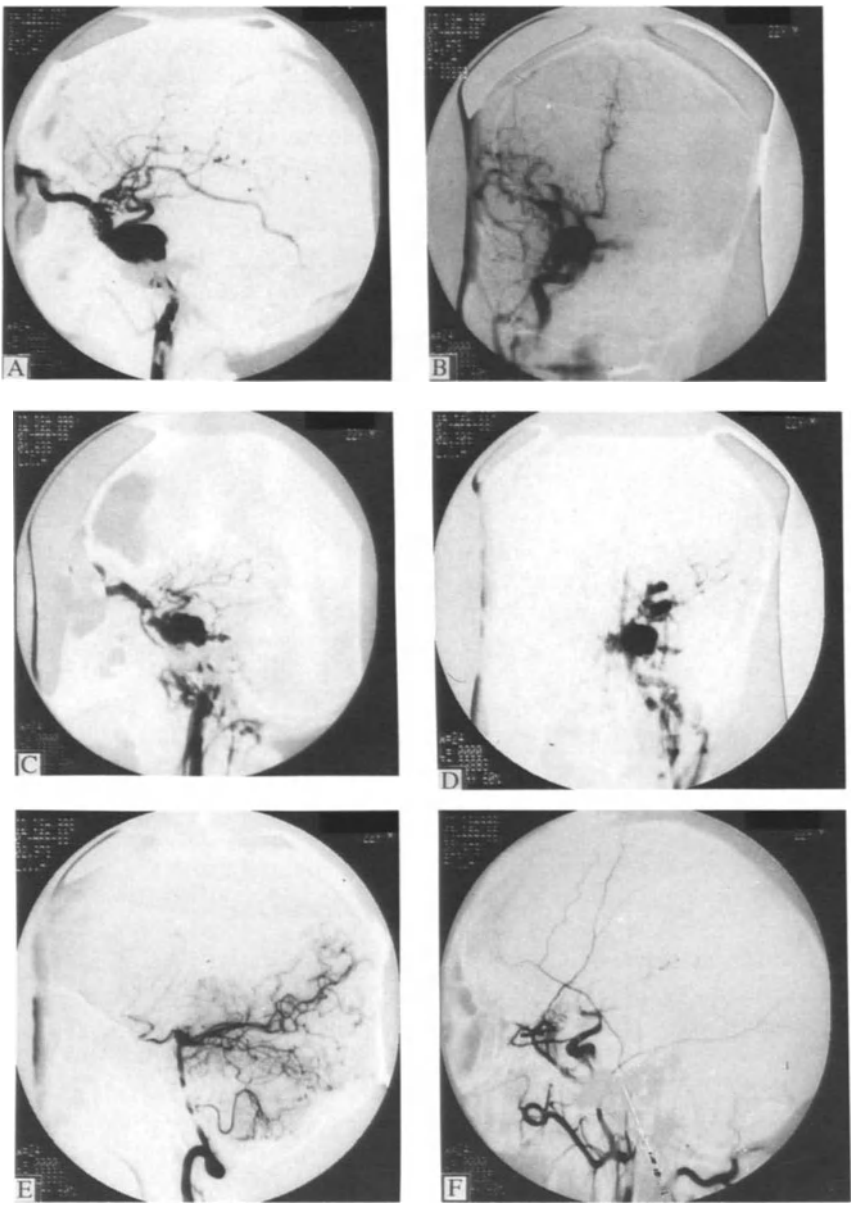

Figure 11.6. Bilateral TCCF. **(A&B)** Right carotid arteriogram before embolization. **(C&D)** Left carotid arteriogram. **(E)** Preembolization angiogram shows the anterior circulation coming from post circulation. **(F)** Postembolization right carotid arteriogram shows that the ICA is blocked and there is an anastomosis between the ECA and the ICA.

Clinical Materials

Among the 12 patients with intracranial AVMs there were 8 men and 4 women whose ages ranged from 9 to 45 years with a mean of 27 years.

The malformations of this groups could be classified as follows: one case of a complex AVM involving the scalp, skull, dura mater, and brain; three cases of dural AVMs, of which two involved the cavernous sinus and one involved the parietooccipital region; eight cases of large cerebral AVMs (greater than 6 cm in size), of which three were located in the Rolandic area and two involved the deep structures.

The symptoms and signs before embolization included headache in 12 cases, epilepsy in seven cases, mental disorder in two cases, transient ischemic attack in one case, and cardiac failure in one case.

Methods

Embolizing Materials

We produced our own leak-calibrated microballoon catheters and IBCA. The catheter tubing's inner diameter was 0.4 mm and outer diameter was 0.8 mm, and it was connected to a latex balloon at an opening in its distal end. IBCA was mixed with Pantopaque in a ratio of 2:1 during the embolization procedure.

Embolizing Procedure

Local anesthesia was utilized after administration of analgesics and sedatives in most cases.

The technique of catheterization is almost the same as that used for TCCFs described above. When the tip of the microballoon catheter reaches the nidus of the AVM, the catheter should be slightly withdrawn to keep its tip in the feeding vessel at least 5 mm away from the nidus of the AVM.

The leak-calibrated microcatheter system must be rinsed with a 5% glucose solution prior to injection of IBCA to prevent the IBCA from hardening within the catheter. The injection method used is called the "sandwich" technique, which means that the predetermined amount of IBCA loaded in a syringe is preceded by the 5% glucose solution, and the IBCA is injected in a "sandwich" fashion. In our experience the total amount of material injected should not exceed 3 ml for the first embolization.

After the IBCA deposition the microballoon catheter should be withdrawn immediately to prevent the tip of the catheter from adhering to the vessel wall.

The connection between the catheter and the needle on the syringe loaded with IBCA must be carefully checked before injection. If the connection is loose or free the injection will fail. Should another injection be required then a new leak-calibrated microballoon catheter is used.

Results

The results of IBCA embolization of intracranial AVMs are shown in Table 11.5. The 12 patients in this group underwent 19 surgical angiographic treatments. In only one case, notably that of a dural AVM, was there complete angiographic occlusion. The other 11 cases were incompletely occluded.

Two of the 12 patients had AVMs involving functional cortex and suffered aphasia and hemiparesis after the embolization. These deficits were transient and disappeared within 3 to 14 days. In two patients the AVMs involved the cavernous sinus, and their signs of exophthalmos and extraocular palsies disappeared. In one patient with a huge AVM involving the cerebral hemisphere there was improvement in his cardiac failure and cerebral ischemia. Symptoms of epilepsy were ameliorated in two patients.

One patient with an AVM involving the Rolandic area underwent three embolizations, and a length of microballoon catheter had to be left in in the feeding vessel because the tip became adherent to the vessel wall. Two years later, at follow-up, no adverse sequelae were observed (Figs. 11.7, 11.8, and 11.9).

Table 11.5. Results of embolization of AVMs with IBCA

Pt. no.	Age	Sex	Involved area	Postembolization clinical status	Feeders	% AVM occlusion
1	22	F	Right hemisphere of cerebrum	Improved	MCA, ACA PCA	40
2	13	M	Cavernous sinus	Improved (Fig. 11.9)	ECA	90
3	6	M	Cavernous sinus	Improved	ECA	90
4	43	M	Scalp, skull, dura, brain	No change	ECA, ACA	70
5	40	F	Left basal ganglion	Improved	MCA, PCA	80
6	45	F	Dura	Improved	ECA	100
7	24	M	Left rolandic, speech	Aphasia, full recovery in 56 hours	MCA, ACA	80
8	23	M	Left rolandic	Hemisparesis, full recovery in 1 week (Fig. 11.8)	MCA, ACA	60
9	27	F	Right frontal	No change (Fig. 11.7)	ACA	80
10	37	M	Right hemisphere	No change	ACA, MCA, PCA	20
11	26	M	Left parietal, occipital	No change	MCA, PCA, ACA	40
12	18	M	Right temporal	No change	MCA	50

MCA = middle cerebral artery; ACA = anterior cerebral artery; PCA = posterior cerebral artery; ECA = external carotid artery; ICA = internal carotid artery.

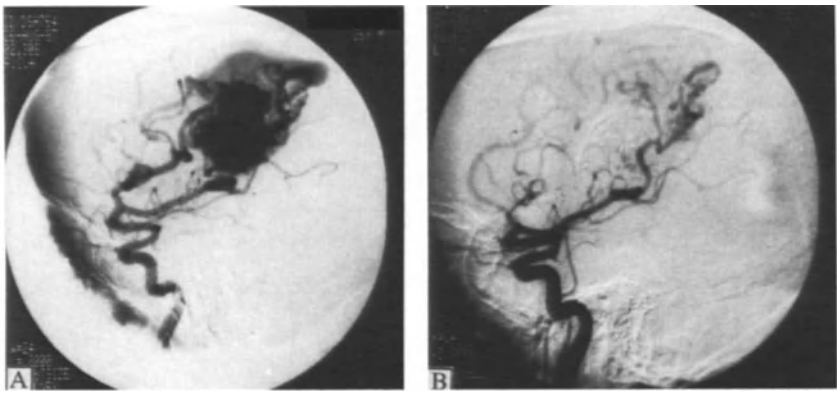

Figure 11.7. AVM. **(A)** Preembolization angiogram showing an AVM in the right rolandic area. **(B)** Postembolization angiogram shows that a large portion of the AVM is no longer visualized.

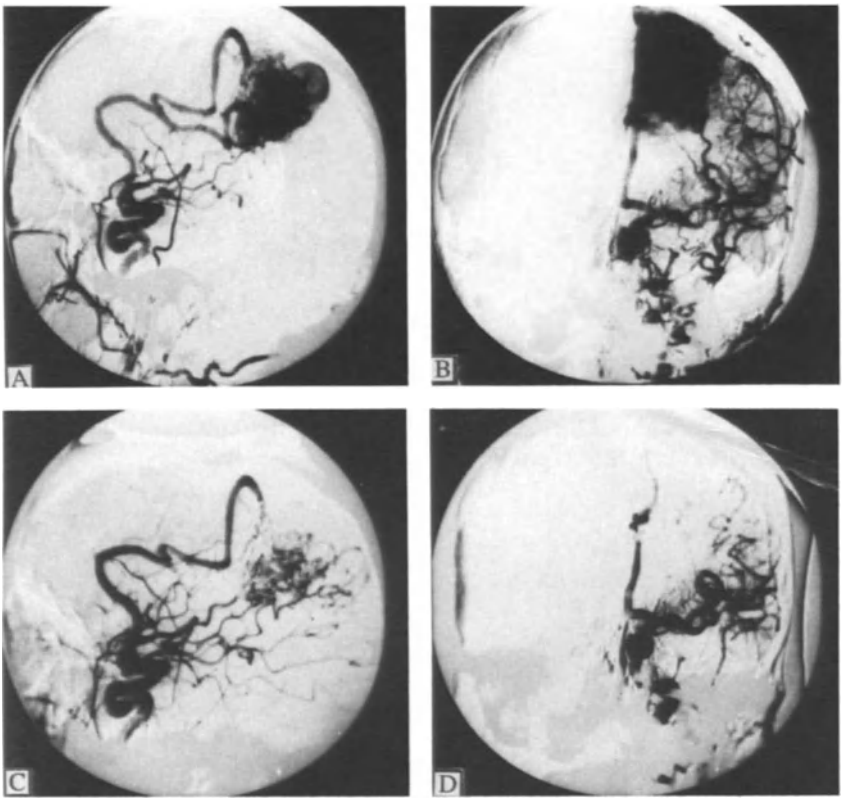

Figure 11.8. AVM. **(A&B)** Preembolization angiogram shows an AVM in the left parietal lobe. **(C&D)** Postembolization angiogram shows that a large portion of the AVM is no longer visualized.

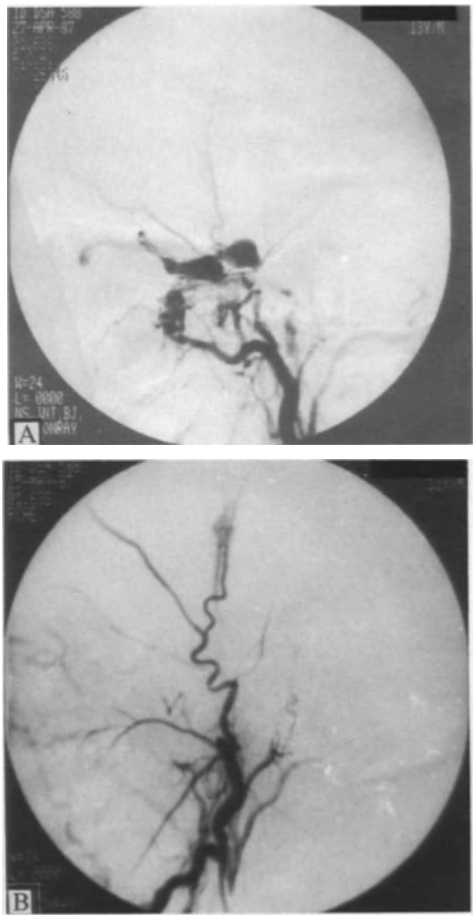

Figure 11.9. Carotid–cavernous AVM. **(A)** Preembolization angiogram shows an AVM feeder from the ECA. **(B)** Postembolization angiogram shows that the AVM is no longer visualized.

Discussion

Intracranial AVMs have been considered more benign than aneurysms. Surgical excision has been the treatment of choice of this disease for more than 20 years. The overall results of surgical excision demonstrate an 11% morbidity and a 2% mortality.[9] The development of endovascular interventional neuroradiology offers an alternative treatment for intracranial AVMs. Generally speaking, the site and size of AVMs are the principal concerns in their surgical removal. AVMs located in deep regions, those located in functionally essential regions, and those occupying extensive areas of the brain represent difficult problems for surgical excision.[10] This is similarly true for some

of the AVMs involving the dura mater. However, utilizing the technique of microballoon catheterization can result in the partial obliteration of these AVMs, which is of value in their management. This technique may be particularly useful for AVMs involving the dura mater and for AVMs in the Rolandic or speech areas or in deep regions of the brain as long as they have large arterial feeders.[11]

IBCA is not the most satisfactory agent for embolizing cerebral AVMs because it does not completely occlude the AVM in most instances. In our series only one AVM involving the dura mater was completely occluded. Hence we believe that this technique will not totally replace surgical excision in most cases. Some authors believe that the clinical status of the patient improves even with the partial occlusion of large AVMs and they speculate that the remainder undergoes thrombosis since IBCA may induce a chronic inflammatory reaction in the vessel walls.[12]

In one patient a length of catheter had to be left within the vessel because its tip became adherent to the wall of the feeding artery. Although no neurological deficits were found after this event, the nature of this problem generated considerable attention.

Many authors including ourselves recommend that the following guidelines be observed to prevent a microballoon catheter from adhering to the vessel wall during embolization procedures.

1. Injection of too great a volume of IBCA during the embolization procedure should be avoided. This is especially true for embolization procedures using a femoral route where the amount of IBCA injected should not exceed 2.5 ml. When a second injection of IBCA is needed through the same AVM feeder the amount of IBCA should be limited carefully even if the angiogram shows no apparent change in the appearance of the AVM in comparison with the preembolization study. This must be stressed because a small amount of IBCA could occlude the AVM feeder.
2. The key point in the use of the "sandwich" or "continuous column" technique is that the rate of injection of IBCA is maintained at a given velocity. It should not be administered with fluctuations of rate or in a stop-and-start fashion.
3. Immediately after injecting the IBCA, the microballoon catheter should be withdrawn rapidly before the retrograde IBCA column can reach the tip of the microballoon catheter.

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CHAPTER 12

Endovascular Therapy of Cerebral Arteriovenous Malformations and Aneurysms with a Proposed Scale for Neurological Outcome

Allan J. Fox

Endovascular therapy has become established as a useful approach to the management of cerebrovascular abnormalities. Much of the basis for this approach has been the development by Luessenhop and Rosa[1] of flow-directed particulate embolization, by Serbinenko[2] of detachable balloons, and by Kerber et al.[3] of leak balloon navigation. The field has been further widened by the development of new microcatheter systems, real-time digital subtraction fluoroscopy, and new embolic materials. A number of centers around the world, including our own at University Hospital in London, Canada, have gained experience in the embolization of various lesions, especially brain arteriovenous malformations (AVMs) and aneurysms.

Cerebral AVMs

The original experience with embolizing brain AVMs was with particles. Our own series from 1976 to 1978 included 15 patients: six embolized with flow-directed plastic spheres via the femoral approach, and nine embolized with a mixture of Pantopaque and Gelfoam via direct operative catheterization of feeders. Follow-up angiography in patients in whom the AVM was not surgically resected invariably showed nidus refilling due to enlarged artery-to-artery collateral networks, recanalization of the Gelfoam mixture, or both. The goal of embolization was subsequently changed to attempt nidus obliteration, and liquid adhesive was used in most instances.

From 1978 to 1986 we treated a series of 115 patients with brain AVMs in various locations and of various sizes using acrylic tissue adhesives.[4–6] Important basic experiences in the field were gained during this time,[7–9] and an evolution in approach occurred. There was 4.3% mortality and a moderate or severe long-term morbidity of 9.4% after embolization in this series. The AVM was completely obliterated by embolization alone in 5.2% of these cases. The AVM was completely resected after embolization in 30% of cases.[10]

Embolization of brain AVMs has been further stimulated by the develop-

ment of directable microcatheters and materials such as tissue adhesives[11,12] and mixtures of particles and thrombotic materials.[13,14] Our series[15] from 1986 to mid-1990 included 43 patients. The results of this series indicate a 4.6% rate of serious complication due to the embolization. The series consisted of large, mostly complex AVMs that were difficult to remove surgically, although 70% were completely resected following the embolization. Mortality due to surgery was 4.6%, and 7.0% had serious neurological sequelae following the surgery. A positive Amytal test or a transient deficit produced by embolization influenced the decision to resect in 9.3% of cases.

Although our own practice has concentrated on embolization to enable surgery for difficult AVMs, other teams are embolizing a growing number of lesions before focused radiosurgery, and some centers have utilized embolization as the sole treatment, with a success rate as high as 18% complete obliteration.

To date, the following conclusions can be offered on the use of embolization for brain AVMs.

1. Small, one- or two-feeder AVMs can be completely obliterated by embolization alone using liquid adhesives.
2. Blockage of feeders alone, whether by particulate emboli or liquid adhesives, does not obliterate the AVM nidus and stimulates growth of artery-to-artery collateral feeders.
3. Embolization before surgery enables resection of large, complex brain AVMs by reducing operating time and bleeding. It can also block difficult-to-access feeders.
4. Incomplete AVM obliteration or removal has not been shown to be of benefit for the treatment of brain AVMs over the long term.

Intracranial Aneurysms

In many centers detachable balloon technology[2] and therapy with preservation of the parent artery quickly became the primary treatment of choice for intracranial and neck fistulas. However, the detachable balloon treatment of brain aneurysms has not gained the same widespread acceptance.

Our own series using detachable balloons to treat patients with cerebral aneurysms[16,17] has been restricted to aneurysms that were not easily clipped, most being giant aneurysms. Initially, during the late 1970s, we treated seven cases of carotid aneurysm with an intraaneurysmal balloon and preservation of the artery. It resulted in recurrence of the aneurysm and some disconcerting neurological complications. We therefore abandoned this approach and for many years used detachable balloons only for proximal parent artery occlusion.[16,17] Our protocol, which includes a test occlusion in the awake patient protected by systemic heparinization, has been performed on 95 patients. In these cases after permanent occlusion of the parent artery 1% had

a permanent deficit due to stroke, and there were no deaths; 83% of the aneurysms were completely obliterated, including those in 16 of 26 patients with supraclinoid aneurysms and in 3 of 6 patients with basilar aneurysms. These results meant that most unclippable aneurysms, when the proximal occlusion did not effect isolation of the aneurysm, thrombosed due to changes in perfusion pattern and biophysical forces.

There have been advances in catheters, balloons, and polymerizing balloon fillers. Moreover, the extraordinary results of Shcheglov's Kiev series[18] and the innovative advances by Hieshima and colleagues in San Francisco[19–21] have spurred new developments. We have therefore resumed treating some unclippable aneurysms with detachable balloons, filling them with HEMA, and preserving the parent artery. With intraaneurysmal balloon treatment we have encountered delayed aneurysm rupture,[22] regrowth of the aneurysm from neck remnants, and stroke caused by propagation of clot from thrombosing aneurysm. Our own series is skewed because of the innovative techniques used by the neurosurgeons with whom we work. Few large-necked aneurysms presenting at our institution do not have some form of surgical treatment such as clipping or parent artery occlusion by clip or tourniquet. Therefore those treated by intraaneurysmal balloons are an even more select group than those treated by other teams.

The experience of regrowth of aneurysm neck remnants after surgical clipping is well known.[23] Aneurysm necks do not have normal arterial wall layers and are subject to the same dynamic flow forces that caused growth of the aneurysm in the first place.[24] Balloons have convex surfaces, and a small space remains between the balloon and the concave surface of the adjacent normal arteries. It is therefore not surprising that aneurysms can regrow from remaining neck remnants.

The following conclusions can be offered on the use of embolization for intracranial aneurysms.

1. Treatment with detachable balloons is a simple, safe approach to effect proximal occlusion of the parent arteries of many unclippable aneurysms.
2. The incidence of aneurysm rupture and regrowth after intraaneurysm balloon treatment of giant unclippable aneurysms with wide necks is of concern.
3. Aneurysms located in many intracranial locations can be entered by endovascular techniques.
4. Balloon treatment may be more successful technically for small-necked, potentially clippable aneurysms.
5. Other endovascular embolic materials presently in the development stage will probably be more successful for treating aneurysms than present materials.

Addendum. Since 1990, we have been using platinum coils for the intraaneurymal emolization of aneurysms, and have not placed a detachable balloon within.

Proposed Standardized Scale for Neurological Outcome of Patients Undergoing Embolization Procedures

The long-term follow-up of patients treated for neurological conditions should address the complications of the treatment, the potential for recurrence, and the effects of the disease itself. Patients who have undergone endovascular therapy of cerebral aneurysms are also subject to the risks of the embolization procedure and to the risk of regrowth from aneurysm neck remnants. Counting hemorrhagic events in the long-term follow-up of patients with embolized AVMs or aneurysms is one method of documenting the relative value of embolization versus other forms of treatment or no treatment at all. Many patients are not permanently or significantly affected by hemorrhage from an AVM, for example; and even some of those severely affected recover. It is important therefore not only to count the incidence of hemorrhage from incompletely embolized brain AVMs but to catalogue the clinical and functional outcome of these events.

A method for following these patients is proposed. The system involves two components: (1) determining the patients' "functional status"; and (2) grading the patients on a "severity scale" according to specific ischemic or hemorrhagic events. This method is utilized in the protocol of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) as a standard method for a multicenter trial. Practical and simply defined criteria are used as an ongoing way to standardize patient assessment and to facilitate

Table 12.1. Functional status

Parameter	Degree of difficulty (score 1–7)
Visual acuity for reading (with glasses)	____
Visual acuity for ambulation (with glasses)	____
Comprehension of language	____
Fluency of speech	____
Swallowing	____
Lower limb function	
Sitting/rising from chair	____
Walking	____
Upper limb function	
Cutting food/pouring beverages	____
Dressing/undressing	____
Toileting (personal hygiene)	____
Integrated function	
Shopping (including travel to stores, walking, carrying)	____
Not applicable or has visited outside usual residence for social reasons	____ no ____ yes

Every time a patient is assessed during follow-up, each category is rated from 1 (normal function) to 4 (moderate difficulty) to 7 (unable to do).

comparisons between treatment centers. The Functional Status Scale (Table 12.1) documents, at regular intervals, the degree of difficulty follow-up patients are experiencing. This assessment includes visual acuity, language comprehension and fluency, swallowing, limb function, and the practical integrated functions of daily living. Each category is scored on a scale of 1 to 7 (from normal to unable to do), and research assistants can perform the evaluations. Comparisons can therefore be made before and after treatment and among groups of patients.

Hemorrhages or ischemic stroke events are also graded in severity (Table 12.2) on a scale of 1 to 11. Specific strokes are graded as to minor or major disruptions of domains of function, such as swallowing, self-care, ambulation, communication, and comprehension. Hemorrhages or ischemic strokes are graded by the level of best recovery on the Stroke Severity Scale.

By utilizing a standardized clinical outcome method such as the one proposed, patients can be documented by total functional status scores at any time, and their specific hemorrhagic or ischemic events can be graded by the severity of the deficit produced. This system allows cooperative study groups to perform standard evaluations on patients before, immediately after, and a long time after endovascular treatment. Good clinical perspective would be gained by including these assessments in the reports of long-term follow-up after endovascular treatment that are now surfacing in the scientific literature. For example, a patient who is severely devastated before treatment but who is neither worse nor better after treatment could not be disguised as "an excellent result" of embolization treatment. Although there might be an ex-

Table 12.2. Stroke severity scale

Severity grade	Impairment	Neurological symptoms	Neurological signs
0	None	None	None
1	None	Present	None
2	None	None	Present
3	None	Present	Present
4	Minor impairment in any domain	Present	Present
5	Major impairment in 1 domain only	Symptoms and signs are not applicable at these high stroke grades	
6	Major impairment in any 2 domains		
7	Major impairment in any 3 domains		
8	Major impairment in any 4 domains		
9	Major impairment in any 5 domains		
10	Reduced consciousness		
11	Death		

The stroke severity scale is used at follow-up to assess the residual deficit and neurological function caused by hemorrhage or stroke. The domains of function—swallowing, self-care, ambulation, communication, and comprehension—are also assessed for status.

cellent vascular anatomical result, and although the treatment might not result in patient decline, the patient would nevertheless always be a neurologically devastated individual. A system of standardized clinical outcome, whether the one proposed here or some other, is recommended for the long-term evaluation of patients with brain AVMs and aneurysms who have undergone endovascular treatment. It might be argued that this system is more rigorous than that usually used for following the outcome of brain AVMs and aneurysms in standard neurosurgical practice. However, the field of intracranial endovascular therapy is now attracting intense scrutiny, and this scrutiny will help validate the procedures in the eyes of the world medical community. If patients with potentially devastating conditions cannot be treated by any other method and are treated by endovascular therapy, a rate of complication higher than that normally tolerated in neurosurgery might be forgiven. However, this justification will not hold if endovascular therapy is to replace, in some instances, standard neurosurgical treatment. If the most successful endovascular treatments involve small one- or two-feeder AVMs and small-necked, easily clipped aneurysms—both of which are conditions managed successfully by surgery—changing to endovascular treatment can be justified only if it results in a better long-term outcome. The results of endovascular therapy must therefore be documented with the highest possible level of objectivity and accuracy.

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Discussion

Aneurysmal Neck Remnants and Aneurysm Regrowth

Dr. Fox: I want to quickly review the paper we published in the *Journal of Neurosurgery* on the regrowth of aneurysms from neck remnants. I think we made an important observation, and the question remains how to integrate it with the work we are doing now and in the future. We defined the neck remnant as a slight outpouching or bulge of the vessel wall proximal to the clip. Normally, the vessel wall is straight. In one case where an aneurysm was clipped during the third trimester of pregnancy, a subarachnoid hemorrhage occurred 5 years later. Angiography demonstrated that the clip had shifted its position, and a neck remnant regrew; it could be called a new aneurysm, implying that the first aneurysm was cured. I think we should call it a neck remnant that grew. We had 17 patients with 19 regrown aneurysms, most of whom had been treated by Dr. Drake.

Dr. Stein: How many aneurysms did you treat overall during that period?

Dr. Fox: Up to 1981 the accumulated aneurysm series of Dr. Drake and his colleagues was 1500 cases. The number with neck remnant cases was approximately 1%. We do not have an accurate number of follow-ups, which can be a problem with a long distance referral center, but we had an informal counting of all the angiograms done during 1985 and angiographically, based on our criteria, we found a neck remnant in about 5% of the cases. I do not know how accurate that is for the first 1500 cases; if it is an accurate number, then 5% have neck remnants and 1% of all aneurysms clipped recur. Hence we suggest that 20% of patients with neck remnants over the next two decades will present again with symptoms and signs due to the same aneurysm. If these figures are real, it suggests a dangerous situation. Unfortunately, we could not include these cases in our report because they are numbers that cannot be absolutely verified. It is unfortunate that we do not have better statistics.

Dr. Debrun: Does Dr. Drake coat the neck of the aneurysm at the end of surgery, and if so does it decrease the regrowth of aneurysms?

Dr. Fox: These aneurysms have been treated variously over many years. Coating is performed when it is obvious that a neck remnant is left. Sometimes the neck remnant is left alone because it was a technically difficult lesion, and the clipping was the best possible choice to avoid damage to the perforating vessels. Those aneurysms that are clipped with an apparently excellent result are not coated.

Dr. Berenstein: Were there any basilar tip remnants?

Dr. Fox: Yes, there was a basilar tip aneurysm as well.

Dr. Berenstein: The shape of the basilar bifurcation is almost universally associated with aneurysms.

Dr. Fox: Those lesions were treated and some did not survive the new presentation or the new treatment. Though they can regrow, we do not know the incidence. This series was compiled as a criticism, in a sense, of surgery and the neurosurgeons' saying that one is cured postoperatively without the need of an angiogram. (Even with an angiogram sometimes there are areas that I cannot interpret.) It is also a major potential criticism of endovascular treatment because we may ask how often a balloon perfectly re-forms the normal artery, how often there is an edge between the aneurysm neck and the balloon, and how often it thromboses? I do not know the answers, but I do know that we are looking at minute lesions that we can barely see. Therefore I think we have to be even more honest than the surgeons.

To quickly review some of the reasons for the attitudes concerning the use of endovascular treatment of aneurysms at our institution: If I treat only the worst aneurysms, almost every one is a disaster. We, like others, have therefore developed a protocol for choosing cases and have been partially lucky and partially intelligent during the process. We place balloons below the aneurysms. It is always done with the occlusion test, with the patient awake, and with systemic heparinization.

Most of the cases have been done without a bypass, although some have been done with a bypass. The procedure is done the day after bypass surgery based on the idea of stressing the bypass to keep it open by occluding the artery soon after. In one instance, with the bypass functioning well and retrograde filling demonstrated down to the distal M_1, at 7 minutes after test occlusion the patient became hemiplegic. This condition was reversed, and he recovered immediately. One week later occlusion again resulted in hemiplegia. One month later, once again after occlusion, he became hemiplegic. The bypass was still open 8 months later, and he passed the occlusion test. We detached two balloons below the aneurysm, and the bypass angiogram looked worse that before. There was retrograde filling, which I interpreted to mean that the bypass was not providing the main collateral supply. The thing that allowed him to pass the occlusion test was the fact that his natural collaterals were better. The excellent bypass originally seen showed that the natural collaterals were bad, and that is why he has failed the first occlusion test.

Dr. Moret: In 1975 I published the fact that surgical bypasses increase normal collateral anastomoses. This point is important. I thought at the beginning that probably the surgical bypass would have reduced the normal vascular anastomoses, but this evidence is to the contrary.

Dr. Fox: In our series we created two groups: aneurysms below the ophthalmic artery, which can be isolated from the circulation by occluding the parent artery, and aneurysms above it, where there are collaterals. We have demonstrated what has been generally known by neurosurgeons, namely, that out-trapping can achieve complete thrombosis of an aneurysm without eliminating it from the circulation simply by the change of flow patterns or whatever other forces happen to coexist. This phenomenon was further exemplified by a case of a right basilar trunk aneurysm previously operated unsuccessfully with clipping of the right vertebral artery. It was reoperated by Dr. Drake, who found that clipping was not possible. Subsequently, balloon occlusion of the left vertebral artery was done below "pica." One week later the occluded vertebral arteries were seen along with retrograde filling of the basilar artery, demonstrating thrombosis of the aneurysm sac with possibly a small neck remnant. We believe that this neck remnant is much less dangerous than a neck remnant that exists when the parent artery is open with anterograde flow because whatever biophysical forces that led to the aneurysm growth have been totally changed. The changes of those forces have led to aneurysmal thombosis. Therefore the neck remnants may be present, but we believe they are less dangerous.

Our results up to November 1988 regarding proximal occlusions, tested by the occlusion test by balloon showed that 75 of 88 aneurysms were completely obliterated by this technique. Of 26 supraclinoid aneurysms, 16 were obliterated, and 3 of 6 basilar aneurysms were treated by vertebral occlusion. About one-third are not really being treated. Hence we subjected the patients to a procedure with its risks, but the aneurysm at follow-up is still growing and needs additional treatment. One other point that remains hidden in our data regards the complications of treatment or the lack of treatment of other patients. We can be blamed as well for having told patients

whose aneurysms were completely isolated that they were cured; we have no follow-up on them. Yet this remains the standard way of reporting many of these cases. One tends to report only that which is of personal advantage and to ignore the questions one cannot answer or describe situations in such a way that people do not notice their questions are not answered.

What about the more elegant treatments? We too have had some experience in trying to treat the aneurysm and preserve the parent artery. Dr. Debrun published our early cases when he was here. We initially had great enthusiasm, but one after another unfortunate outcome led us to abandon this approach. We only started again because of the recent success of Drs. Heishima and Scheglov, who have been using some of the newer materials, although we have attempted it only in the worst cases, from my point of view, because the results are poor.

One such example involved a basilar tip aneurysm. Angiography showed that most of the aneurysm was thrombosed. Dr. Drake was able to get a clip across the neck, but the perforators could not be excluded no matter how the clip was positioned. He thought this was a good case for endovascular occlusion. Dr. Solomon said the same thing the other day. If the perforators come off the neck of the aneurysm, it is a good case for endovascular occlusion. Wrong! It is a terrible case because we cannot occlude the neck for the same reason the surgeon could not. If we leave the aneurysm neck we will cause trouble. Perhaps with enough experience we will find a way to deal effectively with these aneurysms.

The day after surgery we put a balloon in, actively avoiding neck occlusion. Hence we left some neck unoccluded. There was a bit of contrast material around it. The balloon was 1.5 Heishima, and we exchanged it with HEMA. The next day the patient had a pulmonary embolus, and the decision was made to begin anticoagulation. One week later there was thrombosis of the dome of the aneurysm, but the neck enlarged and became a thin "pancake" over the whole front. It was like a saucer going around it. We hoped that it would thrombose when the heparin was discontinued. At 3 months the vascular pulsations pushed the balloon slowly into the clot.

Dr. Scheglov: The balloon was not properly placed. It should have been narrower in its upper portion and wider in its lower portion. The balloon should be modified to the shape of the aneurysm.

Dr. Holtzman: In this aneurysm, though, the perforators emerged from its neck. If the neck was occluded, the perforators would be occluded. How can one possibly insert a balloon that occludes the neck and at the same time preserves the perforators?

Dr. Viñuela: When I was in London, Ontario, Dr. Drake called me to the operating room to show me a vessel emerging from the sac of a superior cerebellar artery aneurysm. He said it was the first time in a thousand cases that he observed such an anomaly.

Dr. Stein: The point to be made here is where is the neck? One has this trouble particularly at the base of the bifurcation, where there is a fusiform dilatation that extends down to the superior cerebellar arteries and sometimes below. Obviously, if you call that area the neck, perforators do come out there because it is a dilatation of the upper apex of the basilar artery. This is not where we would put the clip. We would manufacture a neck distal to the perforators and the posterior cerebral arteries. I think that is the same problem you have with the balloon, that is, to occlude what appears to be neck here, which extends down to the superior cerebellar arteries. You are obviously going to occlude perforators and probably the origin of the posterior cerebral artery and the superior cerebellar arteries so you cannot put a ballon down

there any more than you can put a clip there. That is where the problem arises. You are not at all certain where the neck is radiographically; surgically, we fashion a neck and we say this is where the neck should be. I would agree that, in general, perforators do not emerge from a true aneurysm. When they seem to, they are probably coming from the dilatation of the parent arteries.

Dr. Debrun: If information comes from the neurosurgeons that there are perforators preventing them from clipping an aneurysm, you should not accept the case for endovascular occlusion. In such cases you know there will be trouble because you will have to leave part of the neck open, which does not cure the aneurysm. In such a situation you should say I cannot do better than you. There is one thing that you *can* do. Unlike the neurosurgeon, who is operating under general anesthesia and cannot test the outcome of neck occlusion, you can perform endovascular neck occlusion and see if the patient tolerates it. If he does, you inflate the balloon; if he does not you quit.

Dr. Moret: Yes, that was my point. The answer is to check the patient when the balloon is occluding the neck.

Dr. Fox: In fact, that is the rationale for the Drake tourniquet procedure. It is my strong feeling that even if the result of endovascular occlusion is satisfactory by most standards and the neck is not occluded, such cases are a disaster because the risk of hemorrhage in the future is high.

Dr. Berenstein: Therefore you must treat him again—but it is not a disaster.

Dr. Fox: In this case, he will not come back because of financial factors that are related to his living in Buenos Aires and his ability to return to Canada for further treatment.

Dr. Fox: Another example involves a patient whose opposite carotid artery was occluded some years previously and who presented with an enlarging left cavernous aneurysm and diplopia due to a mild III nerve palsy. We did not want to sacrifice her carotid artery because it was important as a collateral source. Three balloons were introduced. We had to look hard for any neck remnants. The AP and lateral views were reported as complete isolation of the aneurysm. The neck was one of the smallest I have seen and it had a tiny neck remnant. She was watched carefully in the postoperative unit, was awakened every half-hour, and was noted to have a mild drift at 5 hours. She was treated aggressively with volume expansion, hypertensive agents, and heparinization. She reversed the drift and was in excellent condition until the third day when a bruit was auscultated, and there was evidence of a carotid–cavernous fistula. She was ultimately treated successfully with external-internal carotid bypass and balloon occlusion. Her case was not a disaster, just a series of problems; and we simply address them as they arose.

Altered Blood Flow with Proximal Vessel Occlusion and Aneurysm Thrombosis

Dr. Holtzman: Let us address the matter of proximal arterial occlusion and distal aneurysm thrombosis, in particular as it may pertain to disturbed flow, decreased blood flow, or altered pulsatile flow.

Dr. Fox: In effect, the induced stenosis and change in flow patterns are strong factors in assisting thrombosis of most aneurysms. It is the principle on which proximal occlusions with the Selverstone clamp were performed, and it is the principle of the Drake tourniquet used to occlude the basilar trunk.

Dr. Berenstein: Proximal occlusion of a blood vessel induces thrombosis in distally located aneurysms through modifying blood flow. Are there any factors that allow one to predict aneurysm thrombosis, for instance by alterations in the patterns of blood flow?

Dr. Goldsmith: First, there is no *turbulent flow*. We must stop using that phrase. There is no such thing as turbulent flow at the Reynolds numbers that exist in arteries such as these. What we are observing are *disturbed flow patterns*, and they are traceable to well defined patterns. As concerns the aneurysm, we should ask why aneurysms generally do not thrombose. The flow in the center of an aneurysm is brisk; and as it comes back along the sides of the aneurysm there are circulation patterns that also demonstrate brisk flow. Thrombosis tends not to occur in the face of brisk flow. Thrombosis requires that the blood cells hang around for some time and collide frequently with each other and that the shear forces are relatively high. If one reduces the flow rate in an incoming artery, the situation is ripe for thrombosis in a recirculation zone as exists within an aneurysm.

Dr. Fox: We have known it to take 15 minutes for an thrombus to develop. Is this a general experience?

Dr. Goldsmith: It depends on what activating factors are around and how activated are the platelets. Activating the platelets even a little promotes more rapid thrombosis formation.

Dr. Mohr: What about mechanical treatment of aneurysms? Why not take advantage of the hemostatic properties and arrange a balloon at the entrance to the aneurysm so as to reduce the flow into the aneurysm to the extent that endosaccular clotting takes place. The use of thrombotic material may be dangerous because you would not want the substance to reach the main artery. It should be possible to take advantage of the natural thrombogenic processes.

Dr. Stephen Onesti: Cases of aneurysm in the middle cerebral artery have been reported that were treated by bypass procedures and converted to total occlusion.

Dr. Mohr: There are two cases in the literature.

Dr. Onesti: There is a theoretical consideration that increased backflow might promote a more thrombogenic atmosphere. Did you find that patients who had bypasses have a better or higher incidence of complete occlusion of their aneurysms as opposed to patients who did not?

Dr. Fox: I have looked hard for correlations one way or the other. Patients with complications were not a discrete group. Half of them had bypasses, and the other half did not. Half of the patients who failed the occlusion test had bypasses, and we could not find any specific reason. Perhaps in a larger series someone might. Of course, you have to determine the reasons for the bypasses in our cases and maybe that is the problem. We did not find anything specific. A small number had the bypass because they failed some test, but most had bypasses because their surgeons thought it should be done. Thus there were different reasons for the bypass, and so those cases do not represent a homogeneous group.

Experience Derived from the Visit to Dr. Scheglov in Kiev

Dr. Fox: One of the important techniques I learned from Dr. Scheglov and that we have included in our program is to always use two balloons for any case where we intend to use a detachable balloon. Another relates to premedication and the use of

a volume expander to prevent some of the ischemic problems or reduce them by starting treatment earlier. We had not been doing that.

A major point in Dr. Scheglov's series is that all of his cases are "cold" primarily because of the time it takes until they can be treated. That factor represents a difference from our situation. The balloon is the primary treatment for all aneurysms, and most of the aneurysms he treats are the common ones with few in the cavernous sinus, along the ophthalmic, vertebral, and basilar arteries, and giant aneurysms. Our experience represents only a fraction of his, and we are treating the worst aneurysms. I believe that his patients with similar aneusysms have worse complications than the others in his total series. So I am convinced that what Dr. Moret is doing in Paris, despite some criticism from the participants in this conference, is important for us. We wish we could be in an environment of cooperation that would permit us to have those opportunities.

Indications for Endovascular Treatment

Dr. Fox: Dr. Scheglov and I have discussed the indications for endovascular treatment, and I can only conclude that we do not know precisely what they are. What we do know is that something can be done for some patients and that we have an obligation to find a place for the techniques. The important point is that it represents an alternative to surgery. I think that is the future of endovascular treatment—that it will be incorporated into neurosurgical treatment as a real option and not as a competitive modality.

Management of Vasospasm

Dr. Fox: We have had only a small experience with dilating for vasospasm. An example is a patient who had a small anterior communicating artery aneurysm and mild, diffuse spasm. The aneurysm was clipped, and the next day he developed a severe left upper extremity plegia and lower extremity paresis. We were unable to see the M_1 segment. We inferred its filling because there was some contrast in the middle cerebral branches beyond without a large moyamoya pattern. We used two balloons for the dilation. We dilated the supraclinoid carotid and the A_1 segment, and then put a balloon in A_1 and started dilating the bifurcation. Little by little we were able to dilate the first centimeter of M_1. The patient improved on the table. We stopped because he was moving his hand even though the vasodilation was not complete. I think we restored some flow to the lenticulostriate arteries. He had a stormy course, but he never worsened in terms of hand function, and in fact he improved. He did have evidence of infarction in some areas of the frontal cortex, but the deep structures were preserved. This was one of our best successes with dilatation, and it involved an artery we could not see angiographically.

Arteriovenous Malformations

Dr. Fox: Dr. Debrun came to our institution and introduced us to the modern embolization techniques. We were treating AVMs with spheres and Gelfoam. Subsequently, Dr. Berenstein showed us that there could be remarkable success with glue, and Dr. Moret taught us some of the more aggressive ways of using glue to accom-

plish better things. It remains for us to perfect this technology. I think that if we could somehow achieve endovascular obliteration of the draining veins and avoid hemorrhages the AVMs would thrombose. I just cannot think of a way that it can be accomplished. In the cases that evolve to complete thrombosis, such as the two reported here, the draining vein is severely affected. After embolization much of the AVM is left, and at follow-up studies it has disappeared. There was no hematoma formation, and of course that is what we wish to avoid. Achieving complete thrombosis remains a challenge and may be the only solution for the complex AVMs.

Dr. Viñuela: You do not need to mechanically impair the draining vein. What is needed is to slow the flow. The size of the vessel, which is indicative of the flow, should reflect the stagnation of flow at the site in the vein. For example, if there is an AVM with pure venous drainage and you are able to occlude a sufficient number of pedicles to produce partial stagnation in the draining veins, thrombosis begins in those veins and ultimately extends into the AVM. This is something with which we are all familiar and what we are trying to simulate with mechanical or physiological intervention. It is the same process.

Dr. Fox: You may be right. I think there are some differences between the bleeding of dural AVMs and that of brain AVMs: The dural AVMs bleed only from the veins, whereas the brain AVMs may bleed from different sites during the follow-up.

Dr. Viñuela: That is the clinical presentation we are discussing.

Dr. Fox: I am worried about the complications.

Dr. Viñuela: You do not need to involve the vein mechanically to increase the number of complications. If you occlude sufficient pedicles to produce stagnation in the draining vein, that vein will physiologically thrombose.

Dr. Fox: Let me describe our best example of converting what we would call an impossible or nearly impossible surgical case to surgical resectability by embolization. The patient had a large lesion with a huge thalamoperforating artery, multiple lenticulostriate feeders, and an anterior choroidal artery that continued to the distribution of the medial posterior choroidal area. The patient underwent selective injection of glue into five lenticulostriate vessels, the choroidal artery, and the thalamoperforator over some weeks. He remained neurologically intact with some residual small vessels filling the superior thalamic and choroidal areas. The lesion became surgically resectable in Dr. Drake's mind and was removed without incurring a deficit and with only modest bleeding. This was an excellent example of the usefulness of embolization.

On the other hand, in another case a large AVM in the left rolandic region was treated by injecting glue in nine places, both by catheter and with open craniotomy with the patient awake and using cortical mapping techniques. The patient, a 17-year-old girl was hemiplegic after a hemorrhage 2 months previously. She had been absent from school for 3 months with a stable deficit. The embolization was done progressively, and her hand progressively began to move. Not every vessel was taken because of the cortical mapping. We did not use a large amount of glue, as does Dr. Moret, but employed many small shots; the cast filled many parts of the AVM. At the end she was moving everything—complete reversal of her hemiplegia. When she returned 6 months later the angiogram was unchanged, so there filling of the AVM had not recurred. We made up a number and said that it was 90% blocked. She began running several kilometers a day, and she finished high school and entered the university in the fall Four months later she died of a hemorrhage from the residual AVM, 10 months after the treatment. This was an emotional case for us. We cannot base our record on anecdotes, but in fact all series are a group of anecdotes, and this case

prevented me morally from telling patients that the glue would be likely to help even if the AVM was incompletely treated. I removed that part from my informed consent. In fact, we precipitously reduced the number of AVMs we were embolizing by that slight change in one phrase of the informed consent. I do not know what to do about such cases.

Since Dr. Moret taught us to inject glue more aggressively into the nidus of the AVM we have improved our technique, but there are still problems. An example involves a left anterior temporal AVM. We had catheterized two vessels and injected glue. The postinjection angiogram was excellent, but little "things" are filling late. We were hoping it would go on to thrombosis. After 7 months the patient was well, but angiographically the embolization was poor. The glue did not reach the nidus.

Recently we have been utilizing a technique taught us by Dr. Viñuela, that is, using mixtures of ethanol, Avitene, and PVA mostly as a preoperative procedure. An example involves a young boy who suffered a hemorrhage several years before with incomplete treatment of the AVM. We inserted the catheter and the tracker into successive branches and slowly injected the mixture. The angiograms showed progressive occlusion of the individual feeders. The procedures was done slowly with no excitement. The angiogram looked remarkably good except for a small amount of filling during the late phases. It was so good that Dr. Peerless did not want to operate. Four to five months later there was evidence of recurrent partial filling, indicating that this technique is not the answer to permanent obliteration of AVMs. We treated the boy again, embolizing the middle cerebral artery. The collateralized portion remained and was removed surgically.

Similarly, another patient had an occipital lobe AVM, and it was thought that surgical excision would result in a visual field defect. We embolized one pedicle; and the Amytal test in the next pedicle indicated a hemianopia, so we stopped. Surgical excision was then performed with complete resection and no visual field defect. This case points out that one can claim success after the combination of endovascular therapy and surgical therapy. I think either one alone would have resulted in incomplete treatment or a visual field defect consisting of at least quadrantanopia.

Indications and Some Thoughts Regarding Endovascular Therapy

Dr. Fox: First, I must say that I think we do not know absolutely the justifiable indications. Resectable AVMs are the easiest to treat completely with glue, and it becomes a question of the best method for treatment. It is for these lesions that we could contribute the most because they are the more common ones, but surgeons can also take care of them well. Difficult resectability is our best indication at this time. Nonresectable lesions pose a question. If we cannot completely block the AVM and the patient is well and has a nonresectable lesion, I am not sure about the justifications for intervention. We need to study these cases.

There are different points of view regarding the clinical aspects of each case as to which are reasonable ones to treat. I would like to consider some of the psychological aspects. We used to say that when a patient is told he has a "bomb" in his head it is not a sufficient reason to inject a little bit of glue into his AVM. I have seen patients return after 10 years devastated. I specifically recall a good looking man in his thirties running a business, with a wife and family. I embolized his lesion with beads in 1976. We did a bit, not too much as it was in the left rolandic region. When he returned for

follow-up 12 years later he was physically healthy but emotionally broken, with a disrupted home and family and addicted to alcohol. Everything had fallen apart. We had not instituted continuing psychological therapy because he had come from a long distance at great expense.

With preoperative embolization, most operated patients do not require blood replacement at surgery, and the surrounding necrosis produced after embolization helps the surgeon because the plane is there. If sufficient time elapses and the nidus is occluded with glue or one of the other mixtures, it is not the same as having feeder occlusions with beads or coils.

If we compare our results to the estimated natural history, we believe there is a 2% per year risk of hemorrhage in the unruptured AVMs and 4% per year risk if a rupture has occurred. Over a 30-year period this risk is substantial. These data must be qualified by determining whether the hemorrhages are accompanied by transient or permanent morbidity. At the present time our long-term follow-up is incomplete, and we anticipate more definitive correlation of our intervention with the natural history in the years to come.

III. ENDOVASCULAR EXPERIENCE

B. ANEURYSMS

CHAPTER 13

Surgical Perspectives on the Selection of Patients for Endovascular Treatment

Robert A. Solomon

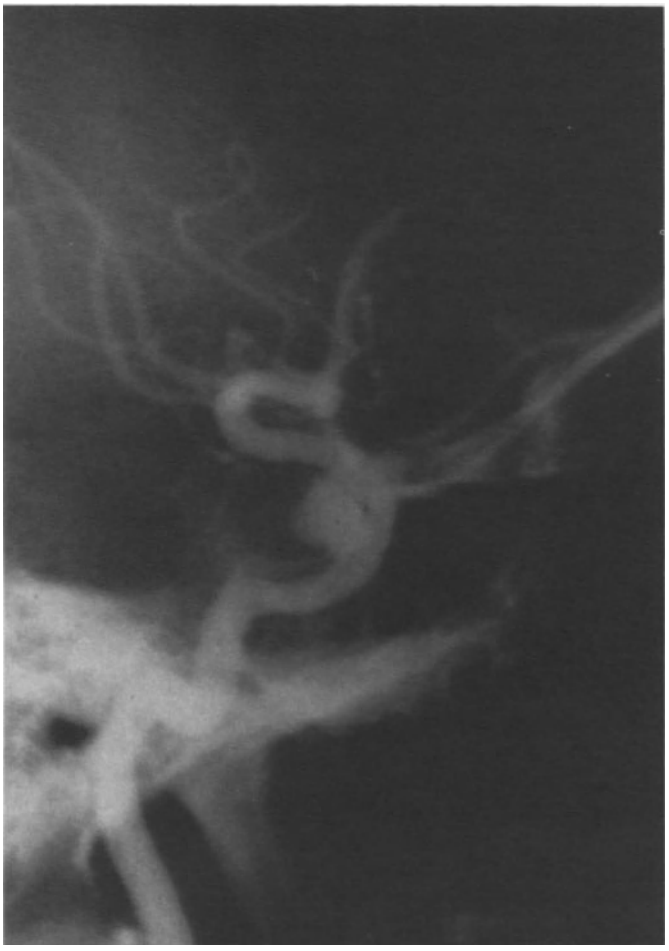
The 1980s saw an explosion of new techniques available for interventional neuroradiology. With the advent of soft latex balloons and more sophisticated endovascular techniques, the interventional radiologist is capable of introducing catheters to almost all regions of the cerebral circulation. A great deal of experience has been gained in the treatment of arteriovenous malformations (AVMs) of the brain, and this type of experience has been applied to the nonoperative treatment of intracranial aneurysms. Significant enthusiasm has been generated by the prospect of treating aneurysms endovascularly, thereby averting many of the potential disasters that accompany surgical treatment of intracranial aneurysms. This form of treatment may eventually serve as a useful adjunct to open surgical approaches.

The current enthusiasm for endovascular treatment of intracranial aneurysms must be tempered, however, by an understanding of the relative success that attends open surgical treatment of aneurysms of the brain. This chapter is meant to demonstrate the current capabilities of modern neurosurgeons and form a baseline that the interventional neuroradiologist can utilize to compare treatment. Intracranial aneurysms are categorized according to location and mode of presentation. For each subgroup the current surgical capabilities are discussed and the possible contribution of endovascular techniques reviewed.

Intracavernous Carotid Aneurysms

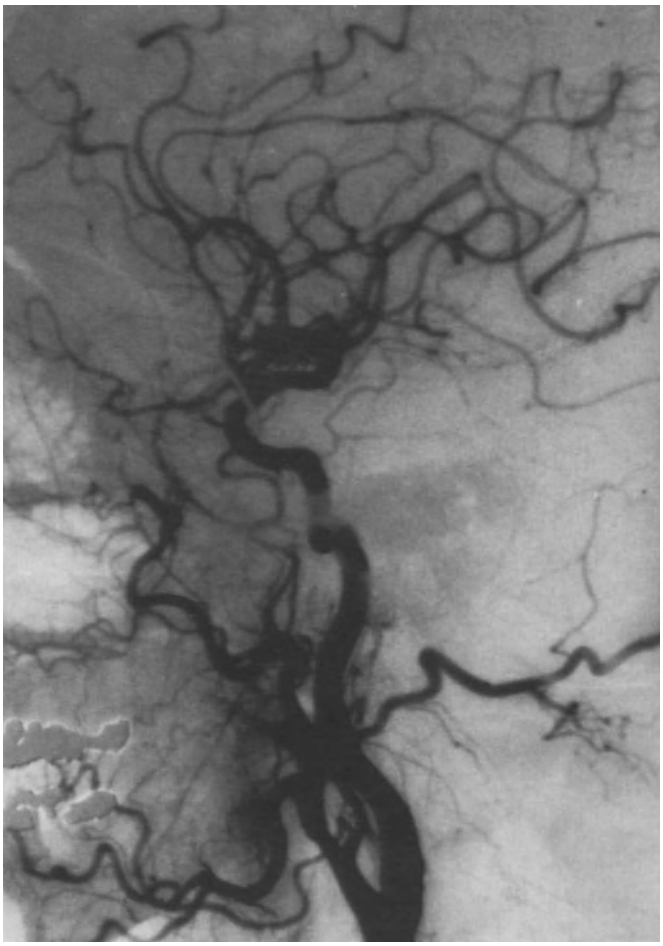
The cavernous sinus has long been considered a surgical "no man's land," and direct surgical treatment of intracavernous lesions has not been routinely performed. However, the last decade has seen a great expansion in surgical techniques aimed at treatment of intracavernous lesions. Most notable has been the work of Dr. Vinko Dolenc in developing surgical techniques for treating intracavernous vascular anomalies, especially arterial aneurysms. Previous attempts to open the cavernous sinus involved a lateral approach and an incision in the wall of the cavernous sinus. Such an approach resulted in the potential for direct injury to the cranial nerves in the wall of the sinus and a blind entry into the sinus without control of the major arteries.

The Dolenc approach, although technically more difficult, offers more controlled entry into the cavernous sinus and one less likely to injure the cranial nerves. With this epidural approach, the roof of the orbit is totally removed, working backward to remove the bone over the superior orbital fissure and optic foramen. Removal of this bone leaves the anterior clinoid process as a free fragment that can be gently disconnected from the petroclinoid ligament. Following this epidural exposure, the top of the cavernous sinus is visible and the optic nerve becomes free to be translocated in a



A

Figure 13.1. Patient with giant intracavernous aneurysm of the left carotid artery. (**A**) Preoperative angiogram showing largely thrombosed giant aneurysm within the cavernous sinus. (**B**) Postoperative angiogram (mirror image of **A**) showing complete obliteration of the aneurysm after clipping.



B

Figure 13.1 (*continued*)

medial direction. The sinus can then be opened from above, medial to the cranial nerves, and the carotid artery can be followed down into the sinus. The venous bleeding that accompanies the opening of the sinus can be controlled with Surgicel packing. In this fashion it is possible to gain distal control of the carotid artery and work proximally along the carotid artery until the neck of the aneurysm within the sinus is defined. We have found it advantageous to gain proximal control of the carotid artery in the cervical portion prior to craniotomy rather than relying on the drilling of the petrous bone as Dolenc reported. With proximal and distal control of the carotid artery and the approach into the sinus sparing the potentially (possibly)

vulnerable cranial nerves, intracavernous aneurysms can be effectively clipped. An example is presented in Figure 13.1.

Just because the surgical capability exists to operate on intracavernous aneurysms, all such aneurysms should not necessarily be treated by surgical clipping. In fact, there is increasing evidence that intracavernous aneurysms behave in a benign fashion clinically. Aneurysms totally within the cavernous sinus never produce life-threatening subarachnoid hemorrhage (SAH), and the most significant complications that these aneurysms produce upon rupture is carotid–cavernous fistula. More often, intracavernous aneurysms present with multiple cranial neuropathies and facial or orbital pain. Although these lesions can produce distressing symptoms, they are rarely fatal. Surgical techniques for clipping such aneurysms are technically challenging and realistically performed by only a few experienced surgeons. The interventional radiologist certainly has a role to play in the treatment of giant cavernous–carotid aneurysms. If flow into the aneurysm can be obliterated, the cranial neuropathies and the facial and orbital pain often resolve even though the mass of the aneurysm is not reduced. Moreover, the large intracavernous aneurysms often do not have a distinct neck as do many of the supraclinoid aneurysms, and manipulation of clips within the sinus is more difficult than manipulation of clips on the supraclinoid carotid aneurysms. Therefore aneurysms without any subarachnoid projection should probably be handled by intravascular techniques. However, aneurysms that are likely to project into the subarachnoid space because of a more distal location within the sinus or origin at the top of the cavernous sinus should be handled by the direct surgical approach. These aneurysms have the potential for rupture and SAH, and therefore direct clipping should be attempted.

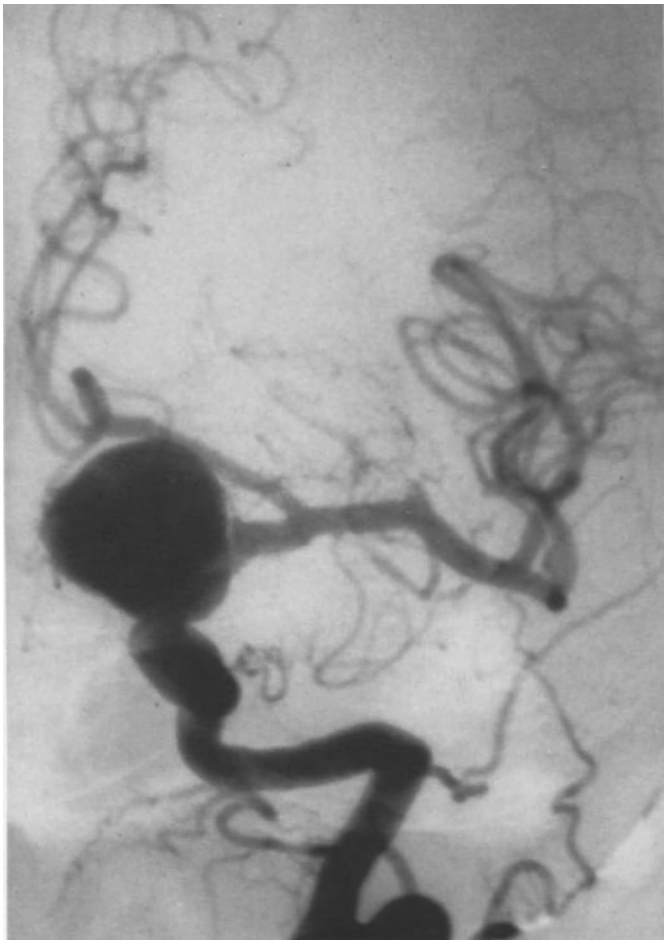
Giant Supraclinoid Carotid Aneurysms

Giant aneurysms of the supraclinoid carotid artery have been grouped under various subheadings including carotid ophthalmic aneurysms, ventral paraclinoid aneurysms, and more traditional posterior communicating aneurysms. These aneurysms often present with impingement on the optic apparatus, but the potential for intracranial hemorrhage must always be considered a risk with aneurysms in the subarachnoid space.

When treating giant aneurysms of the anterior circulation, the operating neurosurgeon has several techniques available to greatly increase the safety and effectiveness of the operation that are not available to the interventional neuroradiologist. The first principle of giant aneurysm surgery is to secure proximal and distal control of the carotid artery. In the case of middle cerebral aneurysms, proximal control of the M_1 segment and distal control of the M_2 segments must be achieved. Once this control is obtained, the safety factor for treating such aneurysms becomes high. We usually employ cortical electrodes to monitor the electroencephalogram (EEG) during operations on

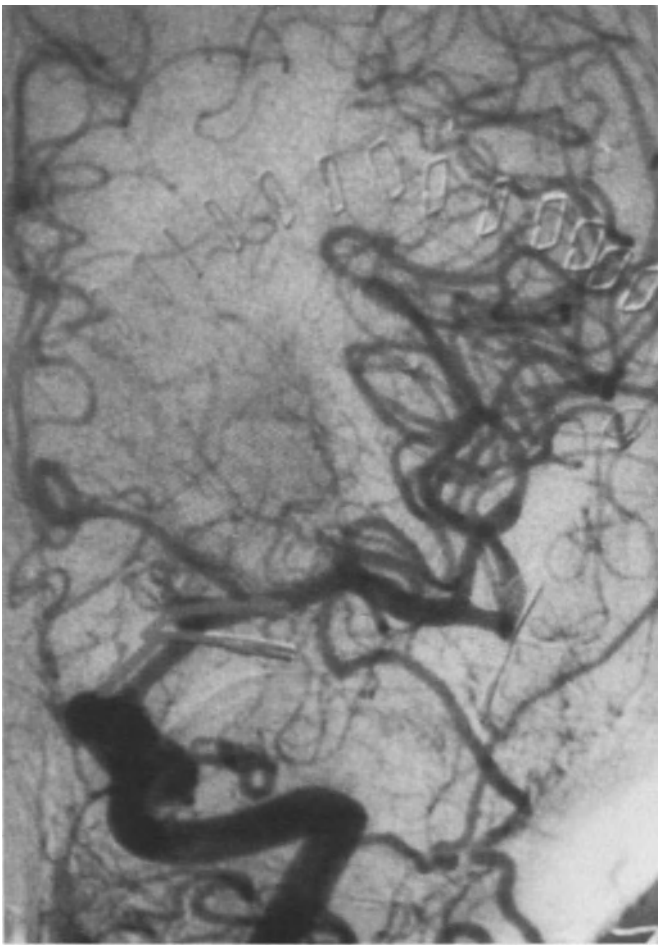
giant aneurysms. Therefore once the aneurysm has been dissected and proximal and distal control is obtained, the parent artery can be completely occluded in a temporary fashion. Monitoring the EEG during temporary occlusion indicates if the brain being occluded is becoming ischemic. If the EEG indicates ischemia, the temporary clips can be removed and more aggressive cerebral protection methods can be utilized.

In cases where there are EEG changes with temporary occlusion or when the M_1 has to be temporarily occluded, the patients are given a loading dose



A

Figure 13.2. An elderly woman with a giant carotid ophthalmic aneurysm presented with bilateral optic nerve compression. (**A**) Preoperative angiogram. (**B**) Postoperative angiogram showing a reconstituted carotid artery traveling through a clip fenestration.



B

Figure 13.2 (*continued*)

of pentobarbital to induce burst suppression on the EEG. Such a dose of barbiturates and the characteristic EEG pattern indicate that the brain has been moved into a hypometabolic state in which the tissue is relatively resistant to cerebral ischemia. Under these circumstances, prolonged temporary occlusion of the carotid artery or the middle cerebral artery can be carried out in many cases for periods up to 30 minutes. During the period of temporary occlusion, the aneurysm can be opened, its contents totally removed, and the sack collapsed. Once the sack is collapsed, the placement of clips to obliterate the aneurysm and restore a normal arterial lumen in the parent

artery can be safely carried out. In most instances, such a procedure requires 5 to 10 minutes of temporary occlusion but we have used periods of as long as 35 minutes without sequelae. In most instances, with proper collateral circulation demonstrated on the angiogram, temporary occlusion of the internal carotid artery can be safely carried out indefinitely during aneurysm procedures.

Once the aneurysm has been satisfactorily clipped, the temporary occlusion is reversed, and flow is restored in the parent vessel. Observation of the aneurysm and the parent artery can identify problems with kinking or possible occlusion of the artery due to improper clip placement. The clips can be adjusted simply in the operating room if problems are identified.

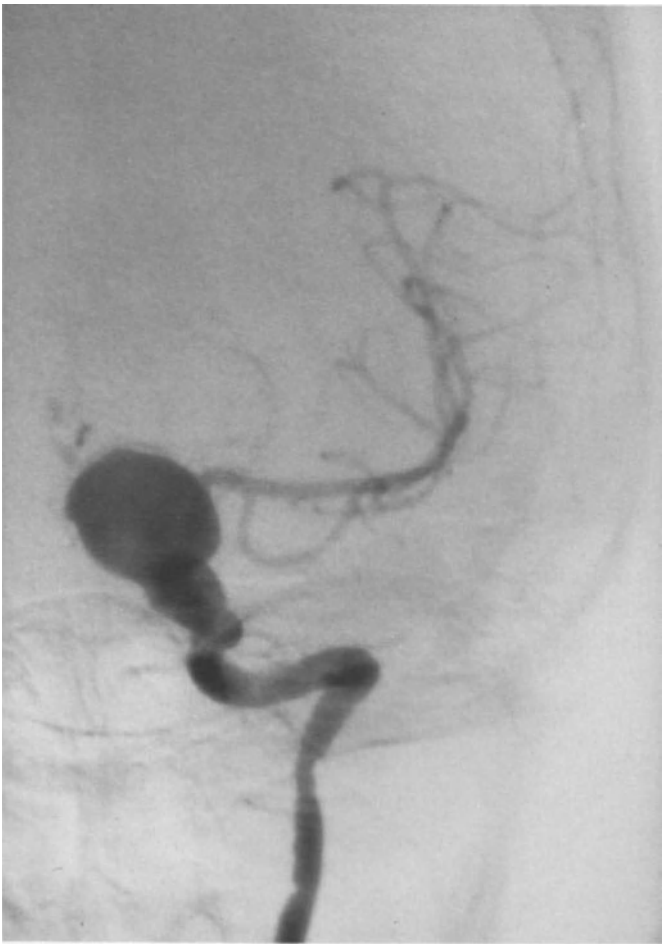
The operating neurosurgeon also has at his or her disposal a large number of highly sophisticated aneurysm clips that can be utilized to reconstruct vessels that have been significantly malformed by the presence of a giant aneurysm. Even aneurysms with broad necks that include part of the parent artery can be obliterated with reconstruction of a normal vessel lumen. Examples of giant anterior circulation aneurysms treated by these techniques are depicted in Figures 13.2 and 13.3. At the present time it does not seem that intravascular techniques offer the degree of safety and effectiveness that the neurosurgeon can offer for these cases.

Giant Basilar Aneurysms

Giant basilar aneurysms remain the one area of intracranial aneurysm surgery that has yet to be advanced to a satisfactory technical level. The morbidity and mortality associated with surgical treatment of giant basilar aneurysms run between 25% and 50% depending on the reporting surgeon. The technical problem with giant basilar aneurysm surgery is that the temporary clips cannot be utilized on the basilar artery in the same fashion that they can be utilized in the anterior circulation. The operative exposure of the basilar apex is confining, and multiple clips cannot be placed at the site of the aneurysm. It is difficult to visualize the contralateral P_2, much less to place a temporary clip there to gain adequate control of the top of the basilar apex. Moreover, the tiny perforating branches that come off the basilar apex cannot be occluded in a temporary fashion because these end-arteries are susceptible to even short periods of ischemia. Infarction of the brainstem can easily occur.

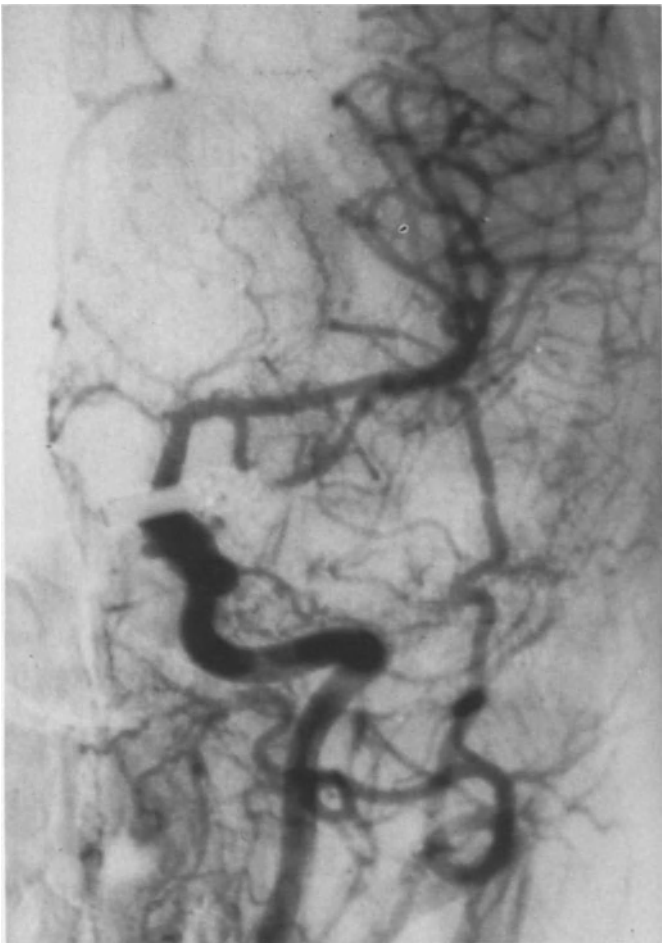
For these reasons, a number of surgeons have introduced the concept of deep hypothermia and complete circulatory arrest for the treatment of giant basilar apex aneurysms. With the advance of modern cardiac surgery techniques, placing the patient on the heart-lung bypass machine can be accomplished with relatively low risk. This technique can be performed either by femoral artery and vein cannulation or by the more traditional midline ster-

notomy. Once the patient has been cooled to 18°C and the heart has stopped beating, the pump can be safely turned off and the systemic blood pressure reduced to zero for up to 1 hour with almost complete safety in regard to brain recovery. Such a maneuver accomplishes the same goal that temporary clips achieve in the anterior circulation. However, with complete circulatory arrest, one does not have to worry about the viability of the brainstem supplied by the small perforating branches that come off the top of the basilar artery. Under complete circulatory arrest, the basilar aneurysm can be opened, its contents evacuated, and the proper clips applied. This technique continues to be somewhat experimental; an example is presented in Figure



A

Figure 13.3. Giant ophthalmic aneurysm in a young woman with visual field defect. (**A**) Preoperative angiogram. (**B**) Postoperative angiogram.



B

Figure 13.3 (*continued*)

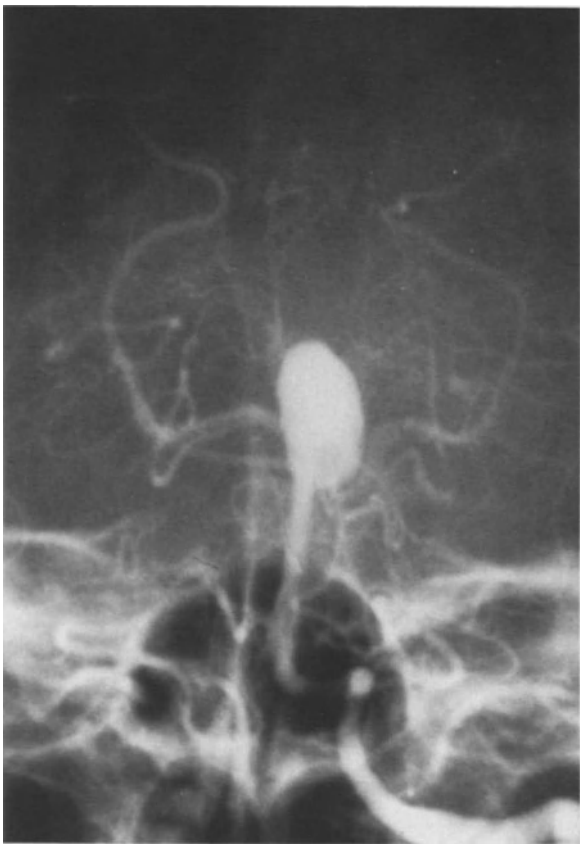
13.4. Excellent results have been obtained on a limited basis, but more experience certainly is needed before this technique is fully understood.

Routine Aneurysms Presenting with SAH

A number of studies have advocated the use of intravascular techniques for the treatment of recently ruptured intracranial aneurysms. However, we must always be aware that the present level of surgical sophistication allows operative clipping of small intracranial aneurysms with low surgical morbid-

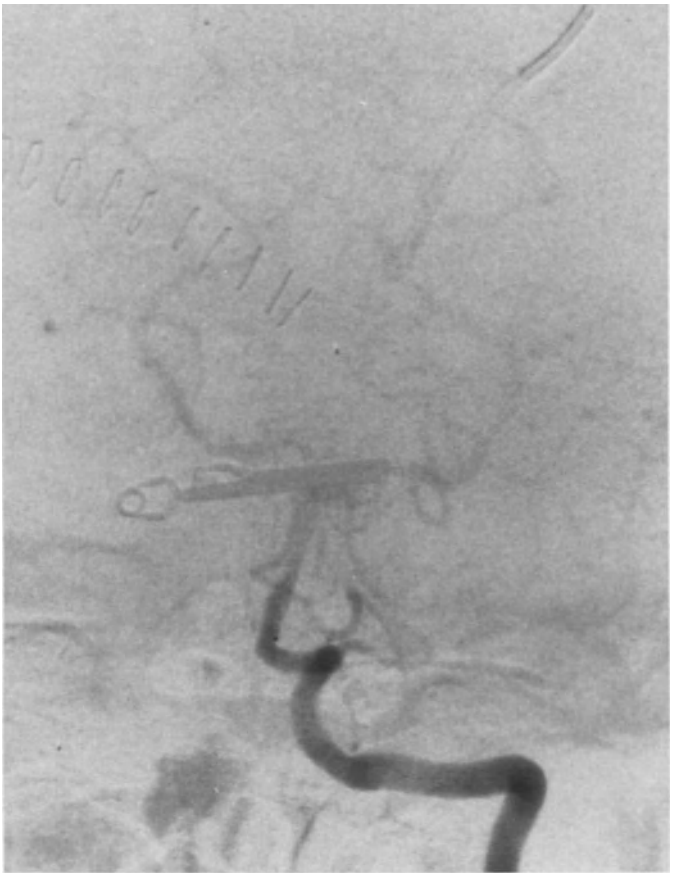
ity. Most of the complications that follow aneurysm surgery in the setting of SAH have to do with the complications of the hemorrhage, such as vasospasm and hydrocephalus, and are not related to the surgical technique.[1-3] In fact, intravascular techniques, even if they are successful, would be expected to have the same level of complications related to vasospasm and hydrocephalus. At surgery most of the subarachnoid blood, especially the local subarachnoid clot, can be evacuated, and postoperative complications may even be reduced. Over a 3-year period we treated more than 120 patients in the acute stages after ruptured aneurysm and an additional 70 patients in the delayed period after SAH. Another 71 patients with unruptured aneurysms were also treated during this time.

Of the group of patients who underwent operation within the first week of



A

Figure 13.4. Giant basilar aneurysm treated by deep hypothermic circulatory arrest. (**A**) Preoperative angiogram. (**B**) Postoperative angiogram demonstrates complete obliteration of the aneurysm.



B

Figure 13.4 (*continued*)

SAH, 100% had successful clipping of the aneurysm as confirmed by postoperative angiography. There was only one direct operative death related to a massive intraoperative rupture and five other deaths during the postoperative period related to the medical complications of the SAH. In total, 89% of the patients made a satisfactory recovery in that 77% of the patients were completely normal neurologically and an additional 12% had some mild impairment but lived an independent life; only 5% had significant impairment that required chronic care. Overall, 4% of the patients had a complication that could be ascribed to the surgical procedure. The 1% operative mortality rate and less than 5% morbidity rate are standard figures that can be achieved by the experienced aneurysm surgeon. In no case in this series did a patient with a documented clipped aneurysm seen by postoperative

angiography experience rebleeding during the 3-year follow-up of the study, and the incidence of this complication in the neurosurgical literature is rare. Most cases of delayed rebleeding after presumably successful aneurysm surgery have been patients without adequate documentation of clip placement at the time of surgery or those with known residual aneurysm.

It is still too soon in the evolution of intravascular techniques to know what the long-term success rate will be for aneurysms that have been angiographically obliterated by balloon placement. A number of cases have already been presented in which angiographically obliterated aneurysms have re-formed rather quickly and even re-hemorrhaged following what was considered perfectly satisfactory embolization and occlusion of the aneurysm. Such experience makes one leery about the safety and effectiveness of intravascular techniques for recently ruptured aneurysms, especially when the surgical treatment of these lesions has been advanced to a high level of sophistication, and successful clipping of the aneurysm is essentially 100% effective in preventing delayed rebleeding.

Discussion and Conclusions

Although the interventional neuroradiological techniques currently being developed and applied to the treatment of intracranial aneurysms form an exciting area, we must use caution when developing selection criteria for patients referred for this approach. Some neuroradiologists liken the present age of interventional techniques to the early days of aneurysm surgery, 30 years ago, when morbidity and mortality ran about 50%. In those days, however, even the poor operative statistics could be favorably compared to the outcomes of untreated intracranial aneurysms. In the present day, however, the surgical mortality for small anterior circulation aneurysms is about 1%, and the morbidity rate is about 5% or less in highly experienced hands. Interventional neuroradiologists must compare their results to the modern surgical statistics and not to the natural history of aneurysmal SAH. Most of the complications that presently occur in patients with ruptured aneurysms are not attributable to surgery but, instead, to the complications of the SAH, and these complications can be expected to be the same for the postoperative patient and the patient after successful embolization treatment of recently ruptured aneurysms. Therefore in most cases of recently ruptured aneurysms, giant anterior circulation aneurysms, and small basilar aneurysms, the surgical techniques are so well developed that there is no need to refer patients at the present time for an interventional neuroradiological technique as a primary procedure.

In some cases when aneurysms are explored, they are found to be unclippable usually because of heavily calcified arterial walls that extend into the neck of the aneurysm. There is no satisfactory way to clip this type of

aneurysm. In some instances, especially with giant basilar aneurysms, the neck or wall of the aneurysm is densely adherent to the brainstem, and mobilization of the aneurysm in a fashion that would allow placement of the clip is hazardous. In these settings interventional neuroradiological techniques seem to be an excellent adjunctive procedure for the operating neurosurgeon, and it is these cases that should be referred to the interventional neuroradiologist. Patient selection should be performed in conjunction with a qualified aneurysm surgeon, and in most cases the referral should be made following an initial exploration of the aneurysm and attempted clipping.

The intracavernous aneurysm is one on which interventional neuroradioly may have a significant impact. These aneurysms are technically demanding lesions, and their natural history is unknown. It seems that, as catheter and balloon techniques advance, the intracavernous aneurysm is ideally suited to be treated by an intravascular technique.

Giant basilar aneurysms continue to be a difficult problem for neurosurgeons. Older patients or patients in whom there are contraindications for undergoing the deep hypothermic circulatory arrest described earlier would certainly be candidates for interventional neuroradiological approaches. However, the young and otherwise healthy individuals, even with giant basilar aneurysms, should undergo exploration of the aneurysm prior to referral for interventional techniques. With the knowledge that a backup procedure is available if the surgeon deems the aneurysm unclippable, the likelihood of performing a dangerous maneuver with the potential for mortality is minimized.

The interventional neuroradiologist may also be of help in treating patients who are elderly with recent SAH, as these patients can be expected to have high anesthesia-related morbidity rates and may do better treated by intravascular techniques. Moreover, some patients with severe cardiac problems and medical instability who are not candidates for general anesthesia and major surgical procedures may also be handled expeditiously by the intravascular neuroradiologist. The short procedure and possibility of performing the procedure under local anesthesia are significant advantages in the elderly and in medically unstable patients.

In conclusion, the interventional neuroradiologist and an experienced aneurysm surgeon must work together in the development of criteria for intravascular embolization of intracranial aneurysms. Unfortunately, because the surgical techniques are so well developed at the present time, the neuroradiologist must gain experience by treating intracranial aneurysms that are thought to be too dangerous or unclippable by a competent neurological surgeon. As the neuroradiologist gains more experience and the surgeon feels more comfortable in evaluating the effectiveness of the radiological procedure, aneurysms of decreasing complexity can be referred to the interventional neuroradiologist. With this type of controlled evolution, the indications for use of endovascular techniques for intracranial aneurysms will become delineated.

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Discussion

Dr. Solomon: from the surgical standpoint it is rarely reported that patients with an angiographically proved clipped aneurysm have recurrence of that aneurysm or repeated SAH at that site. I am not referring to residual masses seen on scanning or angiography.

The problem with balloons when they are placed in the aneurysm sac is that thrombosis may ensue and there may be a nice angiographic appearance, but the defect is still present. We have seen aneurysms that have grown in other directions, from the neck or expanded upward. It remains a problem, and we still do not know the long-term success rate with interventional techniques.

Dr. Berenstein: We have evidence of re-formation of the endothelial lining. Dr. Hilal puts prongs in to stimulate endothelial proliferation.

Dr. Solomon: There are cases where the control angiograms have looked fine, and the patients reappear with recurrent aneurysms.

Dr. Debrun: After surgery? With complete aneurysmal occlusion? Are you performing an angiogram at 6-months and 2 years?

Dr. Solomon: There has never been a group of cases reported of recurrent SAH in patients with angiographically proved clipped aneurysms. Where are those patients if that is happening all the time?

Dr. Fox: There are a small number of cases reported in that category, and I know about them because they are part of the bibliography of the paper we recently published. Our own series, which we called "regrowth from neck remnants" includes some cases that were angiographically interpreted as showing complete aneurysmal obliteration. It was a retrospective study; and with our review and the accumulation of knowledge over the years, we understand the pitfalls of that interpretation. I think we have discussed the immediate postoperative angiograms of AVMs suggesting complete obliteration when it is not there. There is a similarity in the interpretation of postoperative aneurysm angiograms, because the clip can superimpose itself, depending on the direction of the x-ray beam, on a tiny neck remnant. In some of our cases we have inferred the presence of a neck remnant (for example, on a basilar tip aneurysm) by the lateral view. So I would suspect that your series of complete obliteration by clipping with angiographic documentation will include some of the same pitfalls we have encountered.

Dr. Solomon: I am not inferring that there is no potential for aneurysmal regrowth in situations where a residual neck is present. I admit that completely. I think we must carefully look at the quality of the angiograms, and we are going to have to follow the patients long term.

Dr. Berenstein: There is no question in anyone's mind that neurosurgery for berry aneurysms in properly handled cases is an excellent technique. We interventional radiologists will eventually prove that our methods are as good and hopefully better. There is no question that well thought out procedures will prevail. I do think that it is a duty of all of us to examine the socioeconomic aspects of what we do. I am not proposing here today that we should treat all aneurysms with balloons; that would be inappropriate. At the same time I think that it is inappropriate to say that because neurosurgical techniques have reached a particular point all patients are properly assessed. For example, did you have neuropsychological testing on all your patients? In particular, patients with anterior communicating artery aneurysms? Among those

patients, do you know to what extent their function, speech, and affect are altered from their premorbid and preoperative states? Did those patients return to a normal life?

Dr. Solomon: Seven patients who are neurologically normal did not return to their premorbid occupations presumably due to some neuropsychological disturbance that was not apparent on neurological examination. That has been well documented in the literature, and I do not doubt it. I also do not believe that surgery contributes to the development of those defects. I think that they develop because of the SAH and the location of the aneurysm. It is not necessarily related to the procedure.

I do think there is a role for interventional techniques in the treatment of aneurysms. At present, however, although in my institution we are treating 100 aneurysms a year and have a considerable experience with them, I do not think that interventional techniques should be the primary mode of therapy.

I think what Dr. Heishima is doing now is the model approach. The cases should be carefully reviewed by an experienced aneurysm surgeon. If on review of the neuroradiological studies the surgeon believes that the case is going to be too difficult for surgery, the patient should be referred for interventional endovascular therapy. If the surgeon explores the patient and decides not to correct the lesion because it is too difficult, that patient should also be referred to the interventional neuroradiologist.

Another point concerns intracavernous aneurysms. Despite the elegant surgical techniques available, aneurysms that are totally within the sinus are probably better handled by interventional techniques, although in some selected cases direct surgical approaches can be effective.

The last category concerns the elderly or medically unstable patient with an SAH who is at risk of dying from general anesthesia. Those patients deserve a trial with interventional techniques. At this point the onus is on the neuroradiologist, and in other countries they have the opportunity to see these patients primarily. Perhaps we will see from their results over time that the endovascular techniques are superior to what we are doing surgically.

Dr. Apuzzo: We surgeons are outnumbered here. Let me present my thoughts. First, there is a movement toward less invasive techniques when dealing with the brain. This is true for tumors as well as vascular disorders. We can thank neuroimaging for this change. I believe that anybody who does not recognize this fact and tries to stop it or slow it down is not seeing what the future of neurosurgery is and what the treatment of the entire spectrum of disorders of the brain will be in the next 25 to 50 years. This being my basic premise, I believe it is incumbent that we all work toward minimizing the invasive techniques and view the problems we must face.

The problem in regard to endovascular surgery is what to do and at what pace. What Dr. Solomon has done in an eloquent fashion is to outline what a gifted neurosurgeon can do in a major center. He represents a guiding force. Certainly many neurosurgeons at major centers can do the kind of surgery proposed by Dr. Solomon, but many neurosurgeons and probably most neurosurgeons cannot.

What we need to discuss is the state of the art and what constitutes the optimum situation. At my institution I believe that the most difficult lesions that surgeons cannot handle are initially dealt with by the interventional neuroradiologists. Once they demonstrate their abilities and the morbidity of their procedures reach an acceptable level, I believe the patients should be turned over to the endovascular surgeons even for standard cases so we can approach the issue from the endovascular side.

Dr. Viñuela: Your message represents an optimistic view for neuroradiologists. The cases you have shown are the difficult ones, so you should not have any trouble with the easy ones. You are telling me what I want to know: I am well trained because I do the tricky ones. It took us ten years to develop a reputation for embolizing AVMs because the neurosurgeons gave us the opportunity to deal with the difficult ones. Because we have had this experience with cases that have a high morbidity and mortality in the hands of neurosurgeons, we have proved that we are not harming these patients. It seems logical from the neurosurgical viewpoint that we should do only those cases with high risk of morbidity and mortality, but I see that as the neurosurgical community defending itself. It ultimately will not happen that way. Mother Nature, in stating the reality, will speak for herself, and we will do these cases sooner or later.

The point remains that when a neurosurgeon believes there is high morbidity with a given case (perhaps 35%) I may be approached to do a procedure. My answer is "fine," but I know that I too have a 50/50 chance with this case. I may do better or I may do worse, but what does that ultimately prove? Nothing. Thirty years ago the powers that be ever saying why not start with these cases and because there is 35% mortality you should not do the easy ones.

Dr. Solomon: The death rate from a ruptured intracranial aneurysm at that time was 80% if nothing was done, and the operative mortality was 30%. It was worth trying under those circumstances. At the present time the operative mortality for aneurysms is 1% to 2%.

Dr. Berenstein: not all of what Dr. Viñuela has espoused is correct. We should not be in direct competition with neurosurgery where there is a body of experience of 50 years. We are comparing our results, so let us be fair. It is also not correct to say that operative aneurysmal mortality is 1% for all aneurysms. Dr. Solomon, what is your operative mortality and morbidity for the basilar tip aneurysm? I expect it is not 1%.

Dr. Solomon: No, those statistics do not apply for the basilar tip aneurysm; they apply for the giant ophthalmic aneurysms. The basilar aneurysms are a different problem and have a morbidity and mortality of about 25%.

Dr. Berenstein: Dr. Flamm said it may be as high as 40% to 50% among his more than 100 cases, and Dr. Drake indicated that it is under 30%.

Dr. Fox: What you are doing is selecting Dr. Drake's statistics and interpreting them to your advantage. His statistics are for basilar tip aneurysms less than 12 mm in diameter and when the patients are grade I or grade II; then there is 0% mortality and 3% morbidity. Any of us can select statistics and use them to a particular advantage.

Dr. Berenstein: What I am saying is that aneurysm surgery complications are not simply 1%. Perhaps you should let us try the basilar aneurysms first. If we fail, then proceed with surgical intervention. I do agree that interventional procedures, at least in our society, should not start with small berry aneurysms. I will tell you that in the Soviet Union they are treating those, however. In the Neurosurgical Institute of Kiev, where Dr. Scheglov works, they constitute a large percentage of the cases. Acute aneurysms represent a different class, and I do not have an absolute answer as to how they should be treated. I believe that if we are able to handle the giant aneurysms we will later be in a position to deal with the others. There is no rush.

Dr. Fox: There are numerous dilemmas here, and many of us are beginning to understand them. I work with neurosurgeons who are innovative, skillful, and courageous. Some of the giant aneurysms are better treated using their surgical techniques

than by interventional methods. The cases we publish include proximal occlusions of unclippable aneurysms, which represent only a select group of the unclippable ones. Occlusion of the artery does not require a high level of technology; rather, it is a simple, safe procedure and has become established at our institution.

However, with such thorough and aggressive neurosurgeons taking the attitude that Dr. Apuzzo has given us concerning preservation of the parent artery, we are now getting involved with the higher risk cases, which invite the experience of one disaster after another. I believe from seeing the work of Drs. Moret and Scheglov that the aneurysms most amenable to interventional neuroradiological techniques are also the ones that are easiest for the surgeons to clip. Therein lies the dilemma.

Dr. Apuzzo: When I have encountered neurosurgeons at meetings and asked about the results of aneurysm management, they always answer that the results are good. It seems that everyone's results are good.

Dr. Fox: There are problems and adverse outcomes at all institutions, including ours.

Dr. Apuzzo: We never hear about them.

Dr. Fox: Dr. Scheglov's series is presented elsewhere [in this book—Chapter 14]. Though his statistics may not be comparable to the surgical statistics, they are being achieved under adverse conditions. Patient care and materials are not equivalent to those to which we are accustomed; yet he is achieving a remarkable degree of success. Most of the aneurysms he has treated are "cold," but that does not detract in the slightest from his remarkable work. The problem we have now is how to translate that experience to North America where aneurysms are being treated during the first 2 to 3 days under much better conditions. If he were working under our conditions, his results might be even more miraculous.

Dr. Pile-Spellman: What Dr. Fox has said about Dr. Scheglov's work answers several questions: (1) Interventional neuroradiology is technically possible. (2) It works. (3) It can be performed successfully even under adverse conditions. Having been at Dr. Scheglov's clinic for 2 months making rounds and taking care of patients has made me acutely aware of the value of an ICU, a Swan-Ganz catheter, and the availability of anesthesia—factors we take for granted.

Dr. DeBrun: It is difficult to compare our results with surgical outcomes because the surgical result depends so heavily on the institution in which the patients are being treated. The 1% mortality described by Dr. Solomon for three categories of aneurysm would perhaps be 5% or 10% in other hands.

Dr. Berenstein: The same could be said for interventional neuroradiology.

Dr. Debrun: If we want to compete, we should compare good results from both methods, not good results with worst outcomes. All of us must be prepared to have one death among 100 patients. Those of us at this gathering have had one or two deaths. Under these circumstances it is difficult to compete with the neurosurgeons. To emphasize this point I would like to describe two cases in which there were complications. It seems important at this point to bring them to light.

Dr. Solomon: I do not want to be misunderstood that my mortality rate is 1% for all categories of aneurysms. Unruptured aneurysms of the carotid artery carry a 1% mortality rate.

Dr. Debrun: Those cases are ideal for you and ideal for us, and I wish to speak of the aneurysms that have a 1% surgical mortality risk. The way to address this issue is to do what Dr. Moret does when he works with neurosurgeons who tell him to try balloon occlusion first. When he eventually demonstrates 200 or 300 cases with less

than a 1% mortality and a 5-year follow-up showing no regrowth of the aneurysm we will know that the embolization technique is better. We should say now that we have not reached that point with any technique available to us in the world.

My example is a patient sent to me with an aneurysm considered not be clippable, or at least difficult to clip. It was above the ophthalmic artery. I am sure that in Dr. Solomon's hands there world be 1% mortality and a few percent morbidity. We can all agree with that. However, the patient was sent to me for balloon embolization. I told the patient that I could do it—that it was perfectly suitable for that procedure and that we should be able to cure the aneurysm with a low risk of morbidity and mortality. The neurosurgeon discussed the case with the patient and said, no, I think this aneurysm is amenable to surgical clipping and I can do it, but if you want to have an embolization let us go ahead with the balloon technique.

I used a balloon (No. 9) that can usually be inflated with 1 ml of liquid. I inflated this balloon with 0.4 ml of 100% HEMA and had an angiographic result that showed complete obliteration of the aneurysmal sac. The patient was packing her suitcase, leaving the hospital with her relatives, when she experienced a sudden headache, subarachniod hemorrhage, and died.

Dr. Moret: What do you conclude from that case?

Dr. Debrun: The conclusion is that an aneurysm, apparently treated perfectly well with our technique, can still burst. I believe it would not have burst 2 days after an adequate surgical clipping.

Dr. Moret: Why did the aneurysm burst? Are you sure of the mixture you put inside? How was the HEMA? Was it solidified? Were you using a double-lumen catheter?

Dr. Debrun: I was using your double-lumen catheter and 100% HEMA. The balloon was still inflated on CT scan. When the patient had the complication, we repeated the CT scan and the balloon still had homogeneous contrast of HEMA within the balloon inside the aneurysm. The balloon had not moved.

Dr. Holtzman: I would like to raise the point that, on direct visualization of an aneurysm, we surgeons have noticed the presence of multiple microaneurysms that cannot be seen angiographically. Dr. Yasargil mentioned this point to me at this conference many years ago. They are tiny "blisters" that may come off the parent vessel remote from the aneurysmal sac and are delicate. It could well be that your aneurysm was perfectly treated and that the recurrent SAH had nothing to do with the balloon occlusion. It is not impossible to imagine that one of these tiny aneurysms may have ruptured. It might have been seen at surgery and could have been cauterized back into the the blood vessel wall. Dr. Yasargil also recommended that treatment. He said that it strengthened the vessel wall and prevented rerupture. I am not certain what the answer is in this type of situation, but there seems to be no alternative.

Dr. Debrun: It is not only the dome of the aneurysm that may rupture, but the neck sometimes as well. I went to the operating room recently to see a supraophthalmic aneurysm. The surgeon showed me the thin neck. He could not put a clip on it for fear that it might rupture and could only coat the aneurysm. If I had tried to do this case with a balloon it is debatable whether it would have burst.

Dr. Holtzman: Do you have an autopsy for this case?

Dr. Debrun: No, unfortunately not, and the patient did die.

Dr. Berenstein: That is a good point—that a good picture means nothing.

Dr. Debrun: The second case was a basilar tip aneurysm, small but perfectly clippable from the surgical standpoint with, I am sure, 1% mortality and a small

percentage morbidity. According to what Dr. Fox has told us, this type of basilar tip aneurysm in Dr. Drake's hands today carries 1% mortality and a few percent morbidity.

Dr. Fox: Zero percent mortality was recorded in his series of the past 5 years.

Dr. Debrun: Dr. Solomon, in your hands what would the mortality be?

Dr. Solomon: I would say that realistically the patient has a 5% risk of death or major stroke.

Dr. Debrun: This second patient was referred to me by a surgeon who told me that it seemed to be an ideal case for balloon embolization. I treated the aneurysm using a balloon, your catheter, and 100% HEMA.

Dr. Berenstein: ITC HEMA?

Dr. Debrun: Yes, ITC HEMA. The angiographic result after 8 days revealed an apparently beautiful result, and the patient was asmptomatic. The patient went home, returned in 3 months, and a repeat angiogram showed regrowth. The clip was on the right side of the aneurysm. The balloon had moved, and the aneurysm had reappeared. The patient was asymptomatic but not cured. So regrowth can occur despite a good angiographic result in an asymptomatic patient. We also know that we can burst an aneurysm with the balloon. We must be careful to do as well as the neurosurgeons with a 1% or 2% mortality and not higher. If you know then that complications of rupture and regrowth of aneurysms can occur, our techniques cannot compete with surgical results.

Dr. Hilal: What do you to do with such a case? Refer it to a surgeon? Can the surgeon clip the aneurysm with HEMA in it?

Dr. Debrun: We have the option of either attempting balloon occlusion again or trying surgical clipping. The patient has not decided which route she wishes to pursue.

Dr. Berenstein: What would you recommend?

Dr. Debrun: Surgical clipping. I have been given the chance to achieve a cure, and I did not succeed. I prefer the patient to have surgical clipping.

Dr. Fox: When we see such a picture of a balloon and the aneurysm and then the postoperative angiogram—and agree that it shows complete obliteration—I believe we should review those films on the outside chance that there could be a neck remnant that is hidden because of the subtraction artifact of the dense balloon. That is one possibility. It also may be impossible for us to see it because it occurs in aneurysms that have some clot within the sac. In such cases if there is a clot in the aneurysm plus the balloon, the balloon in the proximal portion of the neck is receiving the pulsating force of the blood that is going alongside it and could be pushing it into the clot.

Dr. Taveras: That is the reason why during the acute stage in a "hot" aneurysm that has recently bled, I have wondered whether the balloon treatment would ever be the best. There is partial clotting in the sac and then the balloon is going to move into the clot.

Dr. Berenstein: The question is, are balloons the answer? Balloons are what we have at the present time. Trying to replace the aneurysmal sac entirely with a balloon is probably not the answer.

Dr. Solomon: This discussion brings up another point: the giant aneurysm, such as the giant ophthalmic aneurysm, which usually presents with optic nerve compression rather than rupture. Surgical management with clipping and aneurysmal excision results in decompression of the optic system. Often afterward there is recovery of visual acuity. I wonder if the same would be true with balloon occlusion.

Dr. Viñuela: It is difficult for the vascular community to prove or disprove what you say. It would be extremely difficult to have a randomized prospective study in North America. It would require the full approval of the American Association of Neurological Surgeons. And what would you prove even if that opportunity were to exist: that there could be complications? For many years to come we are going to have the same meetings and the same discussions despite Drs. Moret and Scheglov finding their own way. Someone will always say "Dr. Drake" tried this or that and what will that prove? Zero.

CHAPTER 14

Endosaccular Detachable Balloon Catheter Treatment of Cerebral Saccular Aneurysms*

Victor I. Scheglov

Endovascular technology is rapidly developing and undergoing refinement. The experience of 725 endovascular procedures on saccular aneurysms during the past 14 years at the Neurosurgical Institute of Kiev has shown that the operation is relatively simple and the associated trauma is minimal. Yet the system of occlusion is both complex and demanding, requiring the determination of appropriate balloon shapes for given aneurysms, the "training" of each balloon such that its entry into the aneurysm is facilitated, and the use of one or two additional balloons concomitantly to artificially generate turbulent flow and permit balloon entry into the aneurysm. Strict monitoring of the patient is mandatory during and following each procedure.

Operations are categorized as "reconstructive procedures" during which the aneurysms were occluded and the parent vessels preserved (561 cases, or 91%); and "deconstructive procedures" in which the parent vessel at the level of the aneurysms was occluded along with the aneurysm (56 cases, or 9%).

Most of our operations were performed on ruptured aneurysms in the subacute phase. We have operated on 17 patients with acute aneurysmal rupture and we are continuing this [operative pace] at the rate of two patients per week without mortality. Acute-phase occlusions require special preparations, including specially designed balloons, soaking the latex in thrombin and oil, occluding the aneurysm cavity without dangerously increasing intraluminal pressure, and leaving the catheter in place for at least 24 hours. Following verified occlusion of the aneurysm in the acute phase we have no hesitation to use induced hypertension to overcome the effects of vasospasm or anticoagulation to mitigate against symptoms thought to result from embolic or thrombotic events.

All aneurysms at the Neurosurgical Institute of Kiev are managed by the

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endovascular technique regardless of location. Giant aneurysms (>5 cm) are usually managed with a combined approach of endovascular occlusion utilizing two or three balloons and direct surgical intervention. aneurysms smaller than 0.5 cm are not treated by endovascular methods.

Our results based on the total 617 patients indicate that there was a good outcome in 467, or 80%, and a fair outcome in 117, or 20%; 33 patients died after the operation, representing a mortality of 5.4%. Of those deaths, 9 occurred following operations on 519 patients in fair condition for a rate of 1.7%, and 24, or 24.5%, occurred after operations on 98 patients in poor condition. Four patients died 6 months to 4 years later of unrelated illnesses. Tables 14.1 through 14.8 serve to illuminate the data accumulated during our experience and are based on the total 617 patients.

Table 14.1. Aneurysm location and type of operation

Site of aneurysm	Total cases	Reconstructive operations	Deconstructive operations
Internal carotid	301	266	35
cavernous	52	43	9
ophthalmic	49	42	7
posterior commun.	172	153	19
bifurcation	28	28	—
Anterior communicating artery	207	195	12
Middle Cerebral artery	64	61	3
M_1	5	5	—
M_2 and M_3	59	56	3
Vertebrobasilar artery	17	15	2
Multiple aneurysms	28	24	4
Total	617	561 (91%)	56 (9%)

Table 14.2. Aneurysms that could also be treated by direct surgical methods with comparable results

Parameter	No.
Total	409
Reconstructive operations	376
Deconstructive operation	33
Died after operation	22
Operated in fair condition ($n = 338$)	6 (1.7%)
Operated in poor condition ($n = 71$)	16 (22.0%)

Table 14.3. Giant aneurysms

Parameter	No.
Total	69 (11% of the series)
Reconstructive operations	54
Deconstructive operation	15
Died after operation	6
Aneurysm diameter 2.5 cm	60 (1 died)
Aneurysm diameter 5.0 cm	9 (5 died)

Table 14.4. Ophthalmic and intracavernous aneurysms

Parameter	No.
Ophthalmic artery	49
Reconstructive operations	42
Deconstructive operations	7
Died after operation	2
Intracavernous artery	52
Reconstructive operations	43
Deconstructive operations	9
Died after operation	2

Table 14.5. Vertebrobasilar aneurysms

Parameter	No.
Total	17
Reconstructive operation	15
Deconstructive operation	2
Died after operation	1
Complications	2

Table 14.6. Multiple aneurysms

Parameter	No.
Total	28
Reconstructive operation	24
Deconstructive operation	4
Died after operation	4
In fair condition ($n = 20$)	1
In poor condition ($n = 8$)	3

25 Patients had 2 aneurysms, and 1 patient each had 3, 4, and 5 aneurysms, respectively

Table 14.7. Small aneurysms (< 0.5 cm)

Parameter	No.
Total	17
Reconstructive operation	5
Deconstructive operation	12
Died after operation	0

Table 14.8. False traumatic and carotid–cavernous aneurysms

Parameter	No.
Total	15
Reconstructive operation	14
Deconstructive operation	1
Died after operation	0
Characteristic features: profuse nasal bleeding	

Discussion

Interventional Neuroradiology in Kiev

Dr. Scheglov: My discussion here is a continuation of the outstanding work of Dr. Heishima. He has shown American neuroradiologists that they can eliminate aneurysms from the cerebral circulation, a task that heretofore was exclusively performed by neurosurgeons. We all understand that if we neuroradiologists can interrupt the flow to a difficult aneurysm it will thereafter be simpler to occlude a simple aneurysm. There are great results with microsurgery, and the results of experienced microneurosurgeons are more or less standardized. However, there is no single ideal method, and we cannot say that all operations are ideal. For example, I have had several cases of saccular aneurysms that were operated on by other neurosurgeons. These patients came to my clinic; and after angiography demonstrated filling of their aneurysms, they were retreated by endovascular methods.

It seems to me that it is impossible to compare these two methods. Endovascular techniques are wonderful and represent a development of the twentieth century. They are not yet standardized. With a simple balloon catheter that is now available everywhere it is possible to solve serious problems. To improve the results it is better to "do" than to discuss. If you want to be a great swimmer, you should swim. If you want to be a great runner you should run.

My situation in the Kiev Neurosurgical Institute is luckier than that of my colleagues here. The endovascular operation was the first procedure used to occlude

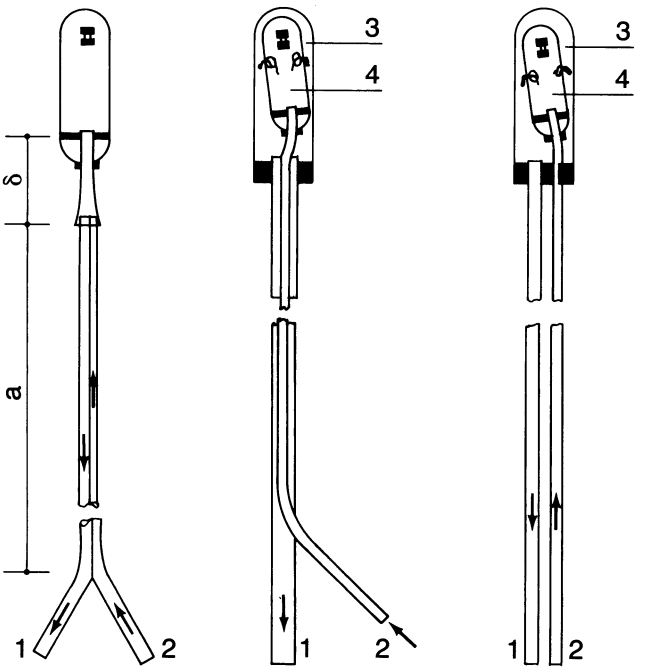


Figure 14.1. Types of balloon catheter used at the Kiev Institute of Neurosurgery.

aneurysms. Our experience with 725 operations has shown that this procedure is relatively simple and the operational trauma minimal. The idea behind the operation is not simply injection of the balloon and occlusion of the aneurysm. It is a whole system of occlusion. It includes special preparation of the balloon, determination of the data for the operation, and following the patient closely during and after the operation. Overall, we have had a small experience, of course, and everyone at our institute is interested in the quality of the operations. The standards that must be maintained include the following: (1) no harm is done to the patient; (2) the procedure should be highly effective; and (3) there should be no residue or hemorrhages. It is necessary to fulfill these criteria without complications or at least with minimal complications.

Two people have changed my fate. The first is Professor Juan Taveras, although he

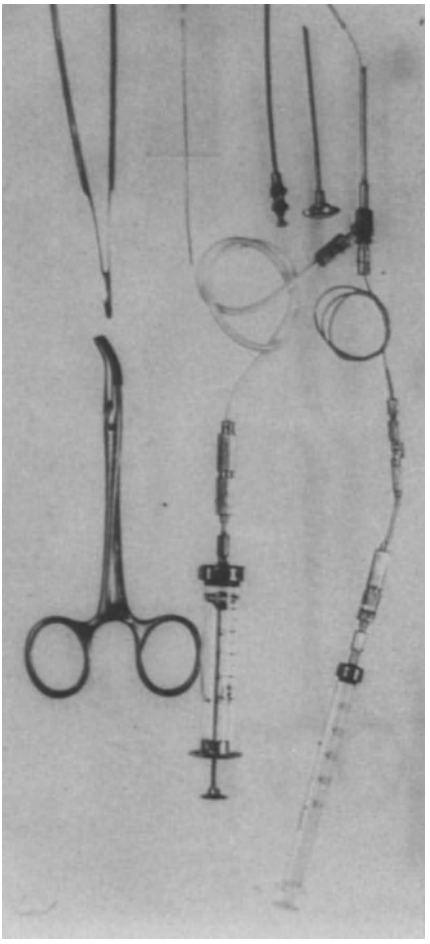


Figure 14.2. General equipment used for the endovascular procedures.

does not know it. The other is Professor Romodanov; he has done it on purpose so he knew about it.

It is valuable to present some examples of the balloons we employ (Fig. 14.1) and the equipment required for performing the procedure (Fig. 14.2). The first case I want to report (Fig. 14.3) is a saccular aneurysm of the supraclinoid carotid before and 1 year after operation. The aneurysm is occluded and the parent vessel is preserved. The second example is that of an anterior communicating artery aneurysm that could be clipped with success by a surgeon. With the help of a balloon it is possible to occlude it in 15 to 20 minutes with the same degree of success and to preserve the anterior communicating artery and the small branches (Fig. 14.4). If we wish to compare this result with a direct surgical approach, imagine how difficult it is for

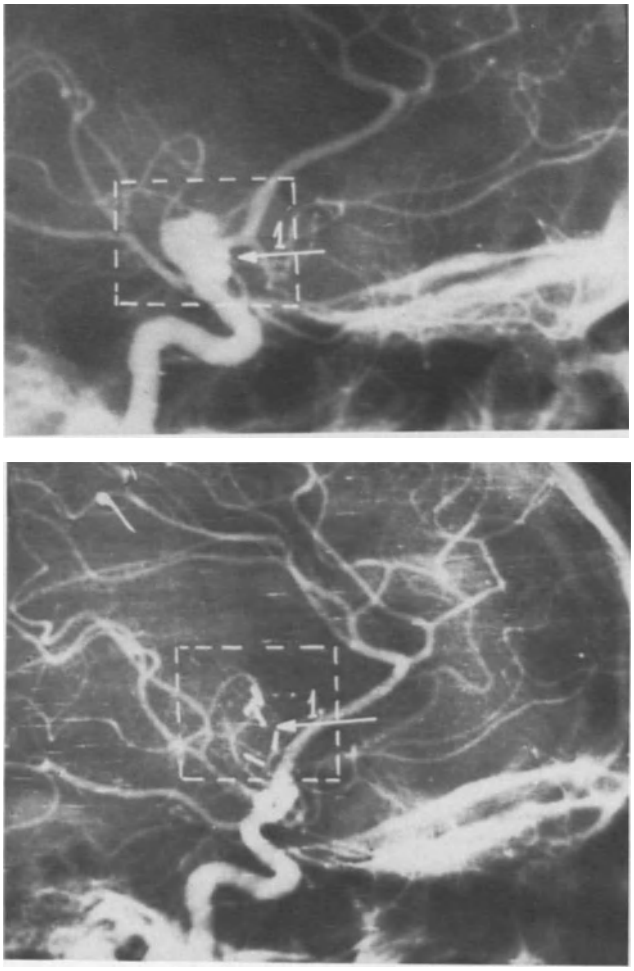


Figure 14.3. Supraclinoid aneurysm before and 1 year after operation. The arrow points to the marker of the balloon.

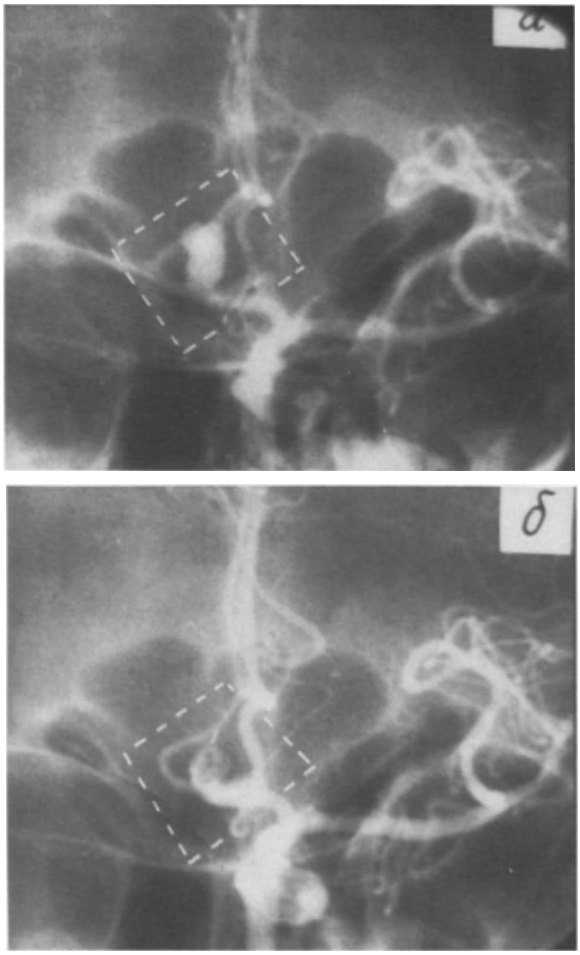


Figure 14.4. Anterior communicating artery aneurysm is occluded but with preservation of of the artery and small branches.

a neurosurgeon to preserve these small brahces. The third example is that of a basilar artery aneurysm before and 1 year after the operation (Fig. 14.5). Often it is suggested that such an aneurysm with a long neck is impossible to occlude by balloon catheter. It is possible to prepare a special balloon with two sections. The first section is introduced into the distal part of the aneurysm and the other part in the proximal portion. The fourth example is that of a middle cerebral artery aneurysm before, immediately after, and 2 years after surgery (Fig. 14.6).

Additional examples include a patient with a large anterior communicating artery aneurysm who refused surgery. On the second admission there was hemorrhage, and she was taken to surgery and the aneurysm occluded by a single balloon. Even today I do not have an explanation as to how it was possible to occlude this aneurysm with

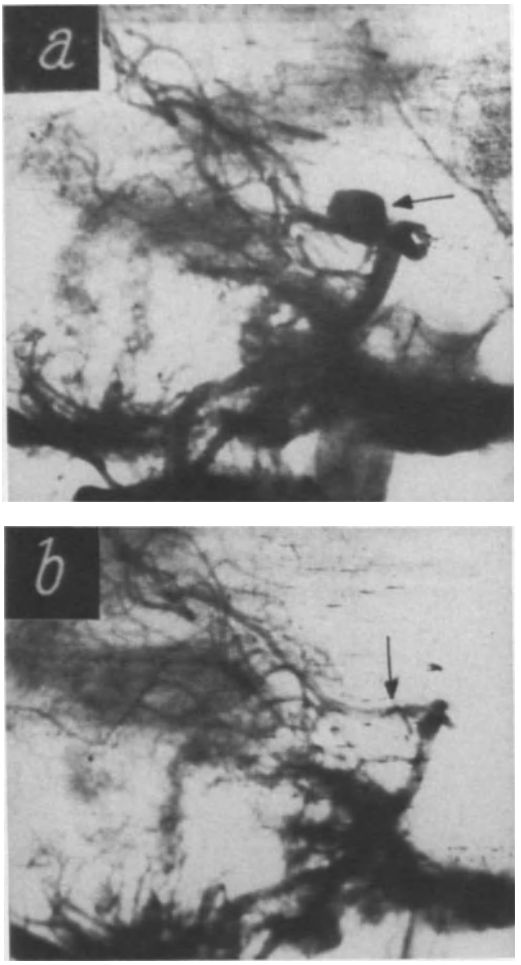


Figure 14.5. Basilar artery aneurysm before and 1 year after occlusion.

a single balloon. Perhaps there were clots in the aneurysm. An aneurysm of the sinus cavernosus after surgery required different modifications for the balloon catheter. A classic balloon is used with a floating marker in it. For large aneurysms, false aneurysms, and traumatic aneurysms we use a special type of balloon that not only occludes the aneurysm but also helps to inject some substances there. This is the second type of balloon we use now. It helps to struggle with the deadspace. With such modifications of balloon catheters it is possible to occlude all types of aneurysm without silicone but using different liquids. It should not be constructed only of latex. Different compounds should be included in the wall of the balloon in order to react with the wall of the aneurysm or intima.

There are different types of balloon and balloon catheters. Previously there was difficulty introducing the balloon into an aneurysm, but now there is no such prob-

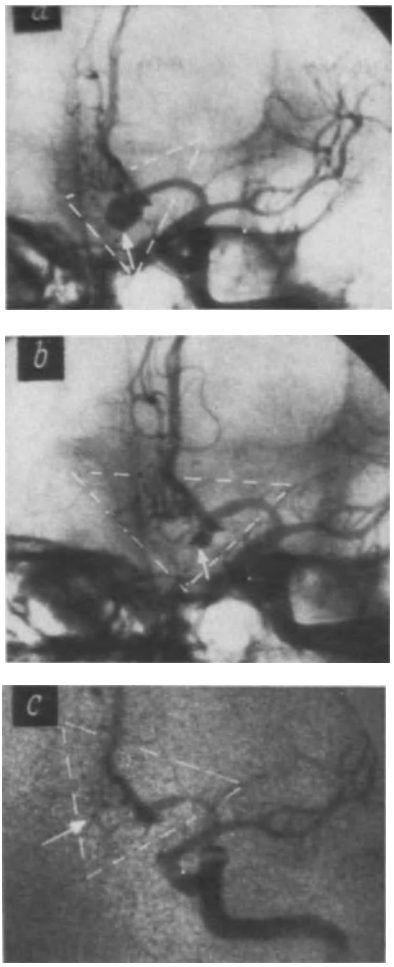


Figure 14.6. Middle cerebral artery aneurysm before, immediately after, and 2 years following occlusion.

lem. It is the special pretraining of the balloon that permits it to flow with the blood into the neck of the aneurysm. We use only a linear change of the blood flow. So they change the linear blood flow to "turbulent" flow. To occlude such an aneurysm we prepare two or three balloons primarily in the upper portion of the balloon because the feeding vessel itself is thin. Such preparation of the balloon helps enormously during its introduction.

In this manner we have operated on easy and difficult aneurysms. Aneurysms larger than 5 cm require combined treatment by the endovascular route and the direct surgical approach. Aneurysms of the cavernous sinus are treated according to size: the larger ones by the intraarterial approach and the smaller ones by the intravenous route. Aneurysms associated with hematomas were managed by occluding the

aneurysm first and then dealing with the hematoma. Multiple aneurysms were usually dealt with in a single sitting beginning with the one that ruptured. Small aneurysms represent a problem, and we occlude them with a simple balloon with no liquid filling. For false aneurysms we use a large balloon with some adhesive substances. We never detach the catheter from the balloon just after the operation, so it is fixed on the neck for 24 hours or more. In one patient who died 6 months later from another cause, at autopsy it was difficult to separate the balloon from the wall of the aneurysm. This case was done with Dr. Pile-Spellman.

Dr. Hilal: Did the balloon shrink?

Dr. Scheglov: As I understand it, the balloon did not shrink because it filled only part of the aneurysm. The aneurysm itself was larger, and so the aneurysm shrinks, not the balloon.

Dr. Berenstein: Was there any endothelium lining the balloon?

Dr. Scheglov: There was some sort of tissue. There was also another case in which the aneurysm shrunk. We could not find the wall of the balloon; it had disappeared. It is necessary to investigate this phenomenon. In this case we found silicone that was from the balloon adjacent to the wall of the aneurysm. According to these preliminary investigations, we achieved an effective, safe occlusion. There were no cases of hemorrhage where there was full occlusion of the aneurysm. The angiographic investigations were repeated at 3, 6, 12, and 24 months and 3 years after the operation.

Dr. Hilal: There was no recurrence of the neck?

Dr. Scheglov: Discussion relative to the neck of the aneurysm is difficult. If there is a neck we occlude the aneurysm itself but never the neck. During preparation of the apparatus often I am questioned by young doctors. I say that "I have had problems but small ones. Each day I perform two or three operations, and you perform three operations a year. You understand that the experience of many cases is the most essential factor." As concerns the balloon available in the United States—the Jacques Moret balloon—it is possible to occlude the saccular aneurysms.

Dr. Berenstein: You never occlude the aneurysm neck?

Dr. Scheglov: Never, because if you dilate the neck the aneurysm will grow. You can occlude an aneurysm with such a neck with a simple balloon. Also there are balloons made of two parts, so the upper part is inflated and occludes the sac, and the part that is not inflated is simply resting in the neck.

Dr. Hilal: Are the cavities of the two balloons communicating, or are they separate chambers?

Dr. Scheglov: No, they are not communicating.

Dr. Hilal: Do you then have one or two catheters? One catheter for inflation of one balloon and one for the second compartment?

Dr. Scheglov: One does not inflate the lower one. The balloon in the upper compartment is inflated.

Dr. Hilal: How does the lower one become inflated, or does it? What do you do with the second balloon to occlude the neck?

Dr. Scheglov: For a balloon with two parts it is necessary to attach the part that represents the second section. That section would not widen and should not be inflated. The inflatable part is used to occlude the aneurysm cavity, and the smaller second section remains resting in the neck. This is the type of balloon for this type of aneurysm. To repeat: There are two parts, one attached to the other. One part is inflatable, the other is not and remains in the neck. It is possible to devise other variations, but in principle it is possible to occlude any aneurysm with one balloon.

Then, of course, it is necessary to "train" the balloon and to make the walls of the balloon of different thicknesses in order for it to adopt the form of the aneurysm.

Dr. Hilal: Do you train them outside the body?

Dr. Berenstein: How do you train them?

Dr. Scheglov: I train them before the operation. I take a part of the balloon and inject some liquid resulting in inflation of the dome portion of the balloon. If the parent vessel is big or wide or small. one the contrary, I compress the lower part of the balloon and that consequently trains the upper part of the balloon by inflation. the trained part of the balloon has a certain degree of liberty compared with other parts of the balloon, so it is going in all directions. The blood flow and the turbulence helps the balloon more into place. It is almost possible to introduce it with your eyes closed.

Dr. Berenstein: Dr. Debrun, what can you tell us about this training?

Dr. Debrun: You hold the balloon, inflate it several times, and then inflate only the distal part of the balloon while holding the proximal part. This action fatigues the distal part. Consequently it is the part of the balloon that infaltes first.

Dr. Hilal: There must be something special to what Dr. Scheglov does because he has no recurrences at the neck. Is it the type of latex you use that is producing a local irritative effect on the artery and makes the balloon adhere better to the artery? It may be important to know what kind of latex you are using, because the experience in the United States is that some patients have a recurrence at the neck. Your balloon must be adhering better to the intima than our balloons, perhaps because of the material.

Dr. Scheglov: The latex comes from India, and it is possible to make a mixture with other latexes.

Dr. Hilal: This factor may be important in creating irritation of the intima.

Dr. Scheglov: There are different sorts of latex tube, and in those cases we see an inflammation or an irritation of the tissues.

Dr. Konovalov: There is a special coating of the latex balloon that makes this balloon adhere—some adhesive substance.

Dr. Scheglov: I would rather not discuss the nature of the coating at this time.

Dr. Fox: How often have you had to re-treat an aneurysm when the patient returned and there was filling on follow-up angiography?

Dr. Scheglov: When we first started using this method we had many experiences, with few roses along this way. It was Professor Romodanov who told me not to stop and to be careful when selecting patients. Hence I performed these operations more and more carefully. At the present time if I occlude the aneurysm myself I rarely see a recurrence. In principle, I think it is possible to perform the operation in such a fashion that there will be no recurrence of the aneurysm. Success is possible at present even with giant aneurysms and false aneurysms with which there are often recurrences due to migration of the balloons. I do not know how many aneurysms of the anterior communicating artery we have mended, which are the easiest to aim for with the balloon catheter. There were only five patients for whom it was necessary to perform a second operation. There are new methods of contructing the balloons, and various liquids are injected or silicone. Polymerization takes place, and additional quantities of substances may be injected. The most important idea was that of Professor Serbinenko—that it is possible to detach the balloon.

Dr. Berenstein: Have you had patients who have had rebleeding after balloon occlusion?

Dr. Scheglov: In the beginning, when the aneurysms were not completely occluded, there were some cases of rebleeding. During the past 12 years there were no cases of rebleeding. The principle to follow is complete occlusion of the aneurysm cavity. The balloons used in the United States are short and spherical, and they occlude the aneurysm in a particular manner. In my opinion they are dangerous because there are no additional materials in the walls of the aneurysm, and they may rupture. In my experience it is necessary to occlude the aneurysm not in this way but by the oval balloon so the latex is touching the walls and the caudal part would be occluding the remaining aneurysmal sac. It is a good guarantee against rupture, because the balloon's volume may actually increase for the first 3 days.

Dr. Holtzman: Do you mean that the balloon may enlarge in size over the first 3 days and then reduce its size?

Dr. Scheglov: I have seen instances when there was occlusion of the aneurysm that was so tight I could sense the danger and possibility of rupture.

Dr. Viñuela: How often have you used the two-balloon systems, and what are the indications?

Dr. Scheglov: Usually I and the younger doctors use two-balloon catheters for injecting the balloons. The balloons change the linear blood flow to turbulent flow, and the circulating blood pushes the balloon into the aneurysmal cavity. We always use two balloons and sometimes three. In some cases there is a small aneurysm; and if a balloon is introduced into this cavity, it escapes. In such cases we first inject the balloon catheter for occlusion of the aneurysm; then we occlude the feeding vessel at the level of the aneurysm; and finally we inject silicone into the first balloon.

There was a case of aneurysmal rupture in Moscow during balloon insertion. The operator immediate took the second balloon and introduced the liquid successfully, aborting the hemorrhage. It is seldom that one can succeed in saving the patient if there is a hemorrhage.

Dr. Viñuela: For what kind of aneurysm would you need more than one balloon to achieve occlusion?

Dr. Scheglov: After detachment of one balloon if we find that it is not sufficient to produce occlusion we introduce a second balloon.

Acute-Phase Endovascular Treatment

Dr. Solomon: Do you operate on patients during the acute period after subarachnoid hemorrhage?

Dr. Scheglov: Yes. We have never seen spasm during the first 2 days; in most cases it develops later. The occlusion of such aneurysms requires a technique that has its peculiarities. We preform a special balloon and then subject it to the action of thrombin with oil. Then it is cleaned, and we occlude the cavity of the aneurysm, but not under high pressure. We do not detach the catheter for 24 hours.

Dr. Solomon: You do not detach the catheter, and it stays in the vessel without provoking thrombosis?

Dr. Scheglov: That is correct. We have had two patients with a slight hemiparesis on the second day; they were given heparin and hypertensive and hormonal therapies. There was no evidence of thrombosis.

Dr. Solomon: Was there any evidence of rupture after the procedure?

Dr. Scheglov: No. In no case was there a rupture. It is well documented.

Dr. Solomon: If patients have developed vasospasm, perhaps 1 week later, and they have the balloon in the aneurysm, we currently treat them with hypertension. Is this technique safe with the balloon in place?

Dr. Scheglov: If the aneurysm is occluded by the balloon, we are not afraid of any elevation of blood pressure or the use of anticoagulants. We never use different coagulating drugs during the acute period. I understand that ε-aminocaproic acid is helpful when the patient is in a good state and dangerous when in a poor state.

A final note: If the procedure is of long duration I think it is wrong to perform it by the transfemoral route. It is necessary to puncture the carotid artery, and the procedure is easier and quicker through the carotid. The duration of the operation itself may be about 6 or 7 minutes. I am uncomfortable saying this, and in my papers I always write that the duration of the operation is about an hour so as not to irritate the neurosurgeons.

CHAPTER 15

Intravascular Treatment of Aneurysms and Angioplasty of Arterial Vasospasm

Randall T. Higashida, Grant B. Hieshima, Van V. Halbach, S.L. Barnwell, Christopher S. Dowd, Bill Dormandy, and Julie Bell

Intravascular Balloon Dilatation Therapy for Intracranial Arterial Vasospasm: Patient Selection, Technique, and Clinical Results*

Intracranial arterial vasospasm due to aneurysmal subarachnoid hemorrhage (SAH) remains a leading cause of major morbidity and mortality among cerebrovascular disorders.[1–3] Despite recent advances in medical and surgical therapy, including calcium antagonists, early removal of thrombus, and cisternal irrigation with thrombolytic agents, it is estimated that 20% to 30% of patients with an acute SAH will develop vasospasm leading to stroke or death.[3–8] Recent advances in interventional neurovascular radiology have now allowed patients with symptomatic vasospasm to be treated by intravascular balloon angioplasty techniques in selected cases. This chapter describes our current clinical protocol for patient selection, angiographic technique, and clinical results from treatment of patients with symptomatic arterial vasospasm by balloon dilatation therapy.

Patient Selection

The indications for treatment by balloon dilatation technique at our institution included clinically symptomatic vasospasm that was not responsive to medical therapy and vasospasm in patients undergoing interventional treatment of an intracranial aneurysm with resultant neurological decline.[9] Prior to treatment a computed tomographic scan of the brain or magnetic resonance imaging head scan was obtained to evaluate for evidence of cerebral infarction, ischemia, and intracerebral hemorrhage.[10,11] Acute hemorrhage (within 6 hours) was a relative contraindication to performing treatment, as systemic anticoagulation was required during the angioplasty procedure.

*Reprinted with permission of Higashida, R.T., Halbach, V.V., Dowd, C.F., et al. Intravascular balloon dilation therapy for intracranial arterial vasospasm: patient selection, technique, and clinical results. *Neurosurgical Review* 1992;15:89–95.

Table 15.1. Vascular territories treated by balloon dilatation in 28 patients

Territory	Patients (no.)
Anterior circulation	
Internal carotid artery	25
Middle cerebral artery	24
Anterior cerebral artery	4
Total	53
Posterior circulation	
Vertebral artery	11
Basilar artery	16
Posterior cerebral artery	19
Total	46

Transcranial Doppler was obtained, if available, pre- and and post-procedure to assess changes in cerebral perfusion.[12]

A total of 28 patients, including 17 females and 11 males ranging in age from 15 to 73 years (mean 44.0), were treated. Table 15.1 lists the vascular territories treated in this group of patients. A total of 99 vessels were dilated including 53 vessels in the anterior circulation and 46 vessels involving the posterior circulation. Five patients (17.9%) presented with focal vasospasm affecting only one vascular territory. In 23 patients (82.1%) there was angiographic evidence of diffuse spasm affecting multiple vascular territories.

Angiographic Protocol

All procedures were performed in the interventional neurovascular radiology section from a transfemoral percutaneous approach. High-resolution digital subtraction angiography with road mapping capability is essential for monitoring the progress of the procedure. A complete four-vessel cerebral arteriogram was initially performed to assess degree of stenosis, vascular territories involved, and collateral circulation.[10,13] Correlation with the angiographic vascular territory in spasm and the patient's clinical symptomatology was performed by a neurological specialist. The majority of patients were treated under local anesthesia so that continuous neurological evaluation of the patient's clinical condition could be assessed throughout the procedure.

Treatment of vasospasm was performed utilizing a custom device, a silicone microballoon developed specifically for use in the intracranial circulation (Interventional Therapeutics Corporation, South San Francisco, CA[14]). Two sizes of the balloon are currently available for intracranial use. Uninflated, the smaller balloon, which measures 0.85 × 3.50 mm, accepts a volume of 0.10 ml and expands to 3.5 × 12.0 mm (Fig. 15.1). This balloon was used to treat the supraclinoid internal carotid, middle and anterior cerebral,

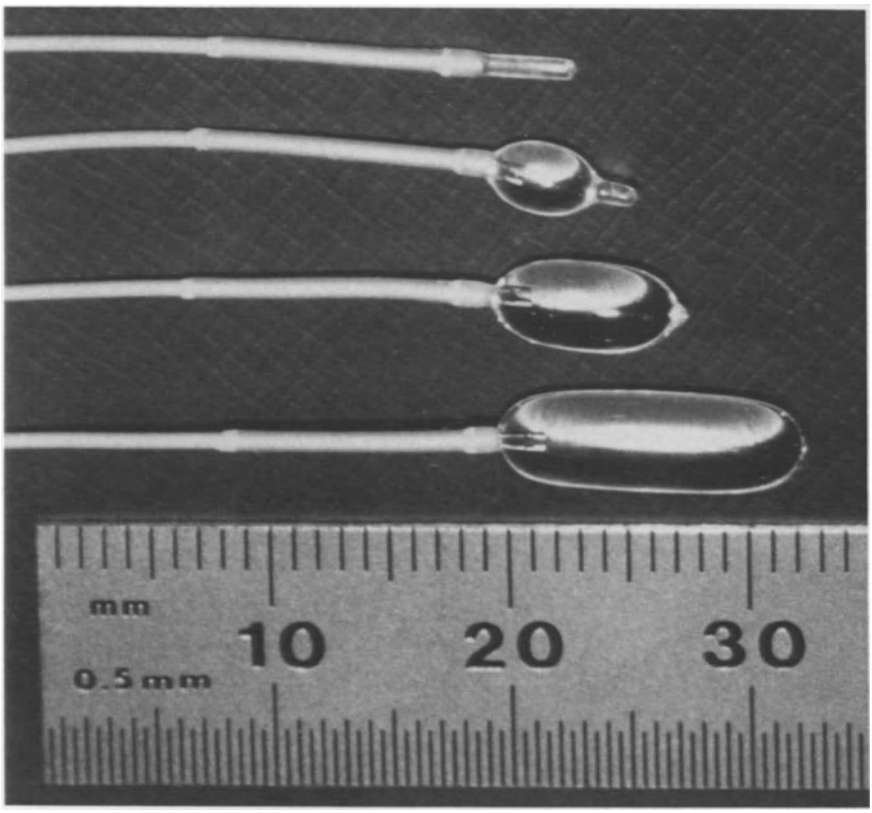


Figure 15.1. Intravascular silicone microballoon used for angioplasty of intracranial arterial vasospasm. Uninflated the balloon measures 0.85 × 3.50 mm. It can accept a volume of 0.10 ml and inflates to 3.5 × 12.0 mm. This balloon inflates from the proximal to distal end and has an elongated contour.

basilar, and posterior cerebral arteries. The larger balloon, which measures 1.5 × 4.0 mm, accepts 0.50 ml of fluid and inflates to 7.5 × 12.5 mm. This balloon was utilized for larger-diameter vessels including the distal vertebral and internal carotid artery. It is important to select the properly sized balloon, as overdilatation beyond the normal luminal diameter of the vessel could result in rupture.

Silicone was chosen for use in the intracranial circulation because of its unique properties of biocompatibility, isotropic expansion capabilities, malleability, and special conformational structure.[14] This material allows the balloon to conform to the vessel lumen without causing excessive pressure on the inner wall. The balloon is chemically bonded onto a 2.0F polyethylene catheter to prevent inadvertent detachment. A special microguide wire, 0.014 inches, can be placed into the catheter to aid in navigation into specific vascu-

lar regions (Target Therapeutics Corporation, San Jose, CA[15]). The balloon is guided to the site of spasm, and with gentle inflation and deflation (with pressures between 0.1 and 1.5 atmospheres) dilatation is performed.

Following the procedure, a postangioplasty arteriogram was obtained in all cases to evaluate the change in caliber of the territories treated and to determine if there was any structural damage to the vessel(s). Patients were monitored by close neurological evaluation throughout the procedure and then observed in the neurosurgical intensive care unit following treatment.

Representative Case Reports

Diffuse Vasospasm Treated by Balloon Dilatation

This 48-year-old man presented with a large subarachnoid hemorrhage (SAH) involving the basal cisterns documented by computed tomography (CT). Over the next several days he became increasingly lethargic and obtunded, with inability to follow commands, and hemiparetic. Cerebral angiography demonstrated a distal left vertebral artery aneurysm. It was treated by interventional techniques utilizing coils to occlude the inflow and outflow of the aneurysm.

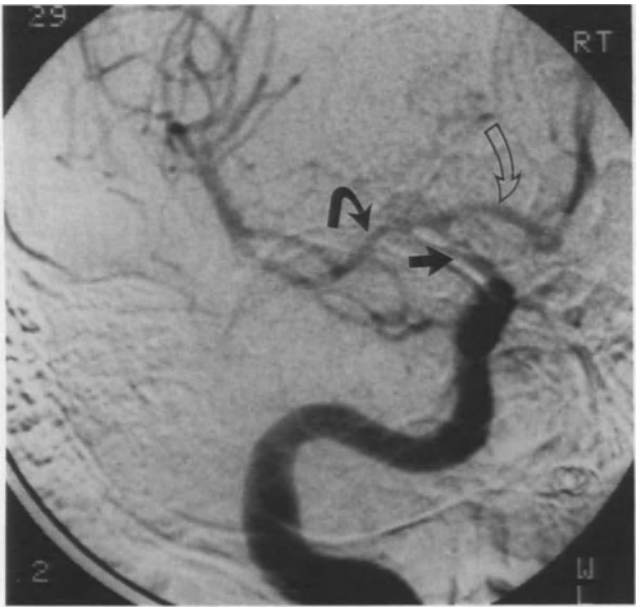


Figure 15.2. (A) Right internal carotid arteriogram demonstrating severe vasospasm of the supraclinoid internal carotid artery (straight arrow), anterior cerebral artery (open arrow), and middle cerebral artery (curved arrow). This patient presented with an acute subarachnoid hemorrhage from rupture of a distal vertebral artery aneurysm.

Despite vigorous medical therapy, including volume expansion, ventriculoperitoneal shunting, and calcium channel blockers, he continued to decline neurologically. A follow-up angiogram demonstrated severe diffuse vasospasm involing both the anterior and posterior circulations (Fig. 15.2A,B). From a transfemoral approach, balloon dilatation of the right and left supraclinoid internal carotid arteries, the right and left middle cerebral arteries, the right vertebral, entire basilar, and the right posterior cerebral arteries was performed. The post dilatation arteriogram demonstrated marked improvement in luminal diameter of the treated vessels to near normal caliber, with angiographic evidence of improved cerebral perfusion (Fig. 15.2C, D). It was confirmed by transcranial Doppler blood flow studies pre-and postprocedure.

Over the next several hours to days the patient had gradual and progressive neurological improvement. He became arousable, followed commands, and was oriented. At 2 months of clinical follow-up he has regained 90% of neurological function and continues to do well with only a mild Wallenberg syndrome secondary to occlusion of the proximal posterior inferior cerebellar artery for treatment of his aneurysm.

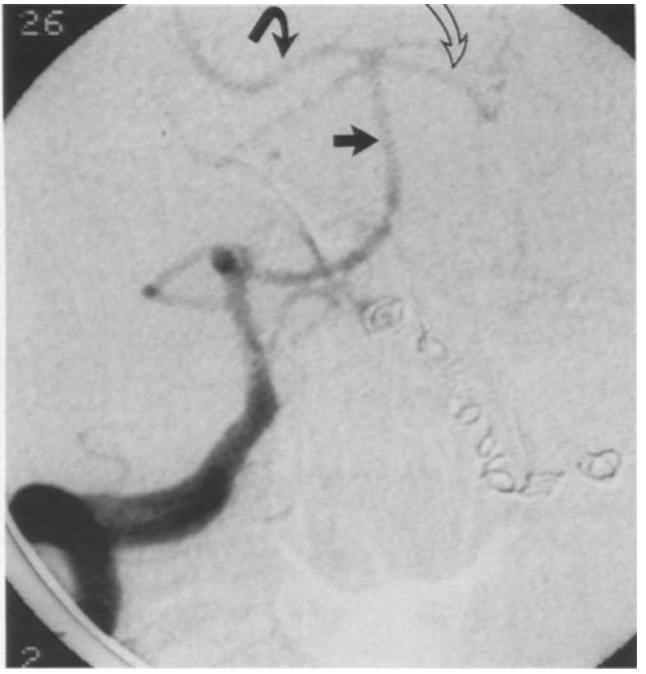


Figure 15.2. (B) Right vertebral angiogram demonstrating severe diffuse vasospasm of the entire basilar artery (straight arrow) and both posterior cerebral arteries (curved arrows).

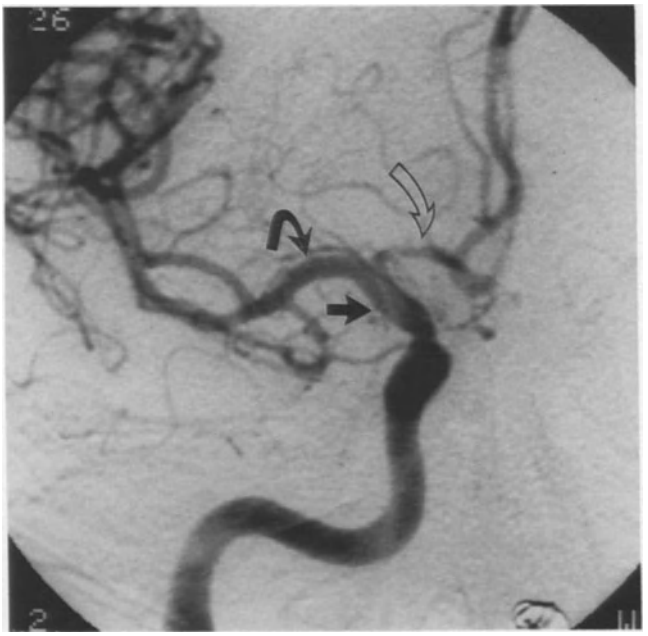


Figure 15.2. (C) Following successful angioplasty of the supraclinoid internal carotid artery (straight arrow) and middle cerebral artery (curved arrow) territories, there is return of normal luminal diameter, with angiographic evidence of improved cerebral perfusion.

Postoperative Vasospasm Treated by Angioplasty

A 27-year-old man presented with an acute subarachnoid hemorrhage and was found to have a right medial temporal lobe arteriovenous malformation (AVM). After recovering from his hemorrhage, he underwent preoperative embolization followed by surgical resection of his AVM. Postoperatively over the next several days, the patient developed progressive left upper extremity paresis with inability to raise his arm but no other focal neurological deficits. Cerebral angiography demonstrated marked vasospasm involving the right supraclinoid internal carotid artery as well as the right middle and anterior cerebral artery (Fig. 15.3A).

From a transfemoral approach, under local anesthesia, transluminal balloon angioplasty of the supraclinoid and middle cerebral arteries was performed without difficulty. The postprocedure arteriogram demonstrated a return to normal luminal diameter of the vessels treated, with angiographic evidence of improved perfusion (Fig. 15.3B). Immediately following this procedure his paresis resolved, and he regained normal motor function of his left arm. He was discharged home several days later in stable neurological condition and at 14 months of follow-up continues to remain well.

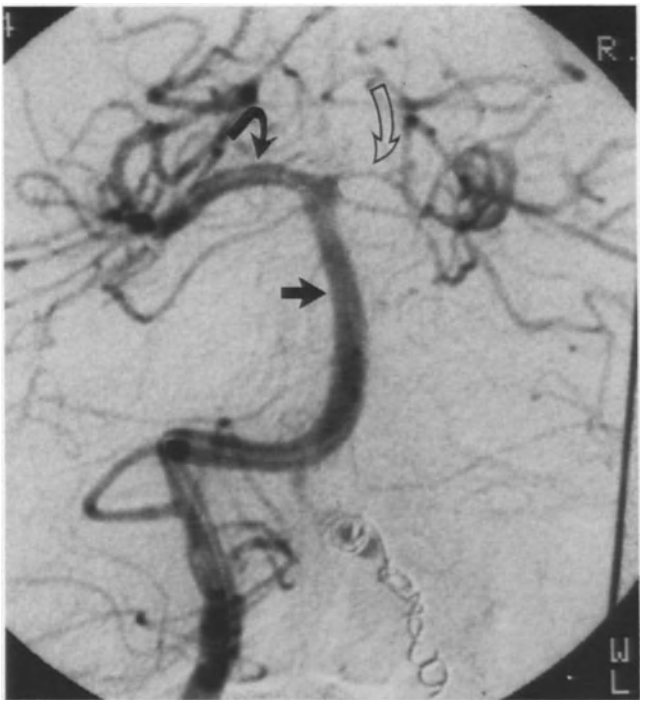


Figure 15.2. (D) Postangioplasty arteriogram following successful dilatation of the entire basilar artery (straight arrow) and the right posterior cerebral artery (curved arrow). Note that the left posterior cerebral artery, which has not been dilated, continues to remain in spasm (open arrow).

Results

Ninety-nine vascular territories were treated in 28 patients by transfemoral balloon dilatation technique. There was angiographic evidence of improved luminal diameter in all cases. Follow-up angiography, performed several days after the procedure demonstrated continued patency of the vessels treated by angioplasty, while the untreated territories continued to remain in spasm. Of the 28 patients treated, there was clinical improvement in the patient's neurological condition in 17 cases (60.7%). The majority of patients had noticeable improvement within minutes to hours following successful dilatation, particularly if the procedure was performed within 24 hours after the onset of neurological decline. If treatment was delayed beyond 24 hours after the onset of symptoms, improvement in neurological condition was slower to evolve. In 11 cases (39.3%), there was no noticeable change in neurological symptoms, despite angiographic evidence of improved luminal diameter of the treated vessels. These patients were in poor neurological

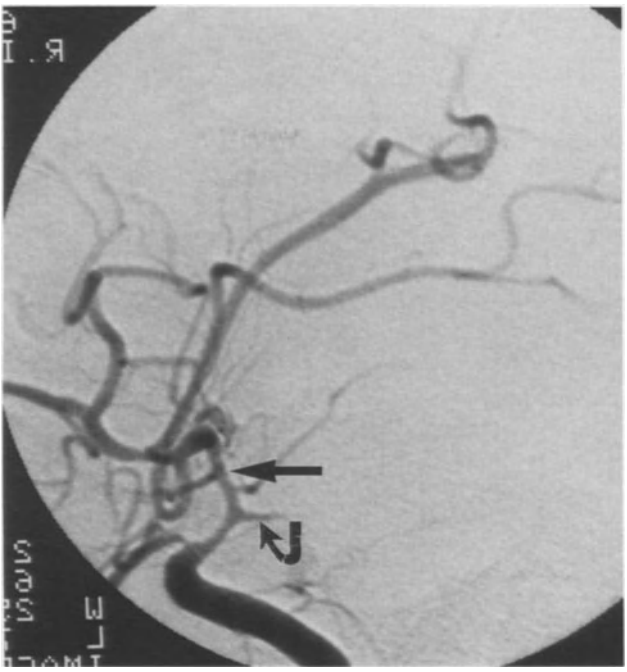


Figure 15.3 (A) Internal carotid arteriogram, lateral view, demonstrating severe vasospasm of the supraclinoid and middle cerebral arteries (straight arrow). The posterior communicating artery also has poor filling (curved arrow).

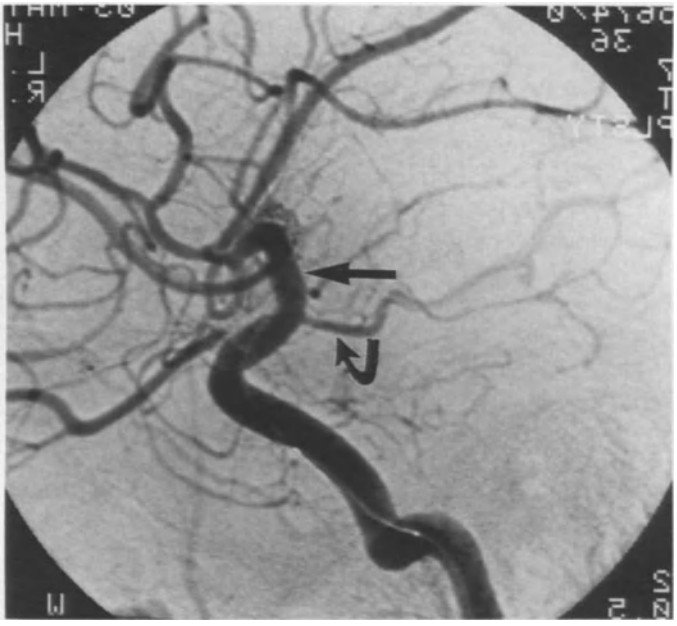


Figure 15.3 (B) Following successful dilatation of the supraclinoid and middle cerebral arteries (straight arrow), there is now improved flow to the anterior circulation as well as through the posterior circulation (curved arrow).

condition (Hunt and Hess grade IV–V) at the time of treatment, and often angioplasty had not been instituted until several days to weeks had passed.

Long-term clinical follow-up demonstrated continued excellent to good outcomes in those 17 patients (60.7%) with initial and prompt response to therapy. Two patients (7.1%) remained in poor neurological condition despite treatment. Nine patients (32.1%) in this series died. Two of the deaths were a result of technical complications from therapy. One that took place early in our experience was due to rupture caused by a latex balloon in the cavernous internal carotid artery leading to a carotid cavernous sinus fistula. The second case involved rupture of a posterior cerebral artery causing an SAH. One patient developed a hemorrhage of the basal ganglia region 24 hours following angioplasy of the middle cerebral artery and subsequently died.[9,16] The remaining six patients died from other unrelated medical problems resulting from the initial hemorrhage, including infection, renal failure, and cardiac and respiratory complications.

Discussion

Dotter and Judkins in 1964 were the first to report on the technique of percutaneous transluminal angioplasty for atherosclerotic disease.[17] It was not until 1984, however, that Zubkov and Nikiforov reported the feasibility of balloon dilatation for spastic intracerebral arteries.[18] They reported the successful treatment of 33 cases, involving 105 vascular territories, with good clinical outcome utilizing latex microballoons. Their initial report prompted our group to study the feasibility of developing and improving this technique to dilate symptomatic spastic blood vessels. Over the next several years, a specially blended silicone elastomer balloon was developed by our group, specifically to treat intracerebral vasospasm.[14,16] The advantages of silicone over other materials are that it is a soft material that conforms to the blood vessel lumen in a gradual and gentle configuration, without exerting high lateral stress against the endothelium. It also expands in a linear fashion from the proximal to distal end, thus aiding in advancement through tight structures. Several studies have compared silicone to latex balloons for vasospasm angioplasty. They have demonstrated that much less endothelial damage is done by the softer silicone balloons.[19–22]

Over the past several years, a number of centers have reported successful treatment for symptomatic spasm by this technique. Mayberg et al. have now performed angioplasty in 21 cases with neurological improvement in 15 patients (71.4%).[23–25] In each case they were able to demonstrate corresponding improvement by transcranial Doppler studies that correlated well with clinical improvement. Takahashi et al. reported successful angioplasty in 22 cases; 15 of them (68.2%) had good to excellent improvement in neurological outcome following treatment.[26] Other centers have reported similar results on smaller groups of patients treated.[20,27] The majority of cases

treated with this technique were patients with progressive neurological deterioration following a trial of medical therapy for symptomatic spasm.

The mechanism and pathophysiology of cerebral vasospasm is still poorly understood. It has been suggested that spasm is due to endothelial damage, myointimal cellular proliferation, or inflammatory changes in the wall of the blood vessels.[1,28–33] Other studies have suggested that vasospasm secondary to subarachnoid bleeding results in a reduction in smooth muscle elasticity similar to an organic vasculopathy.[26] These changes may not be as amenable to therapy by vasodilator medications. Thus far, no pharmacological agent has yet been found that can consistently reverse the effects of spasm due to subarachnoid blood. It is for this reason that balloon angioplasty remains a viable alternative in patients unresponsive to medical therapy.

The mechanism of angioplasty for arterial vasospasm is much different than for atherosclerotic disease in which the balloon acts to disrupt and fracture the plaque that involves the intima and media.[22,34–36] Indeed, on both immediate and delayed follow-up cerebral arteriograms following dilatation for spasm, there is no angiographic evidence to suggest intimal disruption, hypertrophy, dissection, or other vessel damage. The treated vessel lumen appears to be restored to normal caliber, whereas adjacent untreated vessels continue to remain in spasm.[19,22]

In conclusion, intracranial arterial vasospasm can be effectively treated by balloon dilatation techniques in selected cases. We believe that initially patients should be managed by medical therapy to reverse the effects of cerebral ischemia caused by vasospasm. If the patient continues to decline neurologically, intravascular angioplasty should be considered as soon as possible. Radiographically, there is evidence documenting a restoration to normal luminal diameter following dilatation. Clinically, in 60.7% of patients thus far treated, there has been marked improvement in neurological function following angioplasty in patients who might otherwise have progressed to severe stroke with impairment.

Interventional Therapy for Intracranial Aneurysms by Direct Balloon Occlusion: Clinical Protocol and Therapeutic Results*

Interventional neurovascular techniques utilizing detachable balloons were first described in the early 1970s by Serbinenko.[37,38] Since then, with advances in microballoon technology, steerable guidewires and microcatheters, high resolution fluoroscopy with road-mapping capability, and newer poly-

* Reprinted with permission of Higashida, R.T., Halbach, V.V., Barnwell, S.L., et al. Interventional therapy for intracranial aneurysms by direct balloon occlusion: clinical protocol and therapeutic results. *Neuroradiology* 1991;33(supp):139–141.

merizing materials, it has become feasible to guide a balloon directly into the aneurysm for obliteration while preserving the parent vessel.[39–41] Since 1984, 88 patients have been treated by our group using this technique for aneurysms involving both the anterior and posterior circulations. Our current clinical indications, technique, and therapeutic results are described.

Materials and Methods

Since 1981 we have treated 215 patients with an intracranial aneurysm by intravascular detachable balloon occlusion techniques. In 1984, with the development of 2-hydroxyethylmethacrylate (HEMA) as a solidification material within silicone balloons, it became possible to place a balloon directly into the aneurysm and preserve the parent vessel.[42,43] A permanent solidification material within the aneurysm was required to ensure that the aneurysm continued to remain occluded should the balloon shell deterioriate or the valve leak. In 88 cases (40.9%) this treatment goal has been achieved. Patients ranged in age from 15 to 83 years (mean 49 years) and included 63

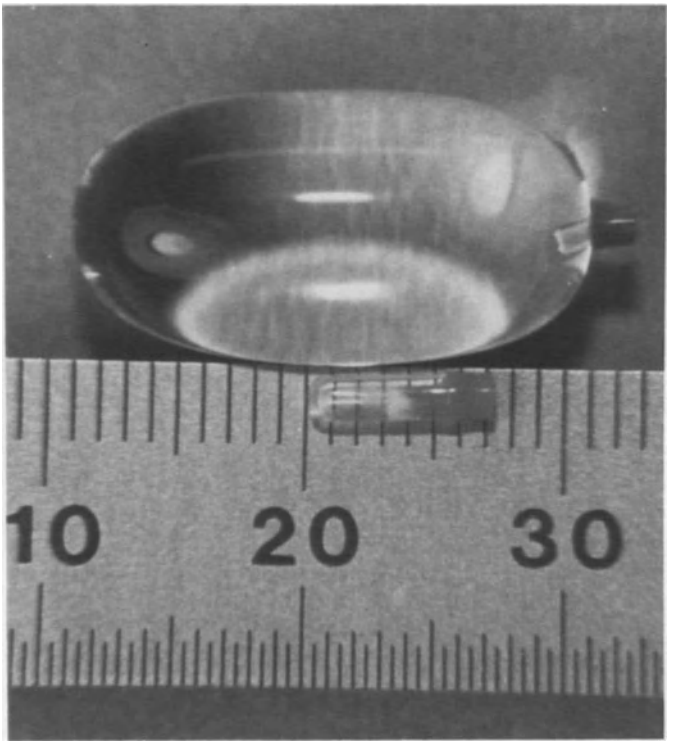
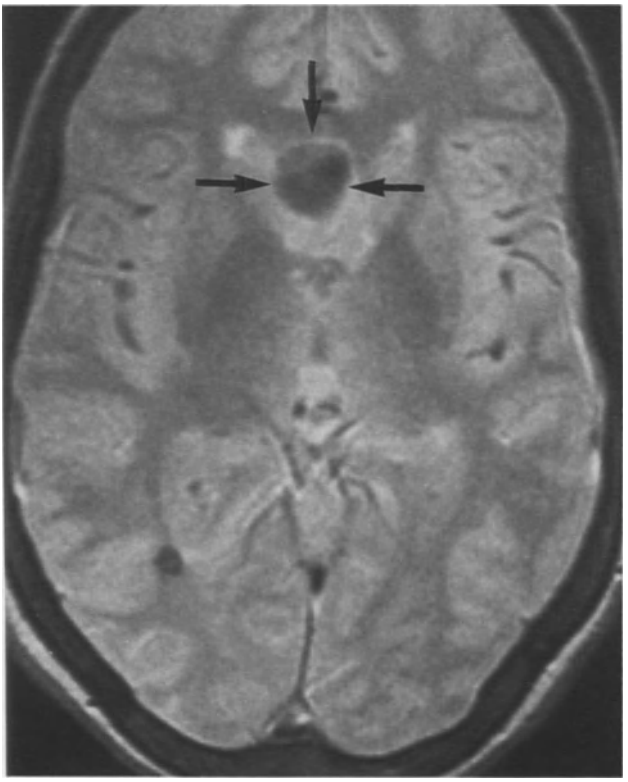


Figure 15.4 ITC detachable silicone balloon system used for direct aneurysm occlusion therapy. The 1.5 DSB balloon measures 1.5 × 7.3 mm uninflated (foreground); it can accept 0.90ml of fluid and expands 8.5 × 21.0mm (background).

cases involving the anterior and 25 the posterior circulation. Twenty patients (22.7%) were treated for a giant aneurysm larger than 2.5 cm.

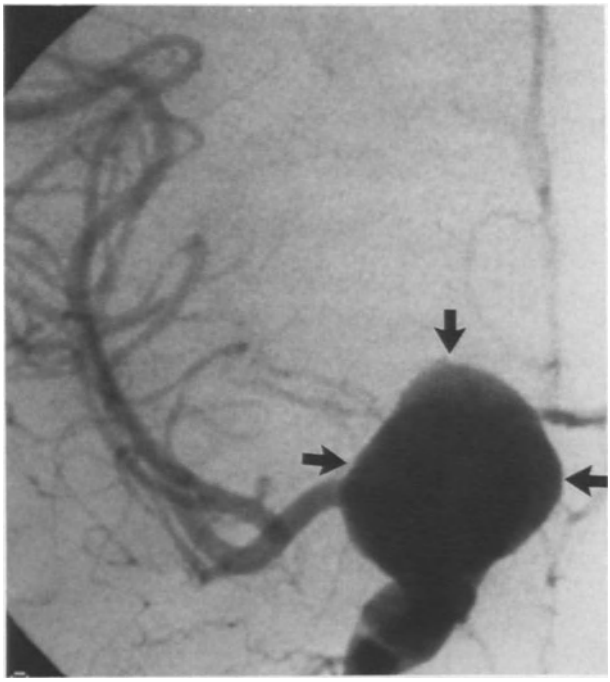
Our current indications for balloon occlusion therapy include surgical exploration with inability to clip the aneurysm, ectatic and broad-based aneurysms without a well defined neck, aneurysms in surgically difficult anatomical locations such as the petrous and cavernous internal carotid artery, and intolerance of general anesthesia.[44]

All procedures were performed in the interventional neurovascular radiology suite under direct fluoroscopic visualization. Patients are mildly sedated with intravenous diazepam, morphine sulfate, and/or midazalom hydrochloride. A high-resolution, rapid-sequence subtraction arteriogram of the aneurysm is obtained to show the size, shape, and relation of the aneurysm

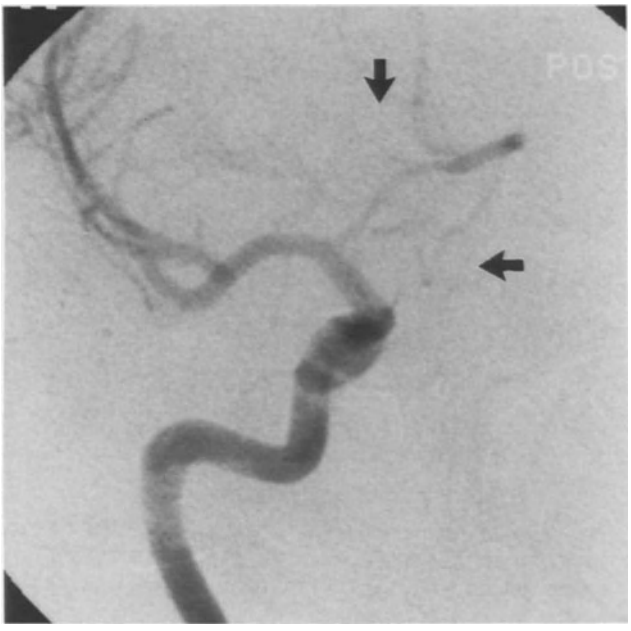


A

Figure 15.5 (A) MRI scan demonstrating a large aneurysm (arrows) that was compressing the optic chiasm. **(B)** Arteriogram confirming the presence of a giant supraclinoid internal carotid artery aneurysm (arrows) projecting superiorly and medially. **(C)** Following placement of a single detachable silicone balloon into the aneurysm (arrows), there is complete obliteration of the aneurysm, with preservation of the normal distal intracranial circulation.



B



C

Figure 15.5 (*continued*)

neck to the parent vessel. Careful measurements are made of the aneurysm size and compared with recent CT and/or MRI studies to look for intraluminal thrombus.[44,45] In the nonacute patient, embolization therapy may be delayed for 6 weeks to allow fresh thrombus to organize or lyse. This step is to avoid inadvertently dislodging clot while placing balloons in the aneurysm.

Patients are then given intravenous heparin (5000 units for a 70 kg patient) for systemic anticoagulation. A guiding 7.3F or 8.0F catheter is placed from the femoral artery into the cervical internal carotid or dominant vertebral artery, depending on aneurysm location. The correct size balloon and configuration are then selected. At our institution we use the ITC detachable balloon occluder system (Interventional Therapeutics Corporation, South San Francisco, Ca) for aneurysm therapy (Fig. 15.4). The advantages of this balloon over latex balloons are that it is biocompatible, nonbiodegradable within the intravascular system, and because of the inherent properties of silicone it is softer and more malleable, thereby decreasing stress on the aneurysm and reducing the risk of inadvertent rupture. Using the road-mapping technique, in which the neurovascular architecture is superimposed over the real-time fluoroscopic image, the balloon can be flow-directed or catheter-guided into the aneurysm. Once the balloon is well situated within the aneurysm, the contrast used to visualize the balloon is aspirated and exchanged with HEMA, which is then allowed to solidify over 40 to 60 minutes (Fig. 15.5). For large and giant aneurysms, more than one balloon may be required for complete aneurysm obliteration (Fig. 15.6).

A postembolization arteriogram is obtained to assess aneurysm exclusion and patency of the parent vessel in all cases. Patients are then observed in the neurosurgical observation unit for 2 to 4 days and, if stable, discharged. Clinical and radiological follow-up is performed at 1, 3, and 12 months posttreatment to ensure continued aneurysm obliteration.

Results

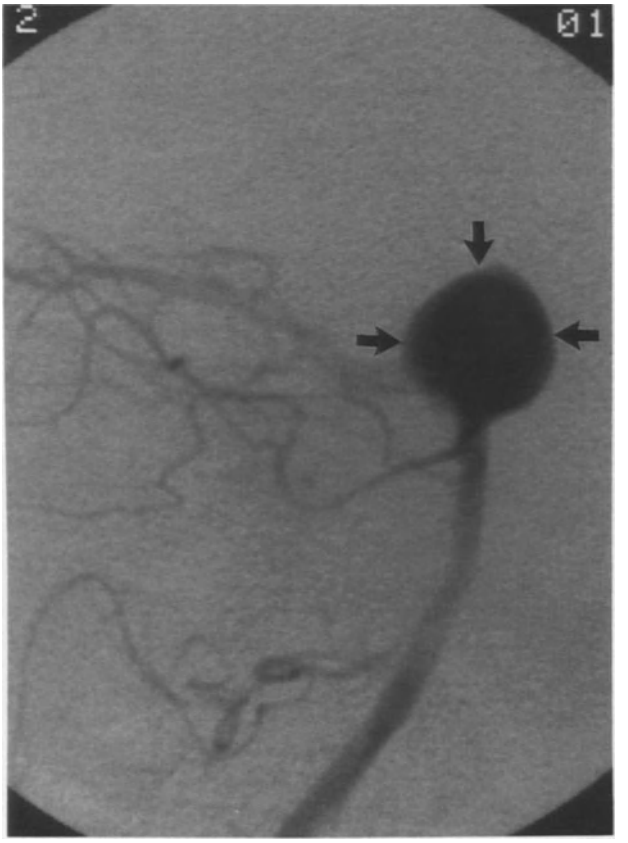
In the 88 patients treated by this technique, our mortality rate was 18.2% (16 deaths).[46] The cause of death in 11 patients was aneurysm rupture due to subtotal occlusion. The other 5 deaths were due to stroke in 2 cases, myocardial infarction in 2 cases, and pulmonary embolus in 1 patient. In general, these patients were in poor medical condition prior to therapy.

Our permanent morbidity rate was 10.2%: nine patients who suffered from a stroke. In five patients it was due to a thromboembolic event during the procedure, either from clot forming on the balloon and catheter or from dislodgement of thrombus from within the aneurysm during balloon placement. These situations occurred despite placing patients on adequate doses of systemic anticoagulants during the procedure. In two cases the balloon shifted after detachment causing occlusion of the parent vessel. In one patient, during the polymerization phase of HEMA solidification, the balloon ruptured causing a stroke. In a second patient, a balloon prematurely

detached resulting in an embolus to the middle cerebral artery. Long-term follow-up in these patients demonstrated that in seven cases (77.8%) there was improvement in neurological function with only mild to moderate functional impairment. Two patients, however, continue to have fixed, dense deficits. Clinical and radiological follow-up has ranged from 6 months to 6 years (mean 39 months).

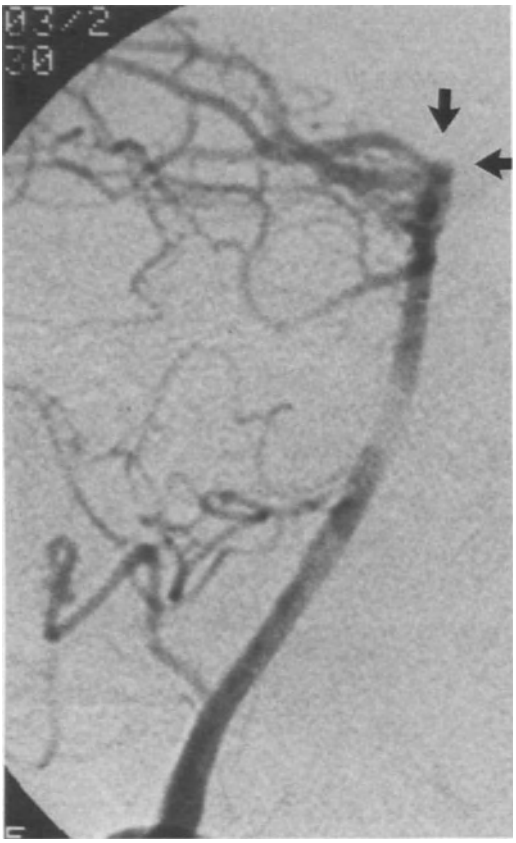
Discussion

Direct endovascular balloon occlusion of intracranial aneurysms is now being performed at several major neurological centers. The largest published



A

Figure 15.6 (A) Vertebral arteriogram, lateral view, demonstrates a large distal basilar artery aneurysm (arrows), in a patient presenting with an acute subarachnoid hemorrhage. **(B)** Following treatment with multiple balloons placed directly into the aneurysm (arrows) from a transfemoral approach, there is complete obliteration with preservation of the basilar artery and distal posterior circulation.



B

Figure 15.6 (*continued*)

series is from the Kiev Neurosurgical Institute by Romodanov and Shcheglov.[47] In 1982 they reported on the treatment of 119 patients with latex balloons for aneurysm therapy. In 78.2% of cases they were able to successfully occlude the aneurysm and preserved the parent vessel. Only 12.6% of patients required parent vessel occlusion, and in only 9.2% of cases were they unable to successfully treat the aneurysm by endovascular balloon occlusion techniques. They reported a 96.7% good to excellent result following therapy.

Moret et al.[48] in 1990 reported a series of 60 patients with saccular aneurysms treated by direct balloon occlusion. Their reported morbidity rate was 10% neurological complications, 10% failure to treat the aneurysm, 8% partial recanalization requiring retreatment, and 4% mortality.

In our current series of 88 patients treated by direct aneurysm occlusion we report an overall mortality rate of 18.2% and a permanent morbidity rate

of 10.2%. The differences in these statistics we believe is due to patient selection criteria. Because we view this technique as an adjunct to surgery, we are accepting only patients who are medically unstable and are poor candidates for general anesthesia. A large percentage of our patients also presented with large and giant intracranial aneurysms that were judged difficult to clip surgically or with acute subarachnoid hemorrhage.

In conclusion, we believe that detachable balloon occlusion therapy of intracranial aneurysms is feasible. However, long-term follow-up of these patients both clinically and radiographically is still required. As continued deveolpments in endovascular occlusion techniques utilizing detachable balloons, catheters, and other materials evolve, the safety, efficacy, and usefulness of these techniques will continue to improve.

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Discussion

Hypertensive Therapy in Vasospasm

Dr. Solomon: Do the neurosurgeons at your institution utilize hypertensive therapy?

Dr. Hieshima: They have an extensive protocol in regard to vasospasm. Now that we are seeing more patients for early treatment we are more able to be aggressive with our therapy. There are still patients who do not respond well to calcium channel blocking medications, and they are devastated by vasospasm. I think that some of those patients can be helped.

The other problem is that although we started this program some years ago we still do not have a large number of referrals with acute SAH. We have our share of acute patients but probably see no more than 15 acute SAHs per year. The large percentage of patients do not develop vasospasm, or if they do it is not clinically evident because the calcium channel blockers have been effective.

Vasospasm, Double-Blind Studies, and Bypass Procedure

Dr. Hieshima: Our progress in angioplasty has been slow. However, I think that in some cases we have definitely been able to provide a service for the patient population because all other existing therapeutic managements have failed.

We are not in a position to conduct a double-blind study with patients at this point because the surgical results of aneurysm clipping for the standard aneurysm has low morbidity and mortality, ranging from 3% to 5%, and I am not certain that I can duplicate those figures. Even if I could, I have a problem because I do not have long-term data. Fortunately, Dr. Scheglov does have such data, but I am not sure I can equal Dr. Scheglov's results so I think that for the moment we will just have to continue to work with aneurysms that are surgically unclippable. I am in agreement with the need for clinical trials in a paired fashion, but I am not personally prepared to do them at this time.

Dr. Fox: When you summarized your results, did you include the complications of just the cases treated with parent artery preservation or those for the combined series?

Dr. Hieshima: Both are included. We had almost as many complications in the vessel occlusion series, and there were a significant number of complications with the bypasses that were done. In fact, almost half of the major morbidity and mortality in that figure was associated with bypass or aspects of the bypass. On the other hand, if we had not done it, these would have been more strokes after our occlusive therapy because patients clearly did not tolerate occlusion.

Dr. Konovalov: How often do you use this method in cases of arterial vasospasm?

Dr. Hieshima: We have done it in 28 cases. We use it rarely because we see a group of patients with vasospasm that is not clinically significant. Another group of patients do have vasospasm, but when it becomes clinically significant they are managed medically to the point where the vasospasm is no longer clinically significant. Then there is a third group in whom the symptom complex is too mild to warrant an invasive procedure and a fourth group who are so clinically devastated by vasospasm that we do not treat it. Hence only a small percentage of the patients are treated with angioplasty. It is never done for asymptomatic patients.

Dr. Konovalov: How often do you use bypass surgery?

Dr. Hieshima: We use bypass surgery predominantly on patients who have failed test occlusion. When we consider the possibility of performing parent vessel occlusion we expect that roughly 25% of those patients will fail the test occlusion. The number actually turns out to be a little lower, about 18% to 20%.

Management of Surgically Accessible Aneurysms

Dr. Kachkov: Why did you not include aneurysms that were accessible to neurosurgeons in your material?

Dr. Hieshima: We thought that the aneurysms that were accessible (at least in our institution) have such an excellent outcome from surgery we would be unable to duplicate those results. Our surgeons have low morbidity and mortality rates for standard posterior communicating, anterior communicating, and middle cerebral aneurysms.

Dr. Kachkov: Is it not possible with this method to occlude, for example, an anterior communicating artery aneurysm?

Dr. Hieshima: It is possible. It is also possible that our results could be as good or maybe even better in terms of morbidity and mortality of treatment. I have no long-term data to show that the therapy is as good, though. My longest follow-up for such cases is 6 years. Six years is not enough time to evaluate parent artery occlusion because we see patients coming back at 8, 12, 15, 20, and 25 years with rehemorrhage from aneurysms that were treated and theoretically cured by parent artery occlusion.

Recanalization During Endovascular Treatment

Dr. Moret: You did not mention recanalization following endovascular treatment. Does that mean it has not occurred?

Dr. Hieshima: No, it means that if it occurs we re-treat it or the patient dies.

Dr. Moret: How many cases showed evidence of recanalization?

Dr. Hieshima: At least 8% to 10%. Recanalization occurred after what was considered to be an excellent occlusion. Many of those problems would be avoided today: Many of the patients were treated with fresh thrombus remaining in the aneurysmal sac, and shortly thereafter we noted that the balloons were shifting out of the aneurysms. In some of the patients in whom recanalization was seen we had achieved perfect occlusion, but the aneurysms expanded after occlusion. Within weeks after occlusion, we could see that the balloons were now in a different position and the aneurysm was much larger than it had been previously. If we did not treat these patients immediately the aneurysms would ruptured and the patient would die. In our current patients this problem is not often seen, but they have not been followed long enough to draw any firm conclusions.

Dr. Berenstein: In the United States that result would be interpreted differently than in France. In the United States most medical communities of neurosurgeons and neuroradiologists feel confident with surgically clipping aneurysms. There is no longer the sense that this procedure consitutes experimental treatment. It is only a matter of time and accumulated experience before we as interventional neuroradiologists can prove that the long-term effect of our therapy is good, and at that time we will start approaching the smaller aneurysms. A technique that works for large aneurysms should also work for small ones.

Dr. Scheglov: Neurosurgeons sometimes also have problems when clipping small aneurysms.

Dr. Berenstein: Dr. Solomon, what is your feeling about the types of case that Dr. Heishima presented. Are those simple or complex aneurysms in the neurosurgical experience?

Dr. Solomon: Dr. Hiesima's work is excellent and well received in the neurosurgical community. His case selection and his work in close association with neurosurgeons has been ideal and the standard by which we should all proceed. He has taken on difficult aneurysms. Those that can be handled surgically with an acceptable morbidity he has referred for surgery, and I believe that that is the direction we should be taking.

Dr. Berenstein: Do you think that in 15 years it will not have mattered whether aneurysms are managed by neurosurgeons or interventional neuroradiologists?

Dr. Solomon: I would have to consider how things are going with the interventional techniques. To date, no one has presented results that approximate current surgical morbidity and mortality rates. In all deference, Dr. Heisima's results were not equal to those achieved surgically.

We are all open to considering the endovascular approach. I personally am receptive to these techniques and have been working with Dr. Hilal, as his work is exciting. I do think that the present level of neurosurgical capability with the straightforward aneurysm is such that in 90% of the cases the morbidity and mortality rates are sufficiently low that interventional neuroradiologists must demonstrate that degree of success before we can consider it a routine situation where the neuroradiologist sees the aneurysm patient before the neurosurgeon.

Management of Aneurysms in Tertiary Care Centers

Dr. Berenstein: Would the complication rate of neurosurgeons who see 50 cases a year versus a neurosurgeon of equal skill who does 10 aneurysms per year be equivalent?

Dr. Solomon: Absolutely not.

Dr. Berenstein: Therefore the neurosurgeon who is exposed to only 10 cases per year should refer those cases to major centers for expert management.

Dr. Solomon: Obviously, I agree with that position. The treatment of aneurysms should be handled by tertiary referral centers in general, so we can select those that should be treated surgically and those that may be managed by endovascular techniques.

Postoperative Angiography

Dr. Fox: Dr. Heishima, regarding the follow-up care of the patient after parent artery occlusion: About 10 to 25 years ago it was not common to do postoperative angiography in part because many of the occlusions were of the common carotid artery and it seldom isolated the aneurysm. I am wondering about your statement that you had had patients whose aneurysms had regrown after parent artery occlusion. Have any of these aneurysms been proved to be isolated from the circulation after treatment and then observed to recur, or were they never really followed and probably never really treated?

Dr. Hieshima: It probably does not matter. If carotid occlusion was definitive therapy and an aneurysm regrown and ruptures, it is immaterial whether it was once shown to be thrombosed.

Dr. Fox: It makes a difference in that we can learn from this experience. If we now see cases treated with parent artery occlusion that have been proved to be totally isolated from the circulation, your statement is very important.

Dr. Hieshima: There is more to be said. We have seen patients with parent artery occlusion where the aneurysm ruptures after the occlusion. For example, we have seen a basilar aneurysm rupture after occlusion.

Dr. Fox: After it has thrombosed?

Dr. Berenstein: It never thrombosed.

Dr. Hieshima: In these patients we have seen definite evidence of internal carotid occlusion, and in some cases the aneurysm is not thrombosed.

Dr. Fox: Dr. Heishima, you said that patients may come back after 20 years with a new hemorrhage. Has anyone seen cases of complete aneurysmal thrombosis following parent vessel occlusion where the aneurysm recurred? If not, then they all must be considered incompletely treated.

Dr. Hieshima: In your experience, what is the incidence of complete thrombosis of the supraclinoid artery aneurysm after parent artery occlusion.

Dr. Moret: It depends on the site of the occlusion.

Dr. Hieshima: I could disagree with you just on principle. Nothing is 100%.

Dr. Fox: One-third of aneurysms continue to fill after parent vessel occlusion; therefore they are not adequately treated. I would like to believe that they are isolated from the circulation because the flow changes have induced thrombosis and endosaccular occlusion.

Dr. Hieshima: We would like to think that too, but it is not going to be 100% true. Some that you have documented to have been thrombosed completely will be found at follow-up years later to have undergone some degree of recanalization.

Dr. Scheglov: We also see recanalization after clipping.

Dr. Konovalov: How often are you able to preserve the parent artery?

Dr. Hieshima: It depends on the type of aneurysm. With the cavernous aneurysm it is probably about 40% to 50% of the time. If we exclude cavernous aneurysms, it approaches 90%.

Management of Acute Subarachnoid Hemorrhage

Dr. Eliava: You mentioned the indications and contraindications for using these treatment methods in high risk patients. Does it mean that you treat patients who are grade 4 and 5 in the acute stage of hemorrhage?

Dr. Hieshima: Few patients present acutely who are in the grade 4 to 5 categories. It has not been a contraindication for treatment, but we have so few patients that I cannot give you a statistically useful answer. For instance, I showed you the woman with bilateral ICA aneurysms. She was at grade 4 and just 1 to 2 days following her hemorrhage. We treated her, and although we thought she would not recover she is normal today. I must say that I have not faced the aneurysms seen by Dr. Scheglov. His work will guide us in the treatment of aneurysms that once could have been treated only by direct surgery.

CHAPTER 16

Endovascular Treatment of Intracranial Arterial Aneurysms: A Neuroradiologist's Viewpoint

Jacques Moret

It is difficut to be the judge of one's own situation, which is precisely why this analysis made by a neuroradiologist can*not* avoid some degree of a partisan spirit and moreover a degree of partiality, even though it has been edited with the author's intention of avoiding any bias. For the first time since the existence of interventional neuroradiology, one of its most recent therapeutic applications is being considered as a potential replacement for a surgical procedure if only partially but to a degree that is difficult to predict. I refer specifically to the clipping of an intracranial arterial aneurysm. Neuroradiologists who treat the same aneurysm by the endovascular route believe their efforts to be important and glorify them as much as possible. It is possible to comprehend this attitude if the quality of the results is comparable. Alternatively, if neurosurgical treatment is at peak quality with minimal fallibility, it would similarly be glorified as the best approach for intracranial aneurysms. Only by strict scientific honesty will one or the other approaches prevail. It would be detrimental to patients and to the scientific community if the truth of the results were altered in even the slightest degree under the cover of an ill-conceived defense of doing business for business' sake. The primary assumption is therefore to ensure that a competition *not* take place between interventional neuroradiologists and neurosurgeons but between two therapeutic techniques, thereby providing greater benefit to the patient.

In this respect, of concern in the treatment of intracranial aneurysms is that the analysis of the results of both methods of treating intracranial aneurysms presupposes, of course, that equivalent types of aneurysm are compared. It also must reach an agreement as to the definition of what constitutes an anatomical cure and what must be considered a complication of therapy. As anachronistic as this statement may appear, it concerns a fundamental premise. In essence, the value and superiority of one or the other of the two techniques are based on numbers, and these numbers must be derived from similar computations. Let us take, for example, an aneurysm considered cured on an angiogram performed immediately after whichever treatment technique was employed. Will the aneurysm still be cured at 6 months, 1 year, 5 years? What means will be used to obtain this information?

A response to this question is not possible unless the protocols for postoperative follow-up are identical. Let us now take an example of a patient who after treatment of an intracranial aneurysm, irrespective of the technique employed, presented with a discrete neurological deficit such as a quadrantanopsia. Is this deficit counted as a complication unto itself, as a total hemiplegia would be? A response to this question is not possible unless one takes into account the total postoperative neurological deficits, no matter how serious or insignificant, and subjects them to a statistical analysis.

If one looks at the evolution of the indications for the endovascular treatment of intracranial aneurysms in a chronological fashion, as is the case for all new techniques, the first applications arise from what seemed to be the impossible: from difficulties or from the risks attendant to usual neurosurgical procedures. It is also natural that the first candidates for the endovascular approach were those possessing giant aneurysms of the intracavernous internal carotid artery. In fact, these first indications permitted us to establish clearly that internal carotid occlusion, which is one of the effective therapeutic means utilized and often is proposed as the only one that should be achieved by the endovascular route. The superiority of this methodology has been effectively established for the future. Its intraoperative trauma is negligible, and its neurological complications (3% according to my statistics) are infinitely fewer than those seen with surgical ligation, as it allows high occlusion at the carotid siphon. Moreover, it nearly completely avoids the risks of distal embolization (the deadspace of the carotid lumen being the site of thrombosis and the origin of emboli situated upstream from the occlusion). Also more complete clinical control of the patient during the test occlusion (patients are under simple neuroleptanalgesia) and a controlled angiographic technique perfected as an anatomical substitute for the circle of Willis coupled to a self-recording transcranial Doppler and eventually to an electroencephalogram are the necessary parameters to ensure the security and ease of performing and perfecting the endovascular approach. All indications for occluding a feeding vessel of an aneurysm, whatever that vessel (internal carotid, vertebral, anterior cerebral arteries, posterior or middle), are the same as those for endovascular treatment.

Selective exclusion of an aneurysmal sac from the feeding vessel was the logical evolution and goal of endovascular treatment. Giant aneurysms (regardless of whether they are partially thrombosed) pose difficult problems for the neurosurgeon and should naturally be among the first anatomical structures proposed for endovascular treatment: endosaccular balloon occlusion of the aneurysm with preservation of the feeding vessel. Single or multiple inflated balloons are placed within the aneurysmal sac with the assistance of angiographic contrast material and then with polymerizing substances (which ensure preservation of a discrete volume over time) have in fact provided the anticipated results. It is difficult anatomically to obtain a perfect congruence of shape with the small balloons available some of which are

grossly round and some oval, thereby facilitating complete filling of a large aneurysmal sac or the occlusion of a neck that is often large. We have found that the treatment of large or giant aneurysms with respect to the feeding vessel cannot be realized reliably using small balloons. Using the technique of endosaccular thrombosis by means of "coils" (small springs coated with hair-like bristles), biological glues, or electrocoagulation in situ is certainly, on a purely theoretical basis, more satisfactory. Meanwhile controlling the extent and the volume of thrombosis remains a difficult problem. Perhaps the association of thrombogenic methods and balloon occlusion will result in a viable and efficacious treatment. When dealing with a large or giant aneurysm, I still prefer to occlude the feeding vessel whenever possible, always using the endovascular route.

The development of the techniques of intracerebral navigation—first placement and then the release of a small balloon—has progressively rendered the virtual totality of small aneurysms that do not exceed 1.5 cm (the most numerous) accessible to endosaccular occlusion by the endovascular route. Until recently it was impossible to treat some small aneurysms, the major problem being the deadspace of the microcatheters, which made it impossible to effect complete exchange of the contrast material for the polymerizing substance. This problem was resolved thanks to the utilization double pathway systems.

We are thus faced with a paradoxical situation where the best indications for neurosurgical treatment are also the best indications for endovascular treatment. In effect, the small aneurysms lend themselves to balloon occlusion better than large or giant aneurysms—an occlusion that is always achieved in our experience by placing a single balloon in the aneurysmal sac. Three modalities of occlusion may be used: (1) *Endosaccular packing*, where the balloon conforms perfectly to the aneurysmal sac and at the same time obstructs the neck. This endovascular treatment is ideal and should be used each time it is feasible. (2) *Endosaccular valving*, where the balloon in positioned along the major axis of the aneurysm in such a manner that its fundus is occluded by the valve effect on the neck of the aneurysm. (3) *Endosaccular clipping*, where the balloon excludes the aneurysm by occlusion of its neck alone. This technique is useful, but it should not be considered until after trying the other two methods because it is often responsible for recurrences later on.

Personal Experience

My personal experience allows me to submit for comparison a homogeneous series of 100 small aneurysms (< 1.5 cm) treated by the endovascular route, with release of the balloon totally inflated with a polymerizing substance in the aneurysmal sac. All of these aneurysms could have been

managed by the neurosurgical route. Of the 100 patients, 17% were treated as an emergency, that is, within the first 24 to 72 hours after the hemorrhage; 36% were treated somewhat later after the hemorrhage (between the eighth and tenth days); and 47% of the patients had no evidence of aneurysmal bleeding. The follow-up angiography was systematically performed at 4 or 6 months and again at 15 or 18 months; it disclosed a 16% incidence of aneurysmal refilling, which retrospectively could have been anticipated by the semicomplete inflations. In fact, at the beginning of our experience the fear we had in certain cases of rupturing the aneurysmal sac led to leaving a small portion of the aneurysmal neck in the event of overinflation of the balloon. These cases for the most part were the ones that later showed refilling of the aneurysm. Six of these recurrences were retreated by the endovascular route. Among more than 106 endosaccular occlusions there have been 6 deaths (5.5%) and 8 neurological complications (7.5%). These numbers hold to the rule-of-one by complications without taking into consideration the importance of each one. It must be noted that rupture of an aneurysmal sac during the course of treatment occurred on only one occasion for a frequency of 0.9%, and that most of the complications and deaths were in fact related to clotting despite the considerable use of systemic heparin. The association of heparin plus aspirin seems to provide satisfactory control for the clotting phenomenon observed.

If one would wish to compare this endovascular series with a neurosurgical series, it would be necessary that both postulates we posed in the beginning of this chapter are applied. One must be able to ascertain that equivalent complications obey the same rules, and certain parameters in the meantime must modulate the number of complications of endovascular treatment. Therefore 54% of the aneurysms we have treated by endosaccular occlusion were equally located half in the carotid-ophthalmic circulation and the other half in the vertebrobasilar circulation. Except for these sites, the other aneurysms were in incontestably difficult locations for neurosurgical approaches and consequently would involve the most risky operations. This parameter therefore plays a role as a minor factor when considering complications of endovascular treatment. Another factor that minimizes the complications of the endovascular route is the absence of trauma in this therapeutic approach, which makes it possible to envision endovascular intervention in patients whose clinical grade is III or IV. This was the situation in three patients of our series. Among the factors that are major contraindications of endovascular treatment is the fact that the endovascular route does not permit lavage of the subarachnoid spaces. Hence the risk of vasospasm during the postsubarachnoid hemorrhage period is increased. In fact, this argument is not sufficiently supported; and it is posed more as a question than as an argument. The endovascular technique does have the capacity to solve the problem of vasospasm: If the vasospasm became symptomatic, it would greatly benefit from endovascular dilation, on the condition that the

dilation would be most effective during the first hours following the appearance of clinical signs (ideally before the sixth hour).

The evaluation of the two methods is completely different when using the criterion of "cure." It is exceptional for postoperative follow-up in surgical series to include systematic angiographic control at a point remote from the time of the operation. Some neurosurgical teams do not even use immediate systematic angiographic controls. Therefore the percentage of surgical relapse is certainly much more difficult to determine even if the series has stated an incidence of perhaps 5% to 6%.

Discussion

With a success rate of 72%, regardless of the localization of the aneurysm, and taking into account the fact that we reduced the complications associated with endovascular treatment, endosaccular occlusion of small intracranial aneurysms (berry aneurysms) using small balloons has already attained the level of results of neurosurgical treatment. Scientific honesty nevertheless imposes the need to reiterate the fact that we have compared standard neurosurgical results with endovascular results obtained by a team of interventional neuroradiologists having the greatest international experience in this field. This fact signifies that our results today appear, in their totality, perhaps still inferior to the results of the most successful neurosurgical teams.

We believe that the advantages of endovascular treatment are undeniable, and that our results entitle us to propose endovascular treatment for aneurysms at carotid-ophthalmic and vertebrobasilar sites that present problems for the neurosurgeon. With regard to other sites, endovascular treatment remains debatable, and its indications must be evaluated by more than one discussion among various therapeutic teams.

Using the endovascular method initially appears logical, as experience permits us to recognize, during the course of the endovascular treatment, the anatomical and hemodynamic elements that may increase the risk of complications. It is then possible to interrupt the interventional procedure without prejudice or trauma and to pursue the neurosurgical approach.

This approach requires a multidisciplinary team, which will gives rise to some standardization of indications. This possibility, by itself, is as important as the fact that neurosurgery during the last few years has become enriched by the ability to perform intracavernous aneurysm surgery, which until the present was an area reserved for interventional neuroradiology.

Technological progress, which knows no limits or sentiments of business as usual, could one day recapture the ideal that the interests of the patient stand above all other forms of consideration. It is for the reason that the problem is not to know whether the neurosurgeon or the interventional

neuroradiologist should treat intracranial aneurysms. Each of the two disciplines and their proper therapeutic armamentaria necessitate a particular and specific structure that makes them not interchangeable, which is good because of the multiplication and diversification of therapeutic modalities. It provides us the opportunity of expanding the indications and improving the results. It is much more important that each in his or her specialty confront the evidence of creativity on the whole and in this way strengthen the therapeutic arsenal.

Addendum: Endovascular Treatment of Berry Aneurysms by Endosaccular Occlusion

Although there is tremendously more experience in the surgical treatment of aneurysms than there is in endovascular treatment, it is possible to have a good idea of what the future will be. As a matter of fact, we have a better approach to the endovascular treatment possibilities and results even on a long term basis if we refer to our experience in endovascular treatment of berry aneurysms begun in march 1988. In order to avoid comparing "apples and oranges," this study takes into account only what is commonly called "berry aneurysms," that is, typical surgical aneurysms whose sizes are equal or inferior to 1.5 cm and which extend intracranially and, in almost all the cases, totally in the subarachnoid space.

The specificity of our study is double: first, it is indeed strictly comparable to the neurosurgical series regarding the material as it has been described above; second, all the aneurysms have been treated by the same team, using the same endovascular technique, and the same rules of follow-up (first control angiogram 3 months after the endosaccular occlusion, second control angiogram one year after the first one). At the beginning of our experience, all the aneurysms underwent an endosaccular occlusion using a latex balloon filled with 100% polymerizing substance (Polymeran® from Balt company). At the end of 1991, we moved to a combined treatment by association of fiber-coils (from Target), to pack most of the aneurysmal sac, with a balloon to occlude the aneurysmal neck.

Currently, since October 1992, we have completely abandoned the previously described technique, and we use only electrically detachable coils (GDC® from Target) or, more recently, mechanically detachable spirals (MDS® from Balt). Both safely offer a dramatic improvement of treatment capabilities. Navigation and positioning of the coils are achieved with either a Traker® 10 catheter (from Target) or a Mag® catheter (from Balt).

Since then, we have attempted treatment of 324 berry aneurysms in 309 patients (158 with balloon and 166 with detachable coils). The results here consider only the 166 berry aneurysms that have been treated in 156 patients with the detachable coils technique. The localizations are as follows:

• intracavernous (partially)	10
• carotido-ophthalmic	25
• posterior communicating artery	14
• carotid bifurcation	3
• basilar artery (tip or trunk)	46
• middle cerebral artery	28
• anterior communicating or anterior cerebellar artery	32
• posterior cerebelar artery and cerebellar artery	1
• posterior-inferior cerebellar artery	3
• subarachnoid vertebral artery	4
	166

Forty-eight cases were acute patients who bled within 48 hours before treatment; 63 cases were nonacute patients who bled 10 days to some weeks before treatment; 55 patients had never hemorrhaged.

Because of arteriosclerosis or the impossibility of occluding the aneurysmal sac or entering the aneurysmal neck, the endosaccular occlusion failed in 19 cases (1 of those cases has been treated by parent vessel occlusion). Finally, 148 of the 166 cases (89%) were successfully treated (95 cases with GDC®, 41 cases with MDS®, 12 cases with GDC and MDS). Eight patients have had 2 aneurysms and 1 patient had 3 aneurysms treated by endovascular occlusion. Sixteen patients were partially treated (persistence of a part of the aneurysmal neck on the immediate control angiogram) because of technical difficulties in achieving a complete cure. In 8 cases presenting with a broad neck, we have used the reconstructive technique (balloon protection of the neck while the sac is packed with the coils).

The long term follow-up shows: 5 recurrences over the 148 aneurysms treated by selective occlusion of the sac (4%); 103 patients are cured; 24 patients have not yet been controlled.

There were 10 complications over 166 cases (6%). Analysis of those complications reveals 2 deaths and 8 neurological deficits. One of the 2 deaths occurred because of rebleeding after partial treatment, the other one because of rupture of the aneurysm during treatment in an acute case. Six of the 8 neurological deficits are related to clotting phenomena despite the fact that all the treatments were performed under full heparinization associated with aspirin except in cases of emergency.

Using the Hunt and Hess scale, 164 patients were graded between 0 and 2, and only 2 were grade 3. Over the 148 cases that have been treated, the results according to the neurosurgical scale are as follow:

- Excellent: 138(93%);
- Good: 6(5%);
- Poor: 2(1%);
- Bad: 2(1%).

In conclusion, at this stage of our experience we can say that 89% of intracranial berry aneurysms can be treated by endosaccular occlusion using detachable coils regardless the anatomical location, the grade, and the clinical presentation. We do recommend treating the berry aneurysm in emergency as neurosurgeons do, that is, at the same as the diagnostic angiography. Finally, behind the statistics which are absolutely necessary to evaluate the performance of a given technique, it is the philosophy of treatment of berry aneurysms which has changed. Endosaccular occlusion is definitely an alternative treatment whose indications must be discussed in priority for carotido-ophthalmic and basilar aneurysms whatever the circumstances of discovery are. In asymptomatic aneurysms, a careful attempt at endovascular treatment carries few risks and seems to also be the first choice of treatment in most localizations (except the middle cerebral artery), especially since its failure can be immediately followed by a surgical procedure.

Discussion

Endosaccular Berry Aneurysm Occlusion Technique

Dr. Moret: One of the secrets of success in the treatment of berry aneurysms is to fill fully the volume of the balloon with a pure polymerizing substance. Any kind of mixing with the contrast material used for the test occlusion before introducing the polymerizing substance is avoided. An important point is that if you want to use the latex balloon you must avoid having the HEMA come in contact with ether. This is the reason we developed a HEMA (produced by Merck Co.) that provides a better solution and does not degrade the latex. The other problem is to reduce the water content of the solution inside the balloon: HEMA shrinks with drying, and if you wish to avoid shrinking you must decrease the amount of water in the solution.

In the solution we use, instead of using 1 ml of a 3% solution of peroxide we use a 0.1 ml solution of 30% peroxide. This mixture is added to the radiopaque substance, which amounts to adding 1.5 ml of 200 mg of nonionic contrast material. Each time you make this addition you put 6 drops of solution B into solution A, and you always obtain solutions that behave in the same fashion. That point is important.

Brief Exchange Regarding the Technique of Endosaccular Packing

Dr. Moret: I do not think we are changing anything in the sac if we do this kind of endosaccular packing. We had a case in which the balloon completely filled the space within the sac of a posterior communicating artery aneurysm. The catheter was detached, and the aneurysm was completely cured with preservation of the posterior communicating artery.

Dr. Debrun: How could you say the aneurysm was completely cured?

Dr. Moret: There was no more aneurysm visible.

Dr. Fox: In your slide I see a neck with contrast around it.

Dr. Moret: There is a neck, but this is a 3-month follow-up angiogram, and I cannot tell you that it does not represent a recurrence of the sac. The sac is there and is occluded. If there is a small neck, do you think it is going to trouble the patient?

Dr. Debrun: Tell me in 1 year.

Dr. Moret: This case illustrates the various ways of approaching the sac of an aneurysm. A small portion of the neck remains here. It is always a compromise between the size of the aneurysm and the mass effect.

Dr. Fox: That is correct, and you will know with your follow-up, but you should perhaps change your words. You should not say the aneurysm is *completely* filled. You should say the aneurysm is *mostly* filled. Just a matter of terminology.

Dr. Moret: I stand corrected. The aneurysm is almost completely filled. A supraclinoid internal carotid aneurysm was treated with endosaccular placement of a small balloon. A control angiogram 4 months later showed 99.999% occlusion. We can never say 100%.

Treatment of Acute Aneurysmal Rupture

Dr. Tavaras: What percent of patients were in the acute stage of subarachnoid hemorrhage?

Dr. Moret: It was 6% overall: 6 of 35 treated.

Dr. Taveras: That figure represents a relatively lower percentage than is encountered by neurosurgeons when they treat aneurysms.

Dr. Moret: The problem is that we had to convince the neurosurgeons that the procedure was possible; afterward they agreed. Now they know that we are able to treat the difficult cases, and they have developed some confidence with the technique.

Dr. Stein: It is an obviously elegant and useful technique. As a corollary, how do you treat vasospasm when it appears after occlusion of the aneurysm?

Dr. Moret: We anesthetize the patient with nimodipine (the antichannel blocker) and increase the volume of circulating blood. We also utilize hypertensive therapy.

Dr. Stein: Have you had any major problems from delayed ischemia?

Dr. Moret: No. The only problem we ever had concerned the patient with a basilar tip aneurysm, which was treated. That patient finally died from the sequelae of vasospasm that could not be relieved.

Dr. Berenstein: Did you try angioplasty?

Dr. Moret: No.

Dr. Berenstein: Would you try it tomorrow in the same situation?

Dr. Moret: Yes, I would.

Aneurysmal Recurrence

Dr. Kachkov: Did any of the aneurysms recur?

Dr. Moret: Yes, there were two reopenings of aneurysms at long-term follow-up.

Repositioning a Balloon

Dr. Viñuela: Repositioning the balloon is an unfortunate situation because in doing so you leave a space, and the balloon can move back to the original position. Therefore it is not a guarantee that the patient will do well. In just such an instance there was temporary success and recovery, but later the balloon returned to the same position and the patient suffered a stroke.

Dr. Moret: How much later?

Dr. Viñuela: Three days later, after the patient has gone home. Of interest is that she was 72 years old, and we had occluded the aneurysm acutely. The aneurysm had a wide neck with a direct origin from the posterior communicating artery. When the first balloon was positioned, we put the second balloon in to detach it and probably pushed it a bit. When we detached and deflated the second balloon everything was fine. Fifteen minutes later in the radiology suite she developed symptoms (which we recognized because the EEG leads were still in place) and then frank hemiplegia. We moved the second balloon into a different position, and she recovered. She was taken to the ICU and kept there for 3 days using hypertensive techniques. She then went home and developed a stroke at home. After reviewing this case my belief is that when we reposition a balloon we may be creating a "loose balloon."

Dr. Moret: We must know exactly a balloon's position when we reposition it inside an aneurysmal sac.

Dr. Apuzzo: I would be concerned about increasing the systemic arterial pressure because of the possibility of pushing the balloon out into the dome of the aneurysm. How can you reassure me on that account?

Dr. Moret: Mechanically speaking, if the aneurysm neck is completely occluded there is no way to compress fluid. The blood behind the balloon is going to thrombose,

but even when the blood is not thrombosed we are dealing with a fluid. The only way to compress the fluid is to have a sac that is expansile. You can imagine the sac and imagine that the balloon will move after the sac expands. This, of course, is a possibility. I have seen only one such example with recanalization. We will see if the technique of balloon repositioning is valid only after a long-term follow-up.

Dr. Fox: Do you heparinize patients during the procedure so the trapped blood is heparinized blood?

Dr. Moret: Yes, but the heparin is reversed immediately after the procedure is completed.

Dr. Fox: How does the protamine sulfate get into that isolated region of the sac?

Dr. Moret: The vasa vasorum might be a mechanism for protamine entry.

Dr. Hilal: The blood itself eventually degrades the heparin. I have a problem with endovascular clipping. You said correctly that blood is not going to go anywhere because it is not compressible. If after you block the aneurysm neck you produce a chamber behind the balloon that is closed, and if you inflate the balloon a bit more, would it not tend to distend the aneurysm because there is a closed chamber behind the balloon?

Dr. Moret: Mechanically speaking, everything you say is true. The problem is to look at reality. The reality is that it is possible to occlude an aneurysm by doing that endovascular clipping.

Dr. Hilal: Yes, but what is your trick? I am trying to find out how you know when to stop inflating the balloon and when have you trapped the neck?

Dr. Moret: I obtain a control angiogram. When there is no longer any filling of the aneurysm, I deem the neck occluded. Also, before detaching the balloon I always inflate it a bit more (with 0.01 ml) just to be sure the balloon is anchored at the neck.

Dr. Berenstein: What you are doing is remarkable. You are obviously in an environment where you can do it. Your work is important, and you have a major duty to follow these patients closely. I think it is still too early to speak about cures. I know you will continue this work and will improve technically even further. It is important to say that this is what we can do at the present—and time will tell about the results.

III. ENDOVASCULAR EXPERIENCE

C. ARTERIOVENOUS MALFORMATIONS

CHAPTER 17

Clinical Aspects, Diagnostic Evaluation, and Surgical Treatment of Posterior Fossa Arteriovenous Malformations

Yuri M. Filatov and Shalva S. Eliava

The results of clinical examination and treatment of 95 cases (64 males and 31 females aged 8–50) of posterior fossa arteriovenous malformations (AVMs) are reported. There were 45 surgical procedures: 34 total excisions of the AVM and various other operations as described. An anatomicosurgical classification of posterior fossa AVMs is outlined based on angiography, computed tomography (CT), and surgical approaches to the lesions. A total of 83 patients presented with hemorrhage and 12 with only focal neurological deficits. The analysis of the neurological symptoms of posterior fossa AVMs showed relatively poor correlation between the symptoms and the site of the AVM.

This chapter presents an analysis of the indications for surgical treatment of posterior fossa AVMs and the techniques for total excision. It also examines the microsurgical anatomy of anastomoses between the superior cerebellar artery (SCA) and the posterior cerebral artery (PCA), and their importance in regard to posterior fossa AVM surgery.

The AVMs that arise from the vertebrobasilar circulation and are located in the posterior fossa are unusual lesions. Various authors have estimated the frequency of these AVMs at 2.5% to 20.0% of all AVMs of the brain.[1–10] This wide range is due to the fact that until recently vertebral angiography was used rarely because of frequent complications. In our series of about 1250 intracranial AVMs we have encountered 87 malformations in the posterior fossa (7%).

The clinical picture of posterior fossa AVMs was first reported by Clingston in 1908.[11] Dandy in 1928 was the first to describe the surgical treatment of posterior fossa AVMs.[12] In 1932 Olivecrona was the first to totally excise a cerebellar AVM.[13] Fundamental reports on the clinical features, diagnostic evaluation, and surgical treatment of posterior fossa AVMs have been numerous since the 1970s.[1–4,6,7,9,10,14–21] However, more experience is needed to evaluate the clinical picture of posterior fossa AVMs and the potential for their surgical treatment.

The aim of this chapter is to give a detailed description of clinical features, diagnostic evaluation, and surgical treatment of posterior fossa AVMs at different sites in 95 patients. An analysis is made of the sources of blood

supply and the revascularization of AVMs located in midline-oral sections of the cerebellum and in the area of the tentorial incisura. For this purpose, the microsurgical anatomy of anastomoses between the SCA and the PCA was studied.

Clinical Material and Methods

The clinical aspects of 95 cases of posterior fossa AVMs (64 males and 31 females, aged 8–50) are reported. These patients presented at our institute during the last 30 years. Of these 95 patients, 45 underwent various surgical operations. The comprehensive clinical examination of the patients included a detailed neurological examination, vertebral angiography (all patients), and scanning CT (the last 21 patients). With rare exceptions, all the patients presented during the delayed period after bleeding.

The microsurgical anatomy of anastomoses between the SCA and the PCA was studied in 15 brains removed at autopsy after deaths resulting from diseases unrelated to brain pathology. The arteries and veins of the removed brains were perfused with colored latex.

Results and Discussion

Posterior Fossa AVM Classification

An anatomicosurgical classification of posterior fossa AVMs was established after analyzing angiograms, CT data, and surgical approaches to malformations. The clinical material was arranged as shown in Table 17.1.

The group of extensive AVMs comprises large malformations affecting several posterior fossa structures. AVMs are divided into three groups by size: small (2.5 cm), medium (2.5–4.0 cm), and large (>4 cm).

Table 17.1. Anatomicosurgical classification of posterior fossa AVMs

AVM site	No. of cases
Cerebellar AVMs	
Midline oral or slightly extending unilaterally	30
Lateral hemispheric	38
Midline caudal	4
Brainstem	10
Cerebellopontine angle	3
Extended	10
Total	95

Clinical Aspects of Posterior Fossa AVMs

The clinical aspects of posterior fossa AVMs suggest their division into two major groups: those with and those without intracranial hemorrhages, the latter being the so-called pseudotumorous type.

A total of 83 patients had intracranial hemorrhages: 137 hemorrhages were recorded, of which more than 60% were severe causing loss of consciousness. In 58% of patients hemorrhages were recurrent—in more than 50% of cases with interhemorrhage intervals of 1 to 12 months. No relation between the number of hemorrhages, their severity, and the dynamics of clinical syndromes was found.

During the acute bleeding period most patients, in addition to a marked meningeal syndrome, had local symptoms of brainstem or cerebellum dysfunction (or both) that usually persisted over posthemorrhage periods. Ten patients demonstrated crossed paralysis, four of them only at the acute stage of bleeding, and five during both the acute stage and the extended period. One patient with a midline-oral nonbleeding AVM also presented crossed paralysis. In addition to the crossed paralysis, four patients had a marked trigeminal pain syndrome.

Thirteen patients (16%) had clinical signs of intracranial hypertension. In three of these patients the clinical signs regressed following surgical intervention and in nine after drug therapy. A Torkildsen shunt operation was performed in one patient. Analysis of neurological symptoms of posterior fossa AVMs also allowed us to single out a group of cases with marked regression of these symptoms after hemorrhage.

Table 17.2. Dependence of neurological symptoms on site of AVMs associated with intracranial hemorrhages

	No. of patients with neurological symptoms				
AVM site	Mainly brainstem	Mainly cerebellar	Brainstem-cerebellar	With marked regression after hemorrhage in delayed cases	Total
Cerebellum					
Midline-oral regions	11	6	8	2	27
Lateral hemispheric regions	9	4	18	3	34
Midline-caudal regions	0	0	4	—	4
Brainstem	2	0	6	1	9
Cerebellopontine angle	1	0	0	1	2
Extended	1	0	6	—	7
Total	24	10	42	7	83

Table 17.3. Dependence of neurological symptoms on site of AVMs without intracranial hemorrhages: the "pseudotumorous" type

AVM site	No. of patients with neurological symptoms		
	Mainly brainstem	Brainstem-cerebellar	Total
Midline-oral	0	3	3
Lateral hemispheric regions of cerebellum	0	4	4
Brainstem	—	1	1
Cerebellopontine angle	—	1	1
Extended	2	1	3
Total	2	10	12

Except for the brainstem AVMs, all cases demonstrated hypertrophied trunks of the feeding arteries of the malformations, irrespective of the AVM size. Mention should be made of the possibility of the AVM blood supply coming from the PCA basin in cases of marked arteriovenous (AV) shunting. It is via normally existing anastomoses between the SCA and the PCA. These vessels are angiographically visible only in AV shunting owing to the displacement of dynamic equilibrium zones in the vascular system of the brain.

Of special interest is the dependence of clinical symptoms on the site of the posterior fossa AVM in patients with intracranial bleeding. A comparison of the posterior fossa AVM site with neurological symptoms shows relatively poor correlation (Table 17.2).

Of 12 patients with nonbleeding posterior fossa AVMs, 10 had symptoms of both a brainstem lesion and a cerebellar lesion, and two (with extended AVMs) had symptoms only of a brainstem lesion (Table 17.3). Four patients in the group complained of head throbbing simultaneous with the pulse; it disappeared after pressing the carotid artery. All 12 patients were believed to have posterior fossa tumors prior to angiography.

Radiographic Evaluation

Vertebral angiography is currently the most informative diagnostic method for posterior fossa AVMs. An analysis of the angiograms revealed some special angiographic features of this pathology. Blood supply and venous drainage conditions of posterior fossa AVMs are determined not only by the AVM site but also by its size and by the degree of the arteriovenous (AV) shunt.

The angiographic picture of posterior fossa AVMs has been described in detail by many authors, so we concentrate on certain peculiarities of the posterior fossa AVM blood supply, which attracted our attention. A special angiographic picture is observed with brainstem AVMs. Their blood supply involves one or several small arteries of the brainstem arising from the ba-

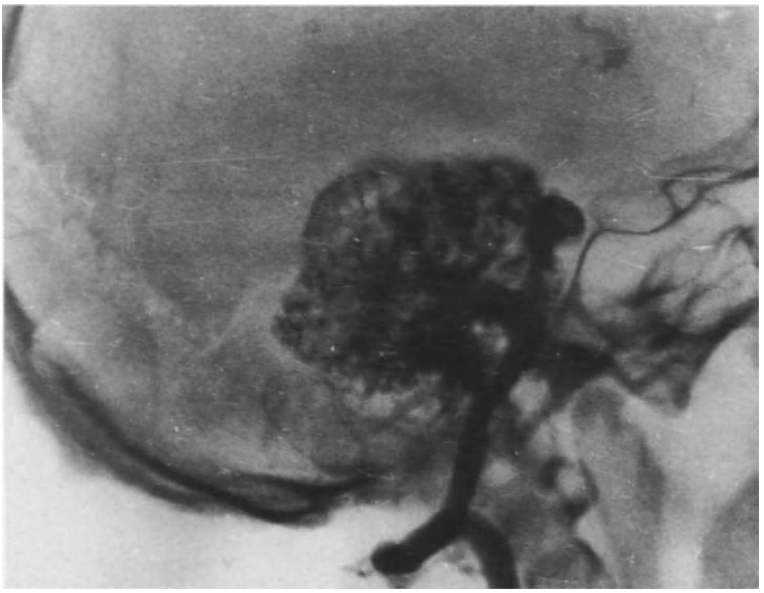


Figure 17.1. Vertebral angiogram, lateral view, showing the extent of the posterior fossa AVM supplied from almost all cerebral arteries.

silar artery. This situation complicates the process of distinguishing the feeding arteries of the malformation, and it is the reason for the absence of hypertrophic changes in the main trunks of the vertebrobasilar arterial system.

Only four of the observed posterior fossa AVMs showed angiographically verified involvement of anastomoses in the blood supply of the malformation. This source of blood supply was verified by carotid angiography when the AVM was located in midline-oral sections of the cerebellar hemispheres, i.e., when the SCA trunks were the principal source of blood supply (Figs. 17.1, 17.2, 17.3).

Computed tomography scans of the brain were obtained in 21 cases. With only one exception, posterior fossa AVMs were shown to be present. In 16 cases there were direct AVM signs: an area with increased density and uneven contour lines. In three cases of a large AVM, draining veins were visualized. In four cases indirect signs of AVMs were seen: areas with decreased density reflecting cystic cavities that formed after intracerebellar hemorrhages. One patient during the acute period of intracranial bleeding demonstrated blood in the cavity of the fourth ventricle. In two cases there was fourth ventricle displacement, which prior to angiography had been thought to be a vascular tumor.

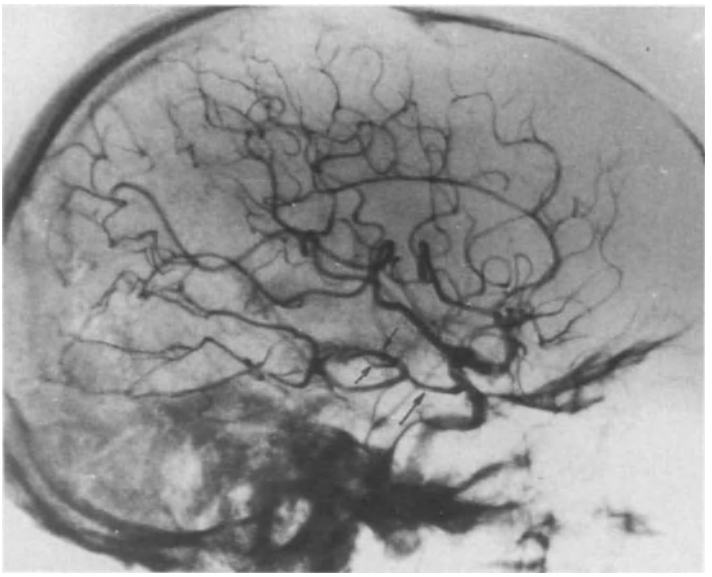


Figure 17.2. Carotid angiogram of the same patient as in Figure 17.1, lateral view. The hypertrophied trunk of the posterior communicating artery is indicated by the long arrow. Short arrows indicate two arteries coming from the precommunicating segment of the PCA (anastomosis-forming arteries) and taking part in the blood supply of the oral portion of the AVM.

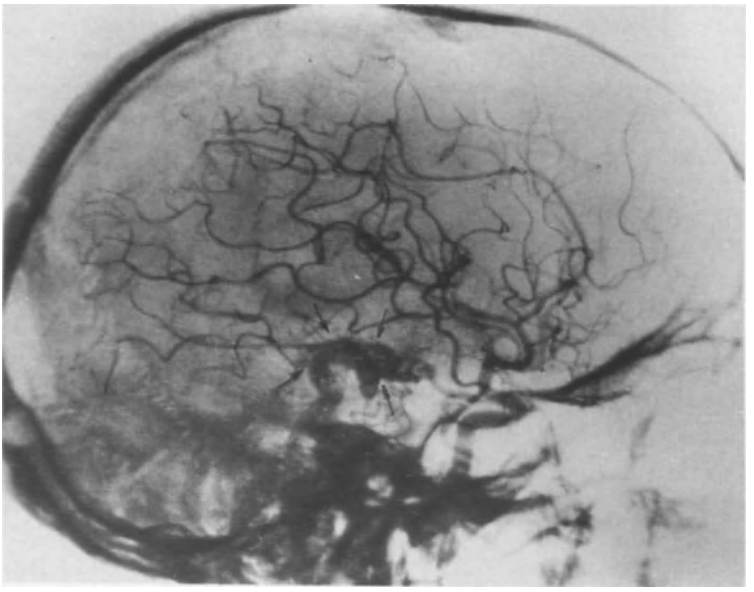


Figure 17.3. Carotid angiogram of the same patient as in Figures 17.1 and 17.2, lateral view. The oral portion of the AVM, which is filled by the anastomoses between the SCA and the PCA, is shown by arrows.

Surgical Treatment of Posterior Fossa AVMs

The reported experience of surgical treatment for posterior fossa AVMs is based on 45 cases of posterior fossa AVMs involving 34 radical operations (total excision of the AVM), 8 palliative operations (clipping of feeding arteries and coagulation of the AVM vessels), and one each of the following: exploratory trephination of the posterior fossa (the operation was discontinued due to anesthetic complication), a Torkildsen shunt operation for occlusive hydrocephalus, and stereotaxic destruction of the Gasserian ganglion in a patient with trigeminal pain syndrome. All patients were operated at least 1 month following the last intracranial hemorrhage.

Table 17.4 presents data on the 34 cases of total excision of posterior fossa AVMs. Most cases (29 of 34) involved medium and small malformations. In only 5 cases was there total excision of large AVMs. Four of the 34 patients died, and death was caused by purulent periventricular encephalitis (two patients), postoperative hematoma (one patient), and thromboembolus of the pulmonary artery (one patient).

The site and size of the malformation are of paramount importance when deciding to operate on posterior fossa AVMs. A malformation was considered inoperable if angiography and CT showed it to extend to brainstem structures (15 cases). Large AVM size was the reason for rejecting radical surgery in 22 cases. AVM hemodynamics and the number and character of feeding arteries and draining veins are also basic considerations before surgery. The blood supply of the malformation by several feeding arteries and multivessel drainage are not absolute contraindications to surgical treatment, although they significantly complicate total excision of the AVM.

Recurrent hemorrhages during a period of 1 month were seen in only four patients. Operations during the acute stage of hemorrhage are often complicated by the presence of edema and hemorrhagic blood. Operations during the delayed period are more expedient. Emergency surgical intervention is indicated only in cases of intracerebral hematoma, the localization of which in the posterior fossa imperils the patient's life.

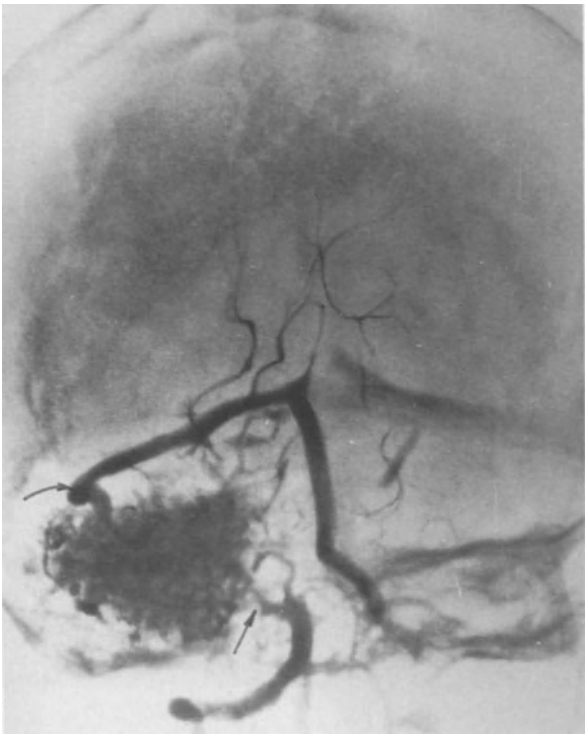
Table 17.4. Data on total excision of posterior fossa AVMs

AVM site	No. of cases	Small AVM	Medium AVM	Large AVM	Mortality (No.)
Cerebellum					
Midline-oral regions	9	1	5	3	4
Lateral regions	16	7	7	2	—
Midline-caudal regions	3	1	2	—	1
Cerebellopontine angle	1	—	1	—	—
Brainstem	5	4	1	—	2
Total	34	13	16	5	4

Patients were operated on in the sitting position, which improved the observation of posterior fossa structures, facilitated orientation in the operative wound, and improved venous drainage. Moderate arterial hypotension was induced.

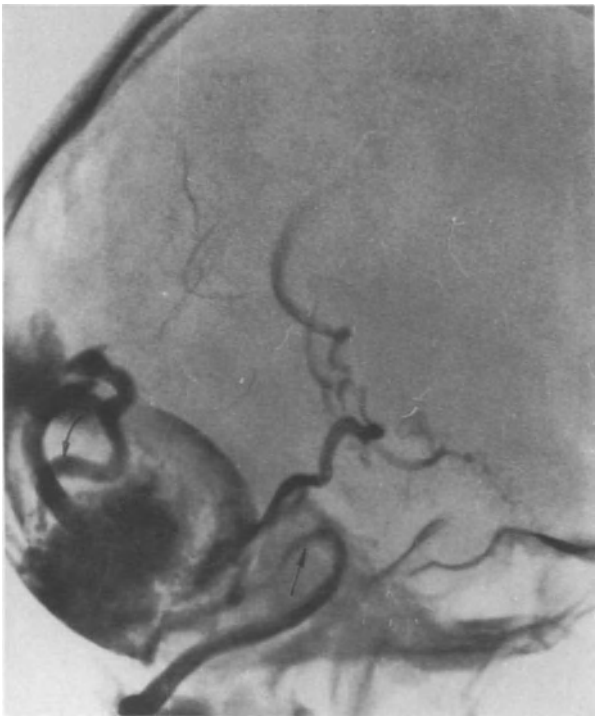
Midline-oral cerebellar AVMs and brainstem AVMs are the most difficult ones for total excision. For surgical treatment of AVMs at this site we used principally the suboccipital supratentorial approach with tentoriotomy. An L-shaped tentoriotomy 3 to 4 cm long was performed parallel to the sinus rectus and 1.2 to 2.0 cm distal from it. Two cases involved exploratory posterior fossa trephination from the midline incision. Both approaches were used for total AVM excision.

To clip the SCA, which supplies blood to AVMs in the oral sections of the cerebellum, we used a subtemporal approach with or without tentoriotomy, depending on the level of bifurcation of the basilar artery. This technique makes it possible to follow the SCA trunk from the point of origin from the



A

Figure 17.4. Vertebral angiograms, AP (**A**) and lateral (**B**) views, of a cerebellar AVM with lateral hemisphere localization. It is supplied from the PICA (straight arrow). Blood drainage from the AVM is mostly through the transverse sinus (curved arrow).



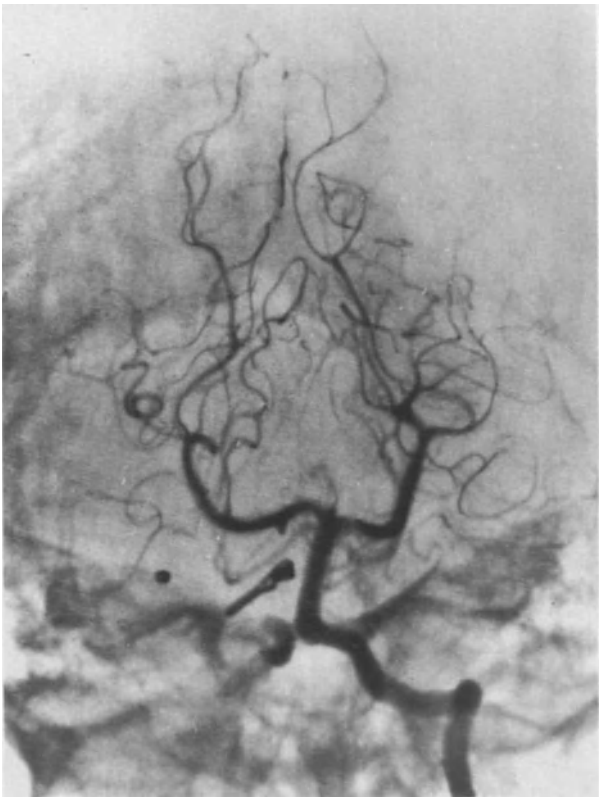
B

Figure 17.4 (*continued*)

main artery to the horizontal segment located in the fissure between the oral sections of the cerebellar hemisphere and the contiguous structures of the mesencephalic segment of the brainstem. Retrospectively, we can say that this approach does not permit visualization of the segment of the SCA that most frequently gives rise to vessels forming anastomoses with the PCA branches. Approaches to AVMs at other sites present no difficulties and are widely used for surgery on posterior fossa lesions.

Direct exposure of the vascular noduli of the malformation was performed with the help of a binocular surgical telelens or microscope, special microsurgical instruments, and bipolar forceps. The exposed feeding arteries were coagulated with bipolar surgical forceps alongside the vessels and divided. Disposable silver clips were used on large vessels to prevent recurrent bleeding after withdrawal from induced arterial hypotension.

Total AVM excision (Figs. 17.4 through 17.7) began with occlusion of most or all arteries feeding the malformation, with further clipping and dividing of the drainage veins. This technique reduces the risk of massive bleeding during excision, which is dangerous because of the proximity of the



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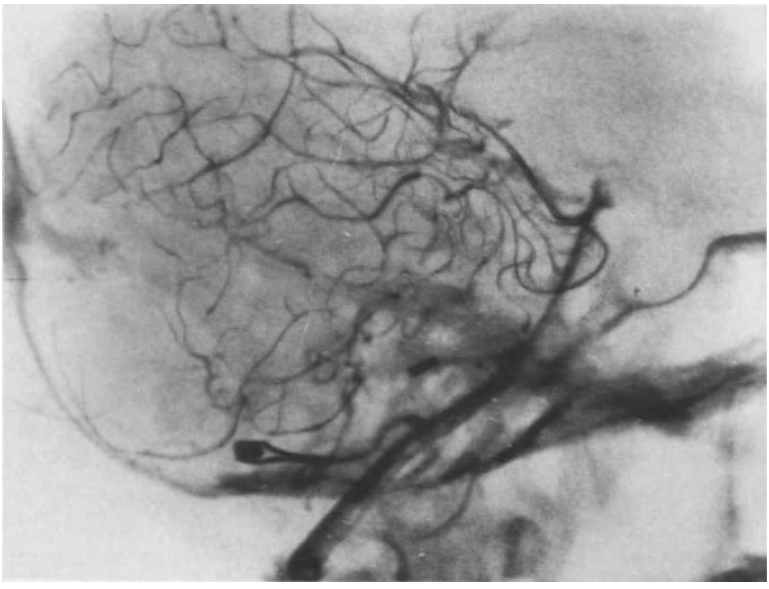
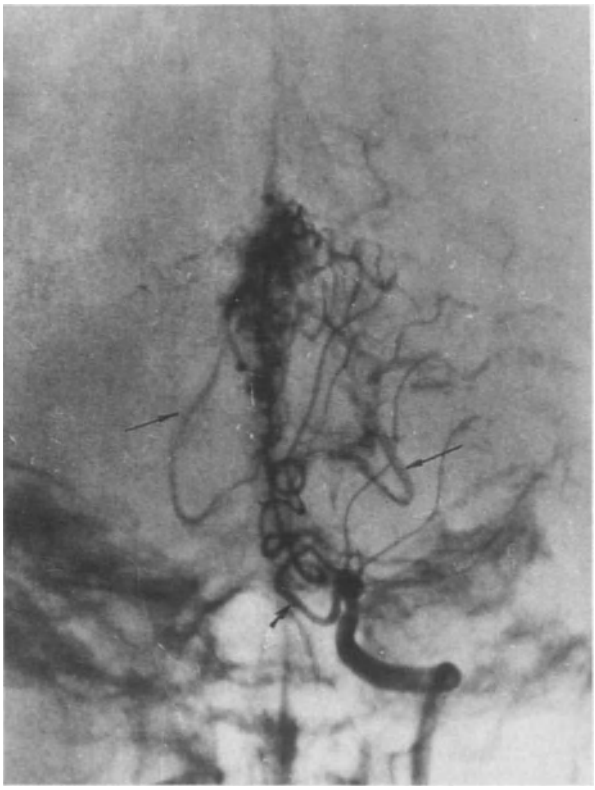


B

Figure 17.5. Postoperative vertebral angiograms, AP (**A**) and lateral (**B**) views, showing the total excision of the AVM. A large clip is positioned on the trunk of the PICA.



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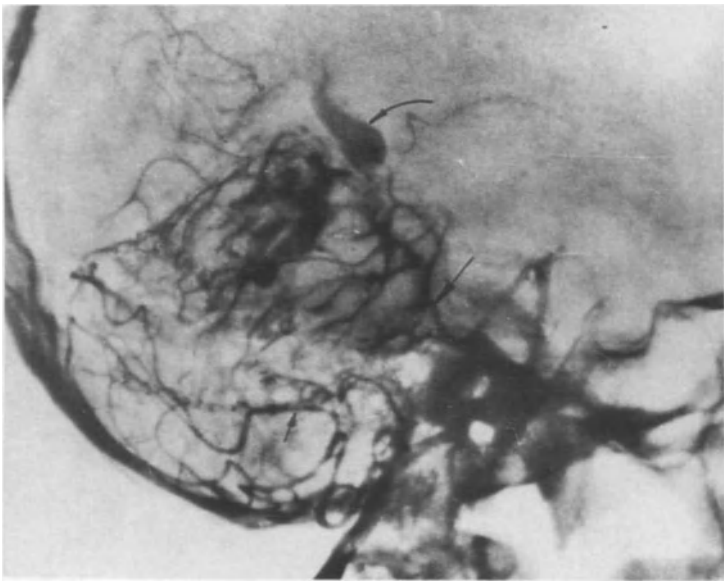
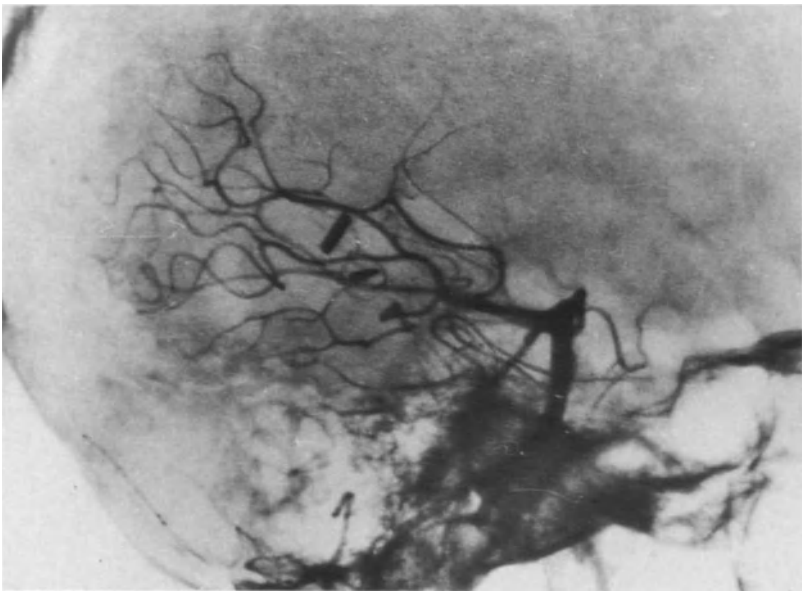


B

Figure 17.6. Vertebral angiograms, AP (**A**) and lateral (**B**) views, of an oral midline cerebellar AVM. It is supplied by both SCAs (long arrows) and the PICA (short arrow). Blood drainage is into the vein of Galen (curved arrow).



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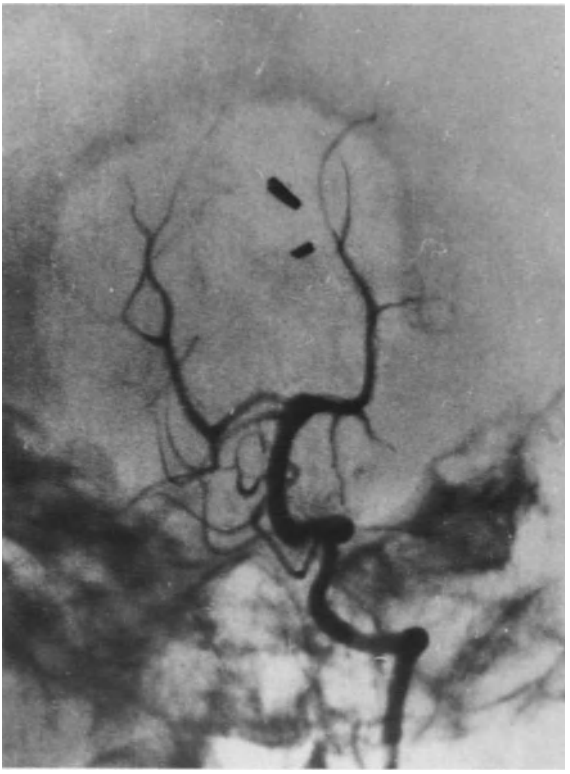


B

Figure 17.7. Postoperative vertebral angiogram, AP (**A**) and lateral (**B**) views, showing total excision of the AVM. The clips are positioned on the trunk and branches of the SCA.

functionally important brainstem structures and the narrow operative field. We sometimes employed a combined method of exposure and excision of AVMs with multichannel blood drainage from the malformation and possible clipping of its large feeding arteries early during the operation. With this method the malformation is exposed from the venous pole. We consider this technique to be technically more feasible and less traumatic.

After hemostasis of the operative wound, Queckenstedt's maneuver was used to assess hemostasis. The dura mater was sutured after the patient's withdrawal from the induced hypotensive state.

Of eight cases of palliative operations that involved clipping the AVM feeding arteries, in only one case was complete (though temporary) exclusion of blood flow from the malformation achieved (Table 17.5). One of these cases is of particular interest: A patient with an AVM in the middle-oral region of the cerebellum (Fig. 17.8) underwent the palliative operation of clipping both SCA trunks feeding the malformation. Control angiography 10 days after the operation demonstrated full exclusion of the AVM from the blood flow (Fig. 17.9). Occlusion of the SCA feeding arteries resulted in considerable regression of brainstem cerebellar symptoms. Over the follow-up period of 5.5 years the patient's condition remained satisfactory. He was later readmitted with recurrent hemorrhage. Angiography was performed and revealed revascularization of the malformation whose size had increased compared with the preoperative size (Fig. 17.10).

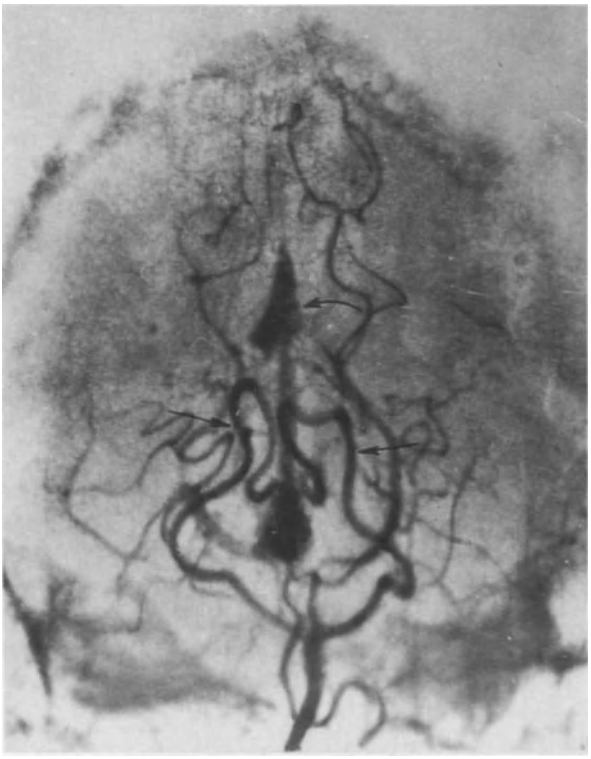
In this patient the malformation consisted of two segments with different blood flow velocities. The segments had separate blood supplies and drainage. The lower segment was fed from the PICA trunk, the involvement of which in the blood supply of the AVM was not demonstrated at preoperative angiography. Blood drainage was into posterior sections of the sinus rectus. We believe that revascularization of the oral part of the malformation was effected via normally existing anastomoses between the SCA and PCA.

Because of the poor results of the palliative operations—most of which involved clipping SCA trunks—we decided to make a special study of the

Table 17.5. Data on clipping AVM feeding arteries

AVM site	No. of cases	Small AVM	Medium AVM	Large AVM	Artery clipped
Cerebellum					
Midline-oral regions	5	2	2	1	SCA
Lateral regions	1	1	—	—	PICA
Cerebellopontine angle	1	—	1	—	AICA
Brainstem	1	—	1	—	SCA
Total	8	3	4	1	

There was no mortality in this group. AICA = anteroinferior cerebellar artery; PICA = posteroinferior cerebellar artery; SCA = superior cerebellar artery.



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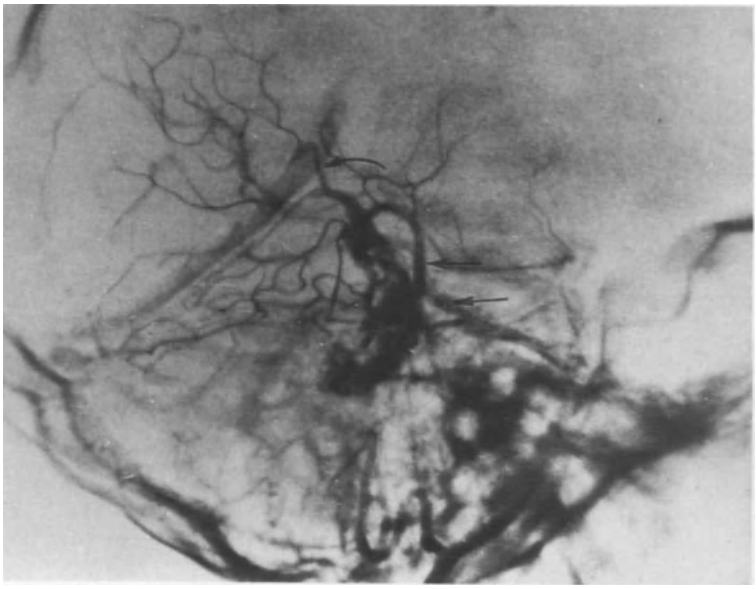
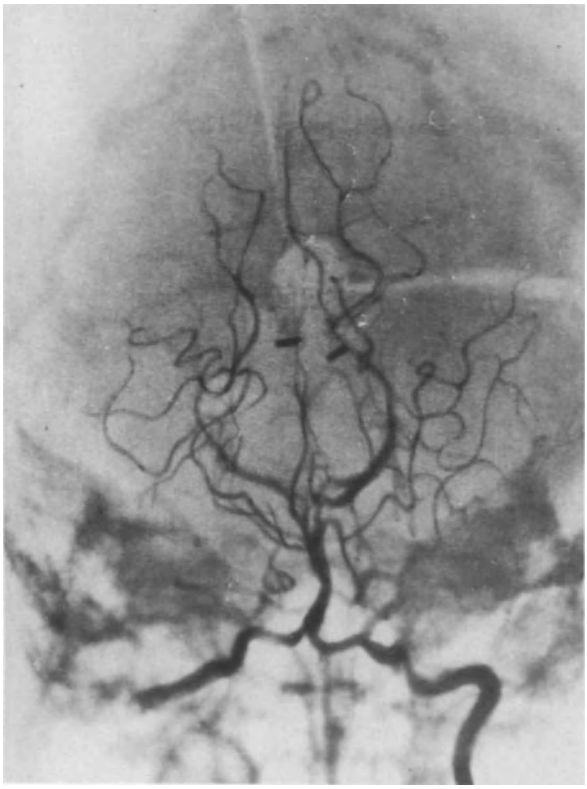


B

Figure 17.8. Vertebral angiograms, AP (**A**) and lateral (**B**) views, of a midline oral cerebellar AVM. Blood supply is from both SCAs (straight arrows). Blood drainage is by the vein of Galen (curved arrow).



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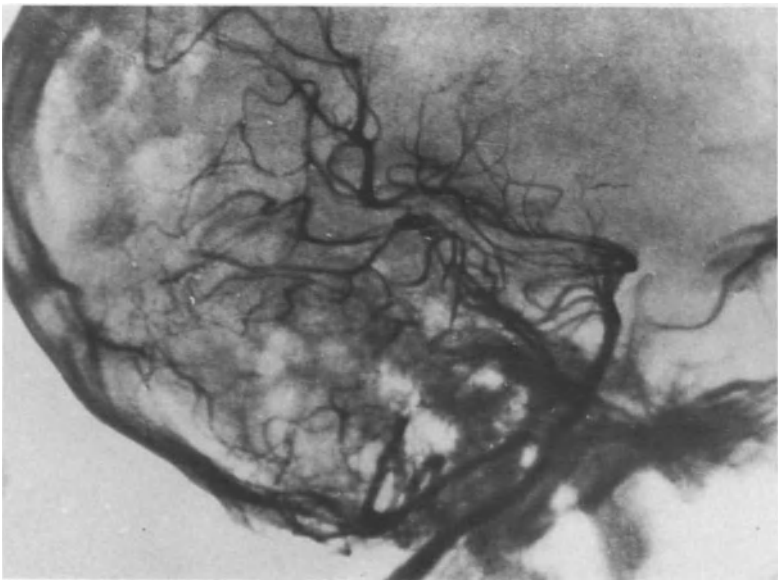
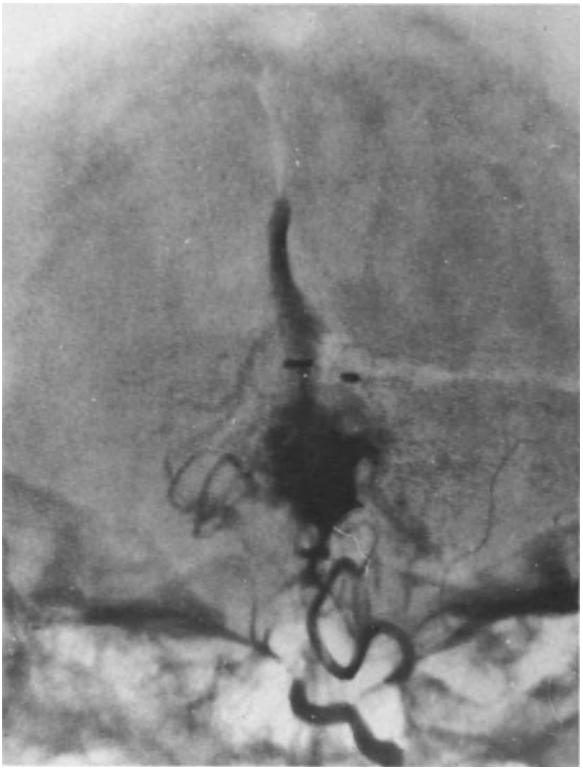


B

Figure 17.9. Postoperative vertebral angiography, AP (**A**) and lateral (**B**) views, after a palliative operation that involved clipping both SCAs. As can be seen, the AVM is not filling.



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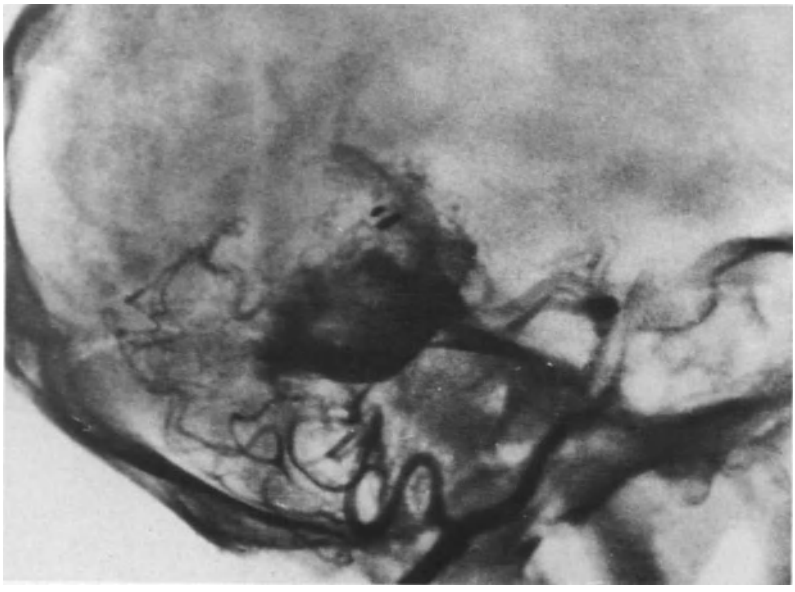

B

Figure 17.10. Vertebral angiography of the same patient as in Figure 17.9. AP (**A**) and lateral (**B**) views show revascularization of the AVM, which is in the midline oral region of the cerebellum. The AVM is now larger than it was before palliative surgery.

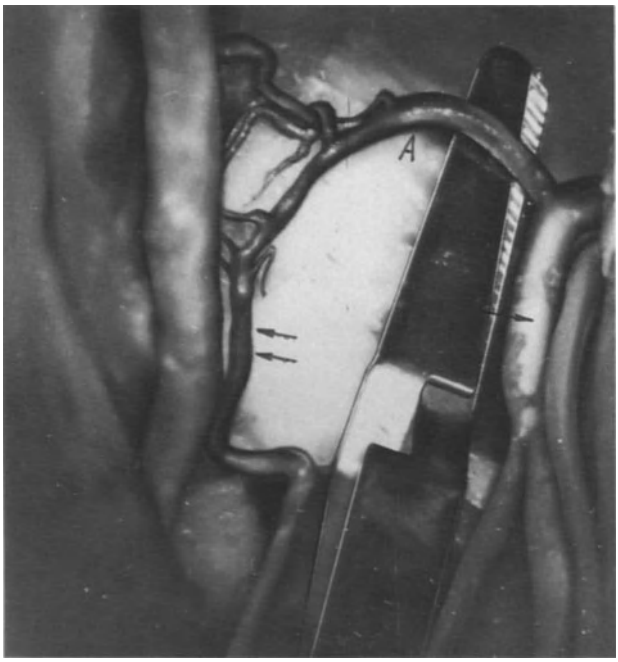

Figure 17.11. One-channel anastomosis (A) between the SCA and the PCA, which is located at the level of the inferior colliculus. The rostral branch of the SCA is indicated by the single arrow. The branch of the PCA is shown by the two arrows. The diameter of the anastomosis is 1.2 mm. (× 6)

microsurgical anatomy of anastomoses between the SCA and the PCA. These anastomoses are localized on the bigemina inferior, or on the lateral surface of the lamina quadrigemina. They are formed by the distal segments of arteries originating from the precommunicating and, more rarely, postcommunicating segments of the PCA and by arteries arising from the rostral branch of the SCA before its transition to the tentorial surface of the cerebellum. In some cases, depending on the structure of arteries of the circle of Willis, anastomoses may also be located on the basal surface of the brainstem and connect the proximal segments of the SCA and the PCA. The anastomoses may be single, double, or triple. The diameters of the vessels forming the anastomoses range from 0.1 to 1.2 mm (Figs. 17.11 and 17.12).

Discussion

The clinical picture of posterior fossa AVMs is varied, which can be explained by the multiplicity of factors determining neurological symptoms. In addition to the direct effect of the malformation mass on the surrounding

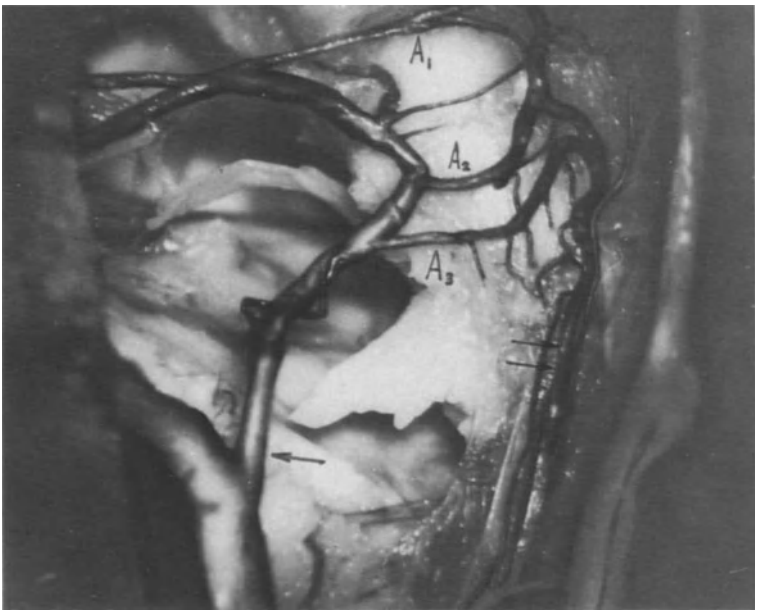

Figure 17.12. Three-channel anastomosis on the lateral surface of the quadrigeminal plate. The rostral branch of the SCA is indicated by the single arrow. Three arteries are seen coming out of the SCA and forming anastomoses (A_1, A_2, A_3). The branch of the PCA is shown by the two arrows. Diameters of the anastomoses are 0.7 to 0.8 mm. ($\times 6$).

posterior fossa structures and their intrahemorrhage destruction, of importance is AV blood shunting, causing blood redistribution in vertebrobasilar vessels, which feed the structures of the brainstem and cerebellum. Clinical diagnosis of AVMs is complicated by infrequent correlation of neurological symptoms with the anatomical location of the malformation. The diagnosis was established on the basis of data over the course of the disease, a history of intracranial bleeding, the age of the patient, and neurological symptoms resulting from lesions of posterior fossa structures.

Vertebral angiography is especially important for diagnosing posterior fossa AVMs, permitting verification of the site and size and evaluating the condition of the blood supply and its drainage. Additional information on the sources of posterior fossa AVM blood supply may be provided by carotid angiography.

Computed tomography is an effective technique for diagnosing posterior fossa AVMs, making it possible to estimate the AVM size, determine its exact site, and assess its relation to brain structures. CT is especially valuable for giving information on the state of the brain tissue: the presence of brain edema, ischemic zones, cystic cavities, or hematomas after intracerebellar

hemorrhage. This information is of great surgical importance and often determines the strategies of the operative intervention. Indications for surgical treatment and the strategies and techniques of AVM excision are evaluated and determined on the basis of these data.

Total excision remains the only radical surgical method for treating cerebral AVMs. When it is not feasible, it is expedient to use the technique for endovascular closure of the malformation or irradiation by proton beams, although the proximity of brainstem structures increases the risk of serious complications following the use of these methods.

Clipping the feeding arteries is not particularly effective and should be regarded only as an extreme measure when the extent of surgical intervention must be limited (i.e., when total AVM excision is impossible). Anastomoses between the branches of neighboring arteries play a special role in cerebral AVM surgery. We have confirmed the existence of anastomoses between the SCA and the PCA, reported by others.[22–25]

In vitro we found anastomoses to be present in all specimens and on both sides. The anastomoses between the SCA and the PCA appear to preserve the brainstem blood supply in the zone of the tentorial incisure. It should also be mentioned that in all cases anastomoses give rise to small arteries that feed the neighboring brainstem structures. Of great surgical importance is the angiographic confirmation (and one case postmortem verification) of the involvement of these anastomoses in feeding the malformations in the oral sections of the posterior fossa.

Our results on the structure of anastomoses between the PCA and the SCA can explain the mechanism of AVM revascularization following the clipping of feeding arteries. This situation must be taken into consideration to prevent or reduce intraoperative bleeding.

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Discussion

Posterior Fossa AVMs: Anastomoses Between Superior Cerebellar and Posterior Cerebral Arteries

What percentage of your specimens demonstrated anastomoses between the superior cerebellar and the posterior cerebral arteries?

Dr. Eliava: Fifteen brains were studied, and anastomoses were found in 100% of them. We decided not to continue our investigations because it was no longer necessary. In only one instance was there no *apparent* anastomosis, presumably due to a lack of filling of the arteries with latex. When we carefully dissected these vessels the anastomoses were present but had not filled with latex.

Management of Subtotally Removed AVMs

Are subtotally removed AVMs at increased risk of bleeding? What is the estimated risk?

Dr. Eliava: Yes, they are. We performed eight "palliative" operations, which entailed clipping the feeding arteries but not excision of the AVM. The postoperative follow-up was from 2 to 7 years. In all cases there was rebleeding, which is why we cannot endorse this method for the treatment of patients with AVMs. I wish to emphasize that nowadays when we decide to operate on a patient with an AVM we always attempt total excision. In some instances it becomes apparent during the operation that complete resection is not possible because vital functional structures are involved. The only measure then available to us is to clip the feeding arteries with the hope that it will help the patient.

Is irradiation of subtotally removed AVMs performed?

Dr. Eliava: Irradiation is undertaken in combination with surgical excision for subtotally removed AVMs. Irradiation here may be more dangerous than in hemispheric AVMs because of the proximity of brainstem structures. Another point relates to the biological results of irradiation: Hemorrhage may occur even a year later.

Concerning embolization: When you talk about total resection, are you talking about embolization with surgery, surgery without embolization, or both?

Dr. Eliava: We generally used clips for the feeding vessels, but in some cases we used a catheter technique with attached balloons, leaving the balloon inflated inside the vessel.

CHAPTER 18

Microsurgical Treatment of Arteriovenous Malformations of the Corpus Callosum and Hippocampus

Yuri M. Filatov, Shalva S. Eliava, O.B. Sazonova, L.I. Moskovichyute, and N.K. Serova

Arteriovenous Malformations of the Corpus Callosum

The problem of surgical treatment of patients with arteriovenous malformations (AVMs) of the cerebral vessels is one of the most pressing in vascular neurosurgery. According to current data, the risk of fatality after the first hemorrhage from an AVM of the large cerebral hemispheres varies from 10% to 35%, and after the recurrence of hemorrhage 20%; disability is noted in almost 40% of those patients who survive.[1–6] If one considers that most cerebral AVMs appear after spontaneous intracranial hemorrhage in young adults, it is possible to understand the need for surgical treatment of such patients. The danger of hemorrhage from AVMs located in the deep structures of the brain and, in part, from corpus callosum AVMs substantially increases owing to the closeness of the ventricle system and the functionally important subcortical structures.[7] Corpus callosum AVMs are relatively rare constituting from 5.0% to 14.5% of all AVMs in all sites,[8,9]; according to data gathered at the Burdenko Institute of Neurosurgery the figure is 5.4%.

Deetz provided the first pathomorphological description of corpus callosum AVMs in 1902,[10] and a corpus callosum AVM was first successfully removed by Basset in 1951.[11] Publications then began to appear that described surgical treatment of patients with corpus callosum AVMs, based on isolated observations or small series of cases.[8,12–17] For this reason, many questions concerning the surgical treatment of corpus callosum AVMs remain unanswered.

The goal of this chapter is to substantiate evidence for surgical treatment and to describe the most effective surgical approaches and methods for removing corpus callosum AVMs based on the largest published series of observations.

Material and Methods

This report is based on analysis of clinical data from 67 patients (37 males and 30 females, ages 10–53) with corpus callosum AVMs who underwent a

series of examinations at the Burdenko Institute. From the total group, 40 patients were operated on (37 total and 3 partial removals of the AVM). The tests included thorough neurological, neuropsychological, and electrophysiological examinations, both pre- and postoperatively. Cerebral angiography and computed tomography (CT) of the brain confirmed the diagnosis and the extent of excision.

Results and Discussion

Based on the analysis of data compiled from the angiography, CT, and other neurophysiological and electrophysiological examinations, an anatomicosurgical classification of corpus callosum AVMs, with regard to the surgical approach to malformations, is proposed. In conformity with this classification, all patients were distributed into four groups (Table 18.1).

The AVMs were categorized according to their size: small (diameter up to 2.5 cm), medium (diameter 2.5–4.0 cm), and large (diameter 4–5 cm). Malformations more than 5 cm in diameter, which occupied all or a large part of the corpus callosum and which spread to contiguous areas and structures of the brain, were included in the group of extensive corpus callosum AVMs.

The classification of corpus callosum AVMs reflects the anatomicotopographical site of the AVM, their correlation with cerebral structures, the circumstances of blood supply and drainage, and the effective surgical approach. According to the data gathered from our series of observations, the illness began with spontaneous intracranial hemorrhage in all cases; 43 patients (64.1%) experienced recurring hemorrhage. In only 16 cases was the interval between recurring hemorrhages less than 1 month.

Analysis of the neurological picture showed that the pyramidal pathways and brainstem structures were affected, with disturbed sensation in various combinations, in most patients. At the same time, in 17 of the patients (25.3%) there were no apparent neurological symptoms during the "cold" period after hemorrhage. The aforementioned patients were categorized in a separate group with marked regression of neurological symptoms.

Nine patients (13.4%) had papilledema, which indicated intracranial hypertension and which arose after spontaneous intracranial hemorrhage.

Table 18.1. Anatomosurgical classification of corpus callosum AVMs

AVM site in corpus callosum	No. of cases
Anterior third and genu of the corpus callosum	10
Middle third of the corpus callosum	18
Posterior third and splenium of the corpus callosum	34
Extended in the corpus callosum	5
Total	67

Table 18.2. Surgical treatment of patients with corpus callosum AVMs

AVM site in corpus callosum	No. of patients	No. of patients, by size of AVM		
		Small	Medium	Large
Anterior third	8	—	8	—
Central third	11[a]	3	7	1
Posterior third and genu	21[a]	8	11	2

[a] Cases of partial removal of AVMs.

Homonymous hemianopia during the remote period of hemorrhage was noted in three patients (4.4%).

The experiment involving surgical treatment was based on a pool of 40 patients with corpus callosum AVMs: There were 37 radical cases (total removal of the AVM); and operations on the other 3 patients were limited to partial removal of malformations and transection of the afferent arteries. A shunting operation was performed on one patient after total removal of the AVM (the shunting operation is not included in Table 18.2). All patients were operated on during the "cold" period after intracranial hemorrhage.

Table 18.2 shows that in most patients small and medium-sized AVMs were removed; in three cases large malformations were completely removed, and two patients died. It should be noted that partial removal of malformations in three patients had not been included in the tactical plan prior to surgery. With the site of the malformations in or near functionally important zones, the surgeon attempted to carry out total removal of the malformation with minimal damage to the surrounding brain tissue, causing the perifocal zone, within which the AVM was visible, to maximally contract. There are three reasons a portion of an AVM may remain attached to brain tissue: (1) the above-mentioned contraction; (2) the diffuse type of structure of the malformation; (3) difficulty in identification of the boundaries of the malformation in "eloquent" brain tissue.

Ten patients refused direct surgical intervention, and endovascular intervention was carried out in three of the ten (endovascular aspects of the problem are not discussed in this report). Seventeen malformations (25.4%) were acknowledged to be inoperable owing to the size of the AVM and its diffusion over the surrounding subcortical ganglions. Their conditions were established by angiographic data and CT scanning.

When discussing the question of surgical treatment of patients, we must take into consideration the clinical course of the disease, the dimensions and site of the AVM, and its conditions of blood supply. Hemorrhage from AVMs is an indicator for surgical treatment if one allows for the size of the malformation. The blood supply of the malformation from several afferent arteries and multichannel blood drainage is not an absolute contraindication for surgical treatment of AVMs, although it markedly complicates the possibility for radical removal.

Operating during the "cold" period of hemorrhage appears to be more advantageous, especially as repeated hemorrhage within the period of 1 month was noted in only 16 cases (11.6% of hemorrhages). Operations performed during the acute stage of hemorrhage were accompanied by additional difficulties, which arose owing to edema of the brain and alterations in the brain tissue. Emergency surgical intervention was performed only in the presence of intracerebral hematoma.

For prophylaxis of intraoperative hemorrhage, a series of measures were undertaken: adequate neuroanesthesiological maintenance during the operation, microsurgical methods, and special methods of AVM removal. The position of the patient on the operating table depended on the AVM site. Patients with AVMs in the posterior third and some of the patients with AVMs in the central third of the corpus callosum were operated on in the sitting or semisitting position, depending on the topography of the parasagittal veins. Such positions created better conditions for orientation within the area of operation. In general, the sitting and semisitting positions are more physiological in nature and improve blood drainage in the venous system. Patients with AVMs in the anterior third and genu of the corpus callosum were operated on lying on their backs, with access from the left or right side depending on the predominant position of the malformation.

During surgery, a surgical binocular lens with a magnification of 3.5 × was used.

The choice of approach to corpus callosum AVMs is of prime importance. It depends on the site of the malformation in the corpus callosum and on its spread to contiguous brain structures.

For most cases of AVM of the anterior third and genu of the corpus

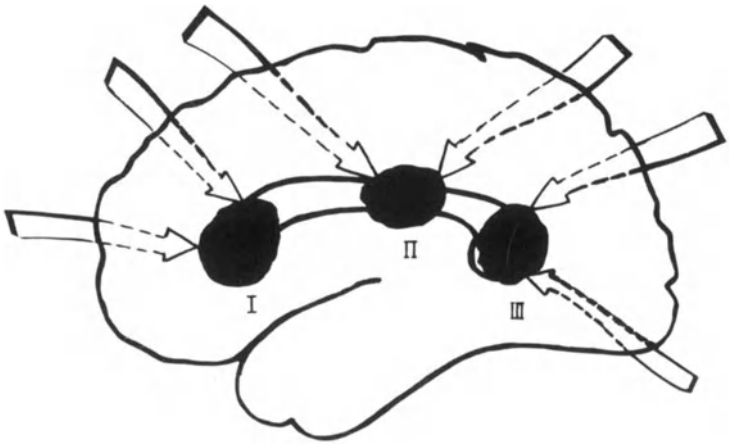
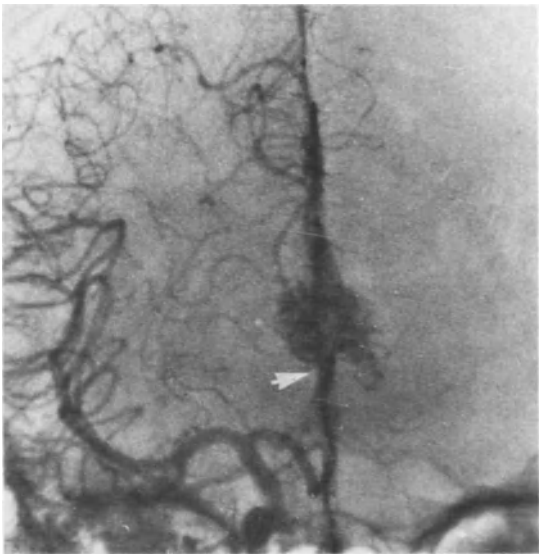


Figure 18.1. Approaches to AVMs of the corpus callosum. I = genu and anterior third of corpus callosum. II = middle third of corpus callosum. III = splenium, posterior third of corpus callosum.

callosum, we used the frontal interhemispheral approach (Fig. 18.1). In two of eight patients with AVMs of the anterior third of the corpus callosum who were operated on, the superior sagittal sinus was occluded (anterior third) while approaching the malformation. In three patients the parasagittal veins, which enter the superior sagittal sinus at this level, were transected. It should be noted that no complications associated with the above-mentioned surgical maneuvers were observed.

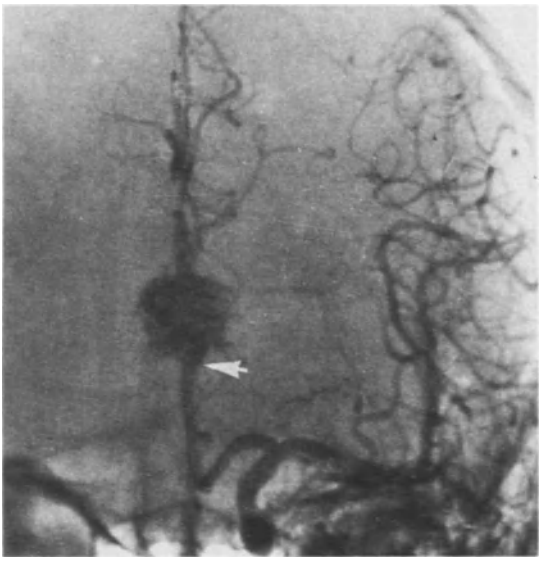
During removal of a malformation, attention should focus on preserving the trunks of the anterior cerebral arteries, especially their proximal segments. According to our surgical experience, the blood supply to corpus callosum malformations proceeds not from the trunks of the pericallosal arteries but from their minor branches, which supply blood to the corpus callosum and which are then gradually coagulated and crossed during removal of the AVM. Figures 18.2 and 18.3 show angiograms of patients with AVMs of the genu of the corpus callosum before and after total removal of the malformation.

Eleven patients were operated on for AVMs of the middle third of the corpus callosum. When the interhemispheric approach in the projection of the premotor zones was used, patients were placed in a lying position. If the projection was of the temporal zone patients were put in the semisitting position (Fig. 18.1). At the time of access, the large parasagittal veins (fron-

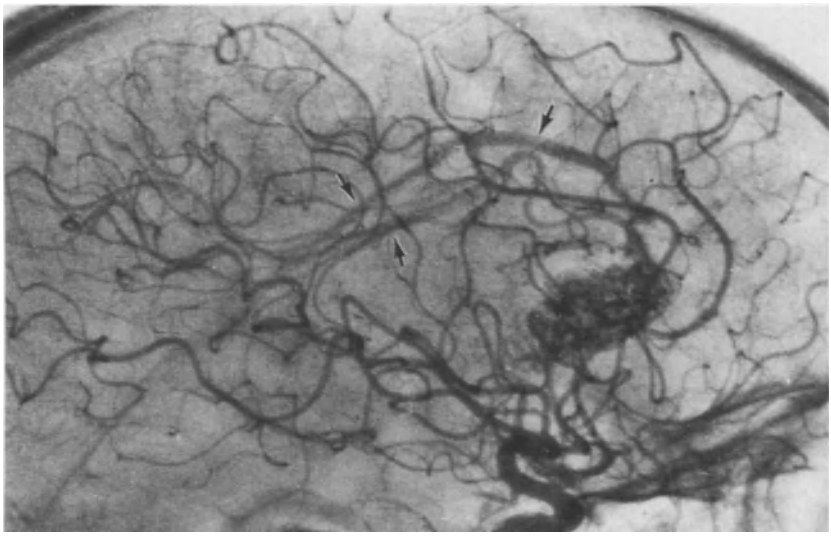


A

Figure 18.2. (**A & B**) Carotid angiograms, AP projection. AVM genu of the corpus callosum, which is supplied by both anterior cerebral arteries, is shown by arrows. (**C**) Carotid angiogram, lateral projection. Draining veins are shown by arrows.

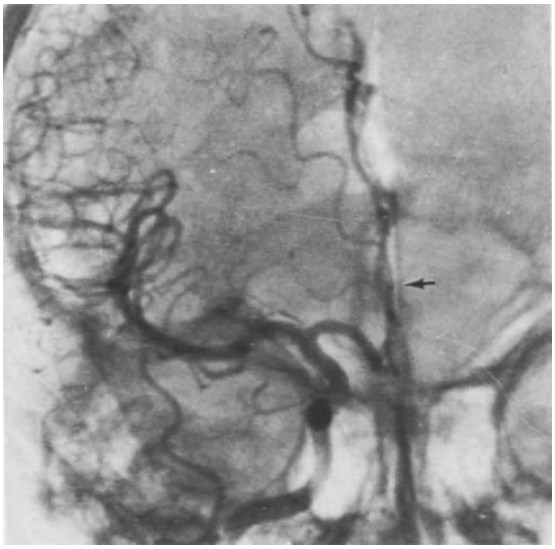


B

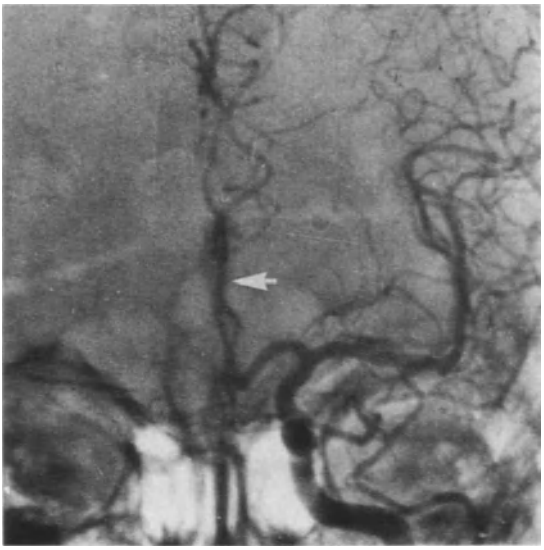


C

Figure 18.2 (*continued*)

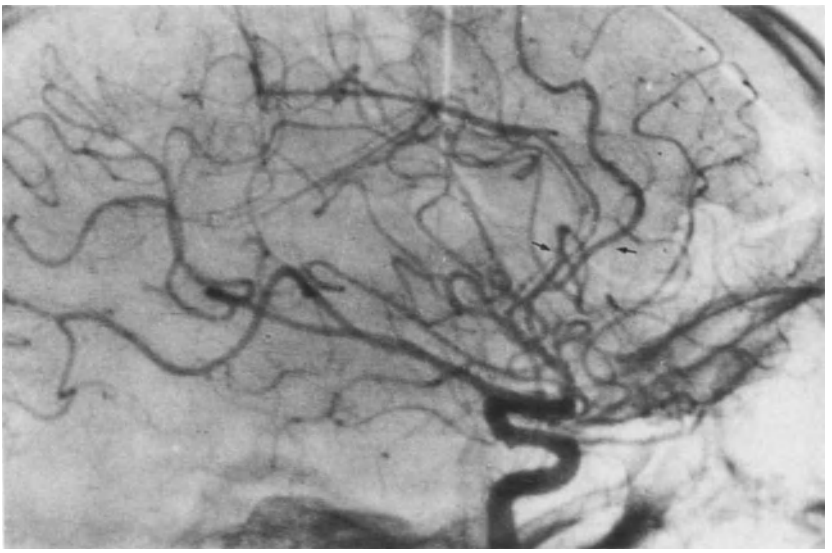


A



B

Figure 18.3. (**A & B**) Carotid angiograms after removal of AVM. Arrows indicate preserved stumps of the anterior cerebral arteries. (**C**) Carotid angiogram after removal of the AVM (lateral projection). Arrows indicate preserved branches of the anterior cerebral artery. Interhemispheric premotor zone approach from the right side.



C

Figure 18.3 (*continued*)

tal, precentral, parietal) were transacted in three patients. Transection of the frontal parasagittal vein caused no neurological side effects. Because of transection of the parasagittal vein, after the operation one patient experienced sensory disturbances, which subsequently regressed almost completely. Because of transection of the left precentral parasagittal vein, one patient experienced marked disorder in the psychoemotional sphere. In this case it was difficult to establish the direct cause of the complication, inasmuch as the trunk of the left pericallosal artery was also transected in its middle section.

The occipital interhemispheric approach was used in 9 of 21 patients with AVMs of the posterior third of the corpus callosum. Of these nine, three were observed to have the tentorium (length 2.0–2.5 cm) in the usual place. The above-mentioned method of access was the most convenient for approaching and opening the upper area of the ambiens cistern and for identifying the trunk of the posterior cerebral artery (PCA) at the boundary between its cisternal and hemispheral segments. Visualization of the trunk of the PCA significantly facilitated identification and transection of the afferent artery of the AVM in the posterior third and splenium of the corpus callosum until the initial stage of removal of the malformation. Such method of access was preferred for operations involving large AVMs. At this point, homonymous hemianopia of the left side during the postoperative period was noted in all nine cases of AVM removal in which the occipital interhemispheric approach was used and in which the trunks of the PCA were

preserved. At the same time, not a single case of hemianopia was noted after removal of the AVM using the parietal interhemispheric approach (in one case hemianopia appeared temporarily).

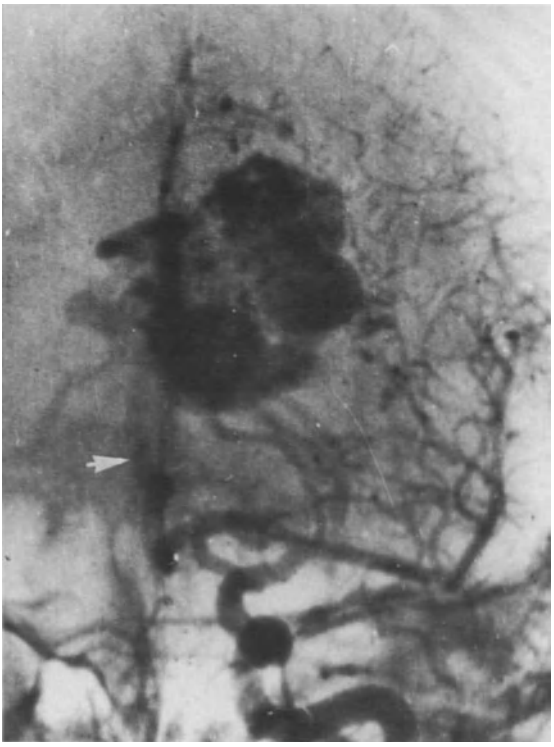
The parietal interhemispheric approach was used in 10 cases and a combined occipital-parietal approach in two. The choice of approach was based on the small size of the malformations, their site in the posterior third of the corpus callosum, and the lack of diffusion into the splenium.

Preserving the parasagittal veins during the approach to the AVM in the splenium and the posterior third of the corpus callosum is important. Therefore it is imperative to undertake preoperative angiographic vizualization of the topography of the parasagittal veins. In four cases, the parasagittal approach, along with economical circular resectioning of the brain in the region of the lobulus parietalis, was used so as to preserve the integrity of the posterior group of parasagittal viens. The method of approach in question does not demand extreme retraction of the adjacent brain structures from the central line and so preserves the parasagittal veins. Figures 18.4 and 18.5 show the angiograms of a patient with an AVM of the posterior third and the genu of the corpus callosum before and after total removal of the malformation.

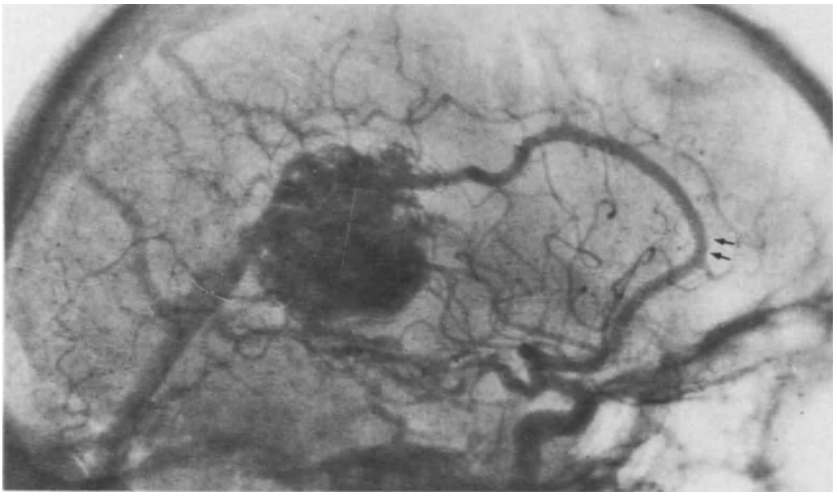
Tactics for the removal of corpus callosum AVMs are based on precise identification of the afferent arteries of the malformation: trunks and branches of the pericallosal and posterior cerebral arteries. Given this fact, we chose to place silver clips on the largest afferent arteries. Immediate separation of the vessels of the AVM was performed using bipolar coagulation and microsurgical instruments. The malformations were separated within the perifocal zone with maximal preservation of the contiguous "eloquent" brain tissue. Lastly, the draining veins were transected, and silver clips were placed on the trunks of the largest veins. To assess hemostasis, especially in the sitting position in patients with AVMs of the posterior third of the corpus callosum, a Queckenstedt maneuver was used.

The connection between corpus callosum AVMs and the choroid plexus should be noted, as it indicates additional sources for nourishment of the malformation from the system of anterior and posterior choroidal arteries. Mainly, malformations of the posterior third and the genu of the corpus callosum, and to a lesser extent AVMs of the middle and anterior thirds, are affected. Thus among the 21 patients with AVMs of the posterior third and genu of the corpus callosum who were operated on, AVMs were found to be connected with the choroid plexus in 11. Of the eight patients with AVMs of the middle and anterior thirds, such a connection was found in four; here immediate removal of the malformation made it necessary to open the walls of the side ventricle and block all additional sources of blood supply from the choroid plexus or to perform partial resection.

An important problem associated with surgery for corpus callosum AVMs is the appearance of hemianopia even when the trunks of the PCA are preserved; preventive measures must be devised here. Preliminary analysis

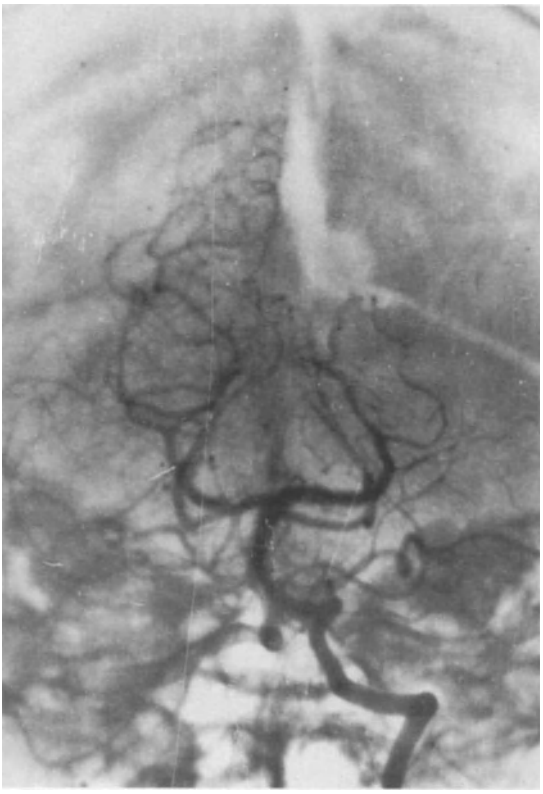


A

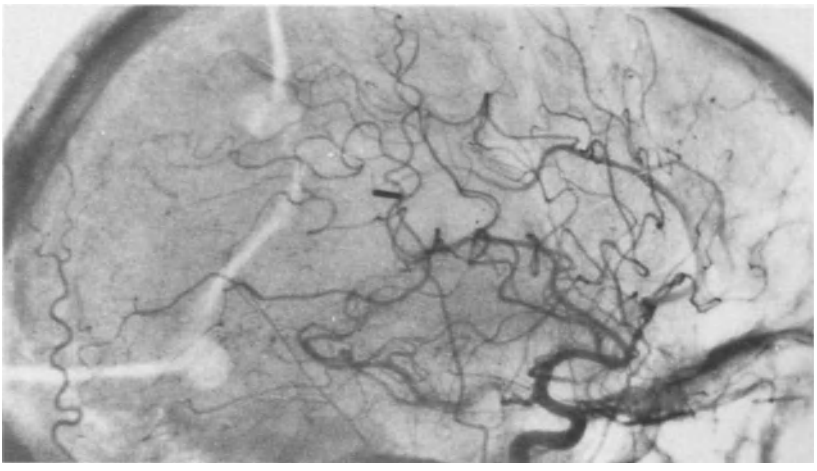


B

Figure 18.4. Carotid angiograms, AP (**A**) and lateral (**B**) projections, of AVMs in the region of the splenium posterior third of the corpus callosum with predominant distribution to the left. The AVM is supplied by the enlarged trunk of the left pericallosal artery (shown by the single arrow) and by branches of the left posterior cerebral artery, which arises from the supraklinoid segment of the internal carotid artery (shown by double arrows). Blood is drained from the AVM through the sinus rectus.



A



B

Figure 18.5. (**A**) Vertebral angiograms (AP projection) after removal of an AVM. The trunks of the posterior cerebral arteries are well visualized. (**B**) Carotid angiogram, lateral projection, after AVM removal. The trunk of the posterior artery is preserved. Clips are visible in the projection of the distal segment of the anterior cerebral artery. Interhemispheric, occipital supratentorial approach.

Table 18.3. AVMs of the hippocampal area: analysis of the dynamics of preoperative and postoperative neurological symptoms at the time of discharge

AVM site in hippocampus	No. of patients	No negative changes in neurological symptoms	With negative changes of neurological symptoms
Anterior third	6	2	4
Middle third	13	4	9
Posterior third	20	7	13
Total			26 (66.6%)

points to three basic factors responsible for the appearance of hemianopia: vascular factors, mechanical damage to the occipital lobes by spatulas, and surgical trauma, which causes damage to the fibers of the visual cortex.

Table 18.3 presents an appraisal of the dynamics of neurological symptoms in patients during the pre- and immediately postoperative periods. Careful analysis of the dynamics of neurological symptoms showed that in only 11 cases was an increase in focal neurological symptoms noted at the time of discharge from the Burdenko Institute. In one of two patients with AVMs of the middle third of the corpus callosum (Table 18.3) deterioration of neurological status was connected with transection of the distal segment of the left anterior cerebral artery, causing the development of a marked psychological defect. The second transection, of the large parasagittal vein, caused the development of sensory disorders. Negative dynamics of the neurological syndrome in nine cases of AVM of the splenium and posterior third of the corpus callosum were connected with the appearance of homonymous hemianopia (Table 18.3). The latter fact emphasizes the relevance of investigating the origins and appearance of homonymous hemianopia, with the goal of its prevention. Hydrocephalus appeared in two patients with AVMs of the posterior third and genu of the corpus callosum during the postoperative period. Regression of the hydrocephalus was noted in one of these patients with conservative therapy. A shunting operation (ventriculoatrialostomia) was performed on the second patient.

When evaluating the results of the surgical treatment of patients according to modern standards, data from neuropsychological and electrophysiological methods of investigation must be taken into consideration. Visual analysis of a pre- and postoperative electroencephalograms (EEGs) in patients with damage in various sections of the corpus callosum showed substantial polymorphism of EEG changes, whose character depended on the site of the AVM and the appropriate surgical approach. In keeping with this fact, more marked changes were noted in cases where the AVM was located in the posterior third and splenium of the corpus callosum after the occipital inter-

hemispheric approach was used. Interhemispheric asymmetry and focal slow waves in the occipital and posterior temporal regions on the side of surgical intervention appeared on the EEG. Local changes were not strongly pronounced after occipital interhemispheric approaches.

Pre- and postoperative neuropsychological investigations of patients showed that transection of various regions of the corpus callosum produced signs of interhemispheric disconnection. The character of these signs depended on the site of the damage. When the anterior sections of the corpus callosum were transected, conventional neurological investigations revealed no deterioration. Transection of the middle section of the corpus callosum revealed disorders of the interaction of the superficial and profound sensory systems. Transection of the posterior third and the splenium of the corpus callosum add anomia, hemianopia, and dysgraphia to the picture. A distinctive feature of neuropsychological symptoms was that the above-mentioned disturbances were reversible, so the symptoms resolved during the 4 weeks following the operation.

The series of pre- and postoperative investigations allowed us to conclude that in 27 of the patients operated on (67.5%), the neurological symptoms at the time of discharge from the Burdenko Institute mainly depended on the patients' preoperative status.

Two of 42 patients died (4.8%). The reason for the death of one patient was occlusion of both PCAs and formation of ischemic zones in both occipital lobes. In the second case, death was caused by anesthesia-related complications; heart activity ceased, and the patient went into a hypoxic coma during removal of a large AVM from the middle-posterior region of the corpus callosum, despite the fact that the operation was conducted without significant blood loss.

Thus defining indicators for the surgical treatment of patients, use of operational optics, and microsurgical methods, as well as accumulated experience in surgical treatment lay the groundwork for successful treatment of corpus callosum AVMs by surgical means. The series of tests performed on patients using pre- and postoperative EEGs and neuropsychological methods of investigation show that the most significant changes were noted during operations on patients with AVMs of the posterior third and splenium of the corpus callosum after use of the occipital interhemispheric approach. These changes were evidenced by temporary symptoms of interhemispheric disconnection and persistent symptoms of homonymous hemianopia. Taking these points into account, the method of approach under discussion could be recommended in connection with corpus callosum AVMs, which, because of the high risk of blood flow, make it necessary to transact the afferent arteries, specifically the branches of the PCA, in advance. Homonymous hemianopia is the most frequent and persistent postoperative complication, appearing in 9 (42.9%) of the 21 patients operated. These complications and the possibility of their prevention calls for further research.

Arteriovenous Malformations of the Hippocampus

There are many terms used to designate AVMs in the region of the hippocampal gyrus. The most widespread are "hippocampal AVM" and "AVM of the medial temporal lobe."[18,19] Malformations in these sites are rarely encountered; and experience involving their surgical treatment, according to the existing literature, is limited to a small number of observations. Surgical treatment of patients with hypocampal AVM is accompanied by a high risk of disability or death after spontaneous intracranial hemorrhage due to components of the malformations located near the brainstem, subcortical nuclei, and ventricular system. Analysis of the dynamics of neurological symptoms in operated patients presents a unique opportunity to investigate the significance of various regions of the hypocampus after destruction of brain tissue that results from spontaneous intracerebral hemorrhage or operational trauma during removal of the malformation. As was previously noted, the hippocampal AVM is a rare lesion, so questions concerning the clinical picture, diagnosis, and tactics for surgical treatment of such patients requires additional research.

The goal here is to substantiate evidence for surgical treatment and to describe the most effective surgical approaches and methodology for removal of a hippocampal AVM. The statements are based on the largest existing series of observations of surgical treatment of patients with this lesion.

Materials and Methods

The clinical data analyzed here are derived from a pool of 56 patients with hippocampal AVM (30 males and 26 females, aged 7–52 years). Patients were subjected to a series of clinical tests and a neurological investigation that included neuropsychological and electrophysiological parameters. Cerebral angiography, CT, and magnetic resonance imaging (MRI) confirmed the diagnosis.

Results and Discussion

The anatomicosurgical classification of the hippocampal AVM with regard to surgical approaches to the malformation is based on the results of angiography, CT, and MRI. In accordance with this classification all patients were categorized into four groups (Table 18.4). AVMs were distributed according to size: small (diameter < 2.5 cm), medium (diameter 2.5–4.0 cm), and large (diameter 4–5 cm). Malformations larger than 5 cm in diameter, which occupied all or a large part of the hippocampus and spread to contiguous brain structures, were included in the group of extended AVMs.

Table 18.4. Anatomicosurgical classification of AVMs of the hippocampus

AVM site in hippocampus	No. of AVMs
Anterior third	8
Middle third	15
Posterior third	29
Extended AVM	4
Total	56

This classification for hippocampal AVMs, in our opinion, reflects the basic parameters (i.e., the anatomicotopographical distribution of the AVM, the nature of its blood supply and drainage, and the size of the malformation) needed to convince the surgeon of the need for choosing the surgical approach to remove the malformation. The classification allows the systematization of neurological symptoms and simplifies the task of describing the clinical picture of hippocampal AVMs at various sites.

According to our series of observations, in all but one patient spontaneous intracranial hemorrhage was the first clinical sign of trouble. Our patients suffered 103 spontaneous internal hemorrhages, 61.5% of which proceeded with varying degrees loss of consciousness and local neurological signs; 23 patients (41.07%) experienced recurring hemorrhages. The maximum number of hemorrhages (five) was noted in two patients. The interval between hemorrhages was less than 1 month in only four cases.

Analysis of the neurological picture revealed that the pyramidal pathways, brainstem structures, and sensation were affected, in various combinations, in most patients. There were no apparent neurological symptoms during the "cold" period of hemorrhage in two patients.

Symptoms of increasing intracranial hemorrhage occurred in six cases, three of them revealed by CT scans. Homonymous, upper quadrant anopsia was evident in 12 patients (21.4%) during the "cold" period of hemorrhage.

Surgical treatment was applied to 39 patients, from whom hippocampal AVMs were totally removed. All patients were operated on during the "cold" period, after intracranial hemorrhage. Table 18.5 indicates the number of patients operated on for hippocampal AVMs and the sizes and sites of the malformations. Note that in most patients it was small and medium AVMs that were removed; large malformations were completely removed in seven cases. There were no deaths. The patients operated on (39 cases) comprised 69.6% of the total number of patients with hippocompal AVMs (56 cases). Three patients refused surgical treatment; and in one case surgical intervention was not indicated, although the size and site of the lesion allowed removal of the total malformation (the patient had an AVM of the

Table 18.5. Sizes and sites of hippocampal AVMs

AVM site in hippocampus	No. of patients	No. of pts., by size of AVM		
		Small	Medium	Large
Anterior third	6	1	3	2
Middle third	13	3	7	3
Posterior third	20	6	12	2

posterior third of the hippocampus, which clinically was not revealed by spontaneous intracranial hemorrhage). Thus surgical treatment was indicated in 43 patients (76.8% of all observed cases). Thirteen cases (23.2%) were acknowledged to be inoperable (the present work does not discuss the endovascular aspects of this problem).

When discussing the question of surgical treatment of patients, we must consider the clinical course of the disease and the size, site, and conditions of the AVM. Hemorrhage from AVMs is an indicator for surgical treatment if one allows for the dimension of the malformation. Blood supply of malformations from several afferent arteries and multichannel blood drainage are not absolute contraindications to surgical treatment of AVMs, although they markedly hamper the possibility of total removal.

We propose that operating during the "cold" period of hemorrhage is advantageous, especially as repeated hemorrhage within the first postoperative month was noted in only 3 cases (7.1%). Our experience shows that operations during the acute stage of hemorrhage were accompanied by additional difficulties that arose owing to edema of the brain and alterations in the brain tissue. Emergency surgical intervention is warranted only in the presence of intracerebral hematoma.

For prophylaxis of intraoperative hemorrhage, a series of measures were undertaken: adequate neuroanesthesiological maintenance during the operation, microsurgical methods, and special methods of AVM removal. The position of the patient on the operating table depended on the AVM site. Patients with an AVM of the posterior third of the hippocampus were operated on in the sitting position. Such a position created better conditions for orientation within the area of operation. In addition, the sitting position is more physiological in nature and improves blood drainage in the venous system. Patients with AVMs in the anterior and middle thirds of the hippocampus were operated on in a prone position, and access was from the left or right side depending on the site of the malformation. During surgery a surgical binocular lens or an operating microscope was used. When dealing with hippocampal AVMs it is important to have a choice of approaches to the malformation (Fig. 18.6). During removal of AVMs of the anterior third of the hippocampus we made our approach, through the sylvian fissure in all six cases. This approach allows good visualization of the afferent arteries of the

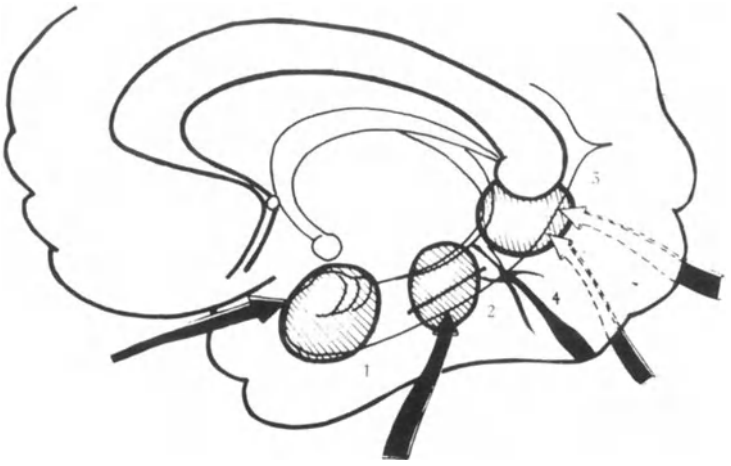
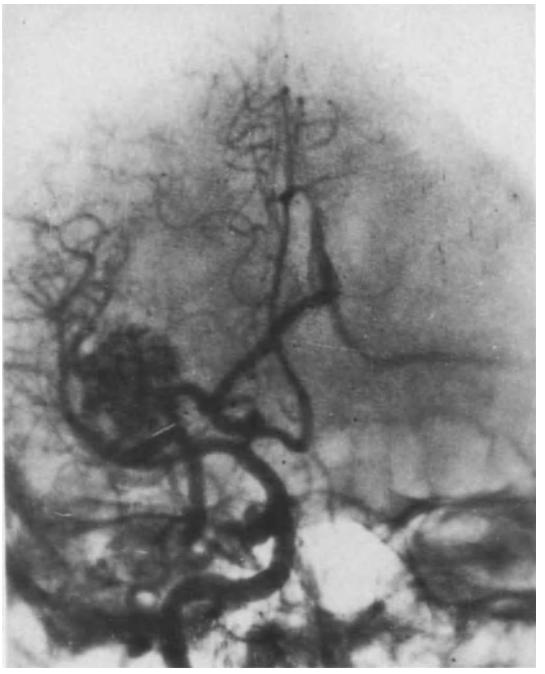


Figure 18.6. surgical approaches to AVMs of the hippocampus.

malformation: temporal branch(es), middle cerebral and posterial cerebral arteries, and branches of the anterior choroidal artery. In both cases in which large AVMs were removed (Table 18.2), malformations were connected to the choroid plexus of the inferior horn of the lateral ventricle and were partially removed together with the malformation. Approaching the AVM through the sylvian fissure also allows good visualization of the draining veins of the malformation in this localization, which lead into the Rosenthal vein or the anterior sphenoparietal sinus. Arteriograms of patients with AVMs of the anterior third of the hippocampus, before and after total removal of the malformation, are shown in Figures 18.7 and 18.8. During hippocampal AVM removal special attention should be given to the topography of the trunk of the anterior choroidal artery, which often participates in supplying blood to the malformation and the transection of which, in its proximal segments, elicits severe local neurological signs (brachiocephalic syndrome).

In 13 patients with AVMs of the central third of the hippocampus we used the transcortical approach through the central or posterior regions of the inferior temporal gyrus, preserving the vein of Labbe. In 7 of the 13 cases, malformations were connected with the choroidal plexus of the inferior horn of the lateral ventricle. In four patients the trunks and large branches of the anterior choroidal arteries were transected. In two of these cases, marked pyramidal symptoms appeared after the operation, apparently connected with transection of the proximal segments of the anterior choroidal arteries.

During the postoperative period upper quadrant anopsia or homonymous hemianopia appeared in three patients. In another three cases hemianopia that had been present prior to the operation worsened. Figures 18.9 and



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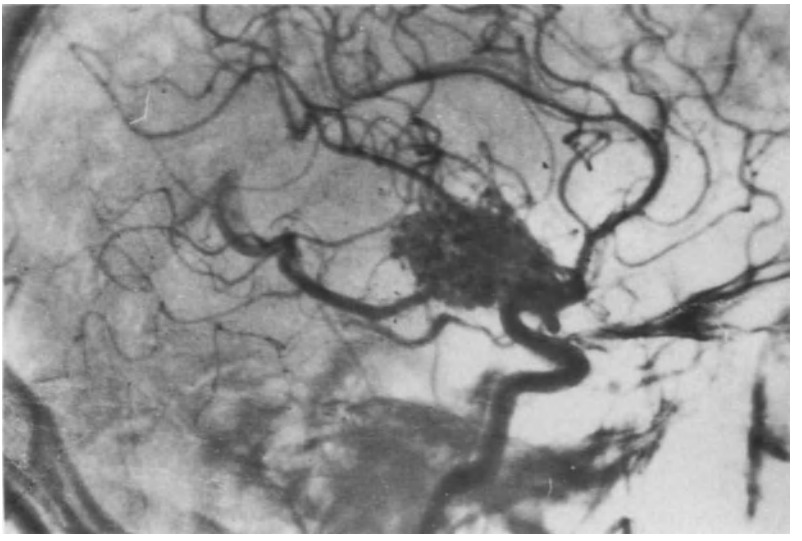
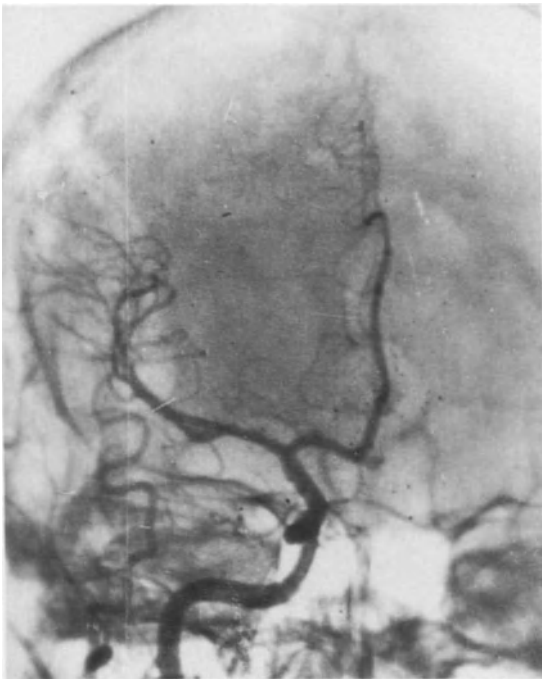


B

Figure 18.7. AP (**A**) and lateral (**B**) angiographic views of an AVM in the anterior third of the hippocampus.



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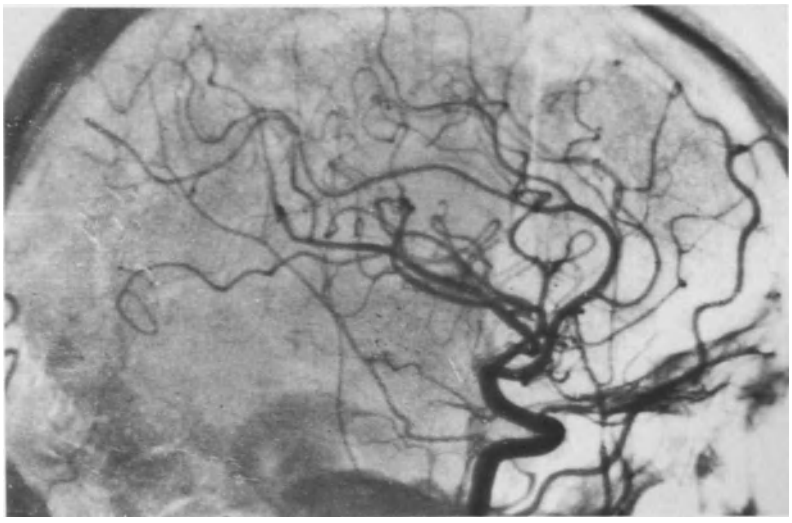

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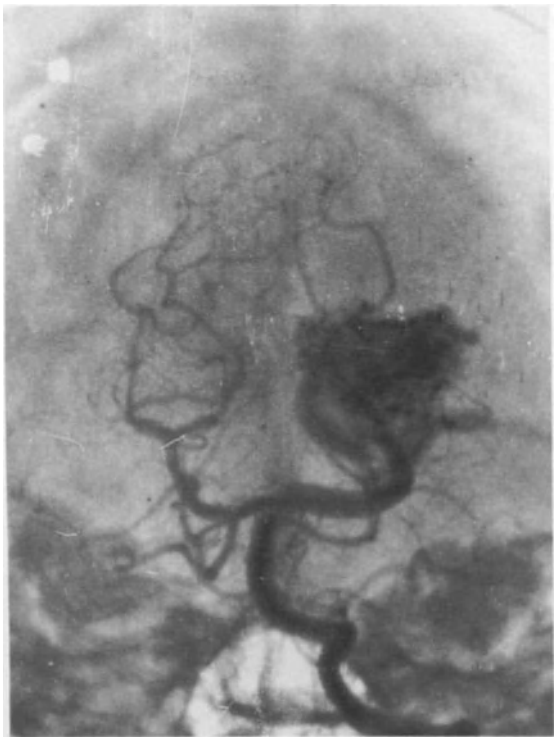
Figure 18.8. AP (**A**) and lateral (**B**) angiograms following excision of the AVM.



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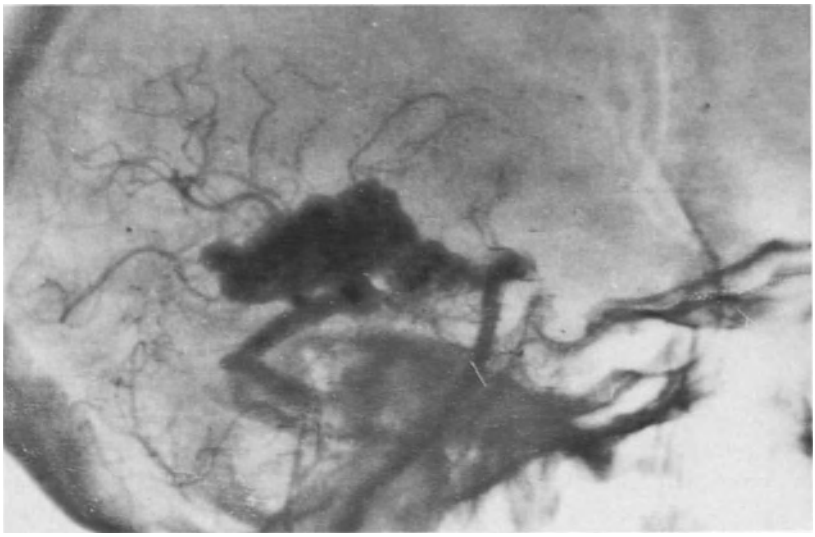

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Figure 18.9. AP (**A**) and lateral (**B**) vertebral angiograms of an AVM of the middle third of the hippocampus.

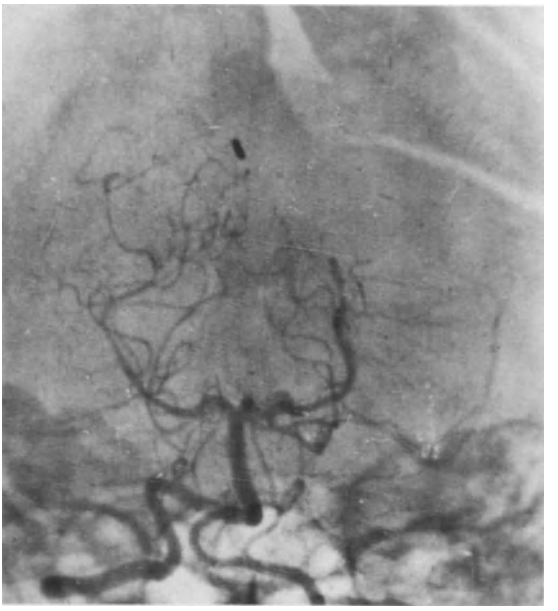
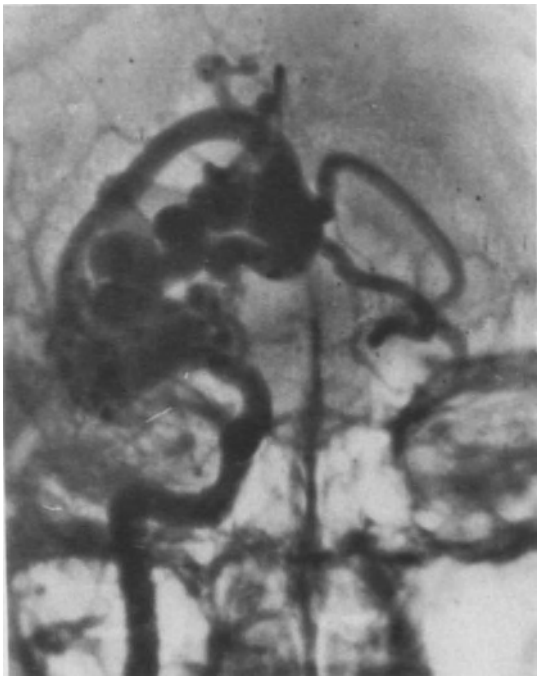


Figure 18.10. AP vertebral angiogram following excision of the AVM.

18.10 show angiograms of patients with AVMs of the central third of the hippocampus before and after total extirpation of the malformation.

In 4 of 20 patients operated on for AVMs of the posterior third of the hippocampus, the transcortical approach through the inferior temporal gyrus in the projection of the ventricular triangle was applied. In the remaining 16 cases the occipital interhemispheric approach was used. Of these 16 patients, 12 were observed to have a tentorium up to 2.0 to 2.5 cm long and in the usual place.

Using the occipital interhemispheric approach, the occipital parasagittal veins were crossed in two patients to prevent neurological damage. We consider the occipital interhemispheric approach to be the most effective for removing AVMs of the posterior third of the hippocampus. The approach allows easy access to the upper regions of the ambiens cistern and visualization of the trunk of the posterior cerebral artery at the point where its ambient segment becomes hemispheric. Visualization of the PCA significantly facilitates identification of the afferent arteries of the malformation (specifically the temporal branches of the PCA and posterior choroidal arteries) and their transection before starting to remove the malformation. At this point the fact that homonymous hemianopia often occurs after the occipital interhemispheric approach is used must be noted. Hemianopia was noted in 15 cases after the above-mentioned approach was used. In three cases preoperative homonymous hemianopia was partial, and no postoperative symptom



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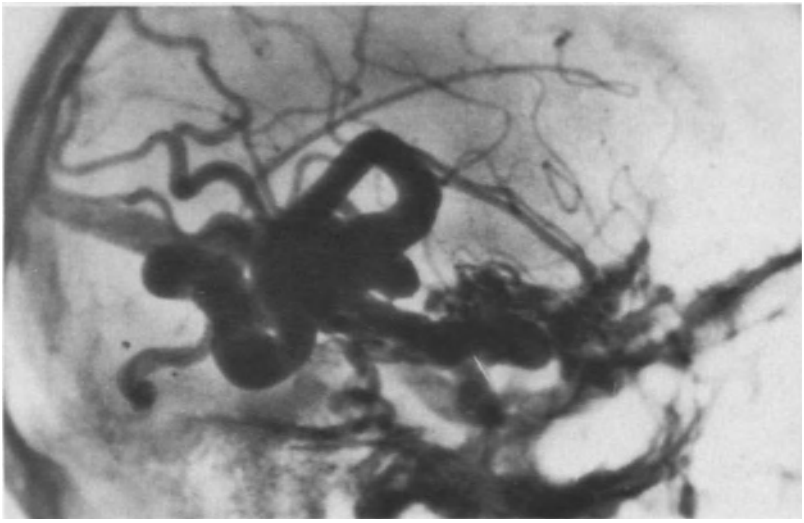


B

Figure 18.11. AP (**A**) and lateral (**B**) carotid angiograms of an AVM of the posterior third of the hippocampus.

worsened. In another three patients, full homonymous hemianopia occurred preoperatively and remained unchanged in the postoperative period. At the same time, one patient of five for whom the transcortical approach through the temporal lobe was used, experienced hemianopia. (In another patient upper-quadrant anopsia was evident prior to the operation, but its intensity did not increase.)

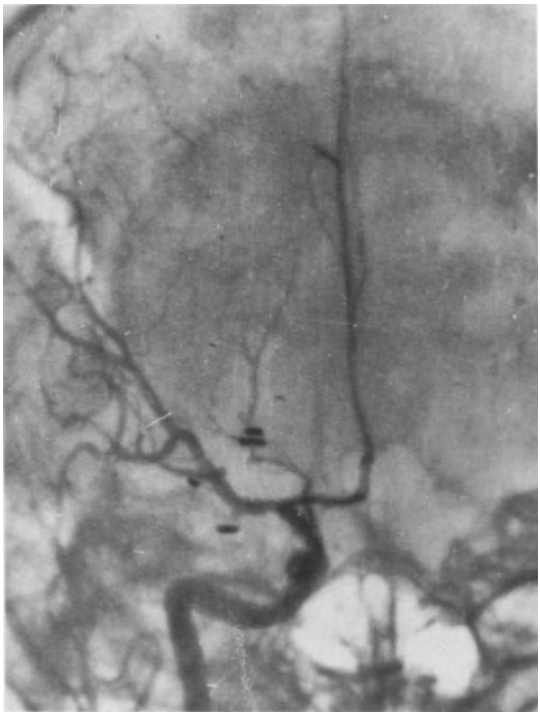
Figures 18.11 and 18.12 show the angiograms of patients with AVMs of the posterior third of the hippocampus before and after total removal of the malformation using the occipital interhemisphoric approach. Tactics for removal of hippocampal AVMs are based on precise identification of the afferent arteries of the malformation: the trunks and branches of the anterior and posterior choroidal arteries and temporal branches of the posterior cerebral arteries. With this fact in mind, we applied the method of preliminary clipping of the largest trunks of the afferent arteries before their occlusion and transection. The anterior choroidal artery warrants special attention, as its transection causes severe local pyramidal symptoms.

We made a close study of the microsurgical anatomy of the anterior choroidal arteries and determined that the branches feed subcortical nuclei and internal capsules directly from the proximal segment of the anterior choroidal arteries. In cases where the anterior choroidal artery arises with two trunks identical in diameter, clipping trunks of the anterior choroidal arteries in their distal segments (Fig. 18.13) does not give rise to neurological symptoms. Vessels can be directly separated from the malformation with the help of bipolar coagulation and microsurgical instruments and techniques. The malformation is then dissected within the perifocal zone with maximum preservation of adjacent "eloquent" brain tissue. Lastly, the draining veins are shrunken and sealed with cautery and silver clips placed on the largest trunks.

The Queckenstedt maneuver is used to check the reliability of the hemostasis, especially when the patient is in the sitting position (during operations on the posterior third of the hippocampus).

The dura mater heals after the patient recovers from the hypotensive state under normal arterial pressure. The connection between hippocampal AVMs and the choroidal plexus warrants attention, as does the examination of additional sources of nourishment for the malformation within the system of anterior and posterior choroidal arteries. Basically, such a study would involve malformations of the posterior third of the hippocampus and to a lesser extent AVMs of the central anterior third of the hippocampus. Furthermore, in 12 of 20 patients operated on for AVMs of the posterior third of the hippocampus (60%) malformations were connected with the choroidal plexus. In 5 of 13 patients operated on for AVMs of the central third of the hippocampus (38.5%) malformations were associated with the choroidal plexus. In these cases total removal of malformations made partial resection of the choroidal plexus necessary.

An important problem during surgery of hippocampal AVMs is explaining the reasons for the appearance of hemianopia, even when the trunks of



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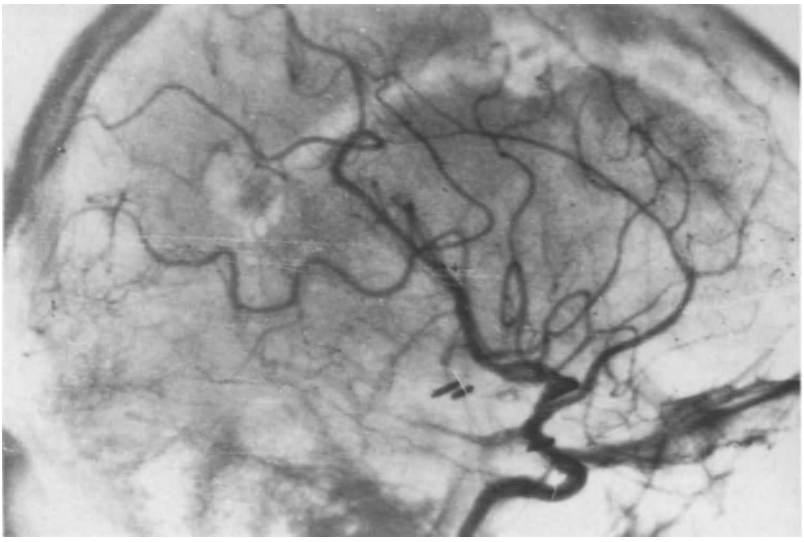

B

Figure 18.12. AP (**A**) and lateral (**B**) carotid angiograms following excision of the AVM.

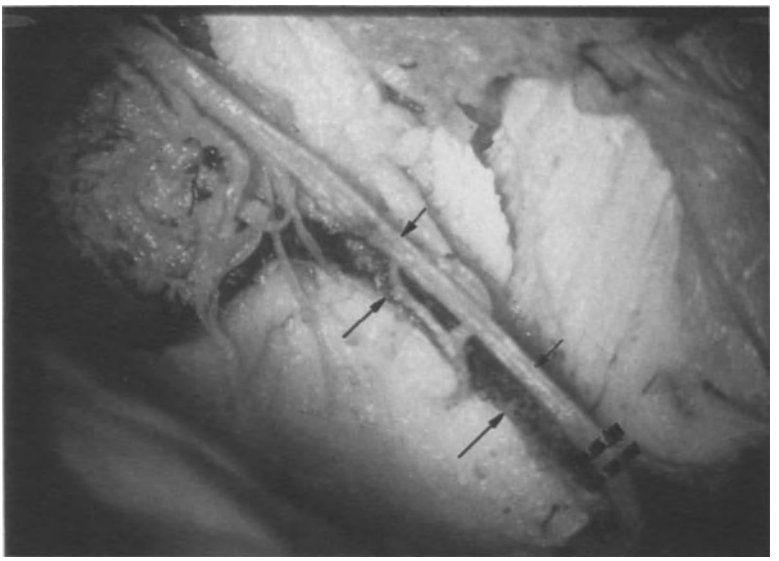

Figure 18.13. Microsurgical appearance of the choroidal artery and possible sites of distal clipping (arrows) prior to AVM excision.

Table 18.6. Neurological symptoms before and immediately after operation

AVM site in hippocampus	Patients (no.)	No increase in neurological symptoms (no. pts.)	Increase in neurological symptoms (no. pts.)
Anterior third	6	2	4
Middle third	13	4	9
Posterior third	20	7	13

the PCA are preserved. In our series of 15 observations involving removal of AVMs of the posterior third of the hippocampus using the occipital interhemispheric approach, in only one case was the posterior cerebral artery transected, causing the hemianopia seen during the postoperative period. In the remaining cases the hemianopia may have been caused by three basic factors: vascular factors, mechanical damage of occipited lobes by spatulas, and surgical trauma, which causes damage to the fibers of the visual analyzer.

Table 18.6 presents an appraisal of the neurological symptoms in patients during the pre- and immediately postoperative periods. Analysis of these symptoms showed that in only 13 cases (33.3%) there no increase in focal neurological symptoms at the time of discharge from the Burdenko Institute.

When evaluating the results of surgical treatment of patients it is essential to consider the data from neurological methods of investigation both pre- and postoperatively. Neurological data show that surgical damage to central

posterior regions of the left hippocampus (in those instances when it combines with damage in other temporal structures) causes the appearance of marked amnestic syndrome (short-term memory deterioration in all spheres). Destruction of memory does not occur using the approach through the interhemispheric fissure. Damage to the right hippocampus leads to defects in knowledge that had been gathered in the past.

Data from neurological and neuropsychological methods of pre- and postoperative investigation help bring to light the reasons for the deepening of neurological problems during the postoperative period and the disturbance of high psychological functions after applying the transcortical approach (nine patients with AVMs in the central third of the hippocampus, four with AVMs of the posterior third of the hippocampus), and disturbance in the visual fields, or homonymous hemianopia (12 patients with AVMs of the posterior third, four with AVMs of the middle third, and one with an AVM of the anterior third of the hippocampus). The mechanism that causes homonymous hemianopia requires further investigation.

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Discussion

Neuropsychological Factors Associated with AVM Removal

Dr. Vinuela: What do you mean by neuropsychological deterioration with a hippocampal lesion in the dominant hemisphere? Do you mean aphasia?

Dr. Eliava: No. In most cases it is some disturbance of short-term memory. I would like to emphasize that this deterioration is irreversible. It represents a significant disturbance. The patient has no focal deficits and full strength in all extremities, but his personality has changed. The transcortical intraventricular approach in the dominant hemisphere carries the risk of this disturbance. The combination of the resection of one of the temporal lobe gyri, either inferior or middle, with resection of an AVM from the hippocampal area always produces such a disturbance. Therefore it is important to use neuropsychological studies when evaluating our surgical results.

Dr. Kachkov: It relates to the social adaptation of patients following the surgical procedure.

Dr. Eliava: In most cases these patients return to their former occupations and function reasonably normally without elaborate support structures. Yet they are changed, and if their work requires higher intellectual activity they cannot perform these jobs.

Direct Versus Endovascular Surgery

Dr. Scheglov: Why did you use direct surgery rather than endovascular surgery?

Dr. Eliava: Endovascular surgery and direct surgery are different types of treatment for the same patients. All of these methods haved their right to exist and now it is rather difficult to come to a common conclusion whether to operate on these patients using direct surgery or endovascular surgery. My opinion is that we shall continue our work and our investigations and accumulate our experience with direct surgery and endovascular surgery. We shall try also to combine these treatment methods. In the future we shall have a chance to show the best one and use the best one. Endovascular surgery for AVMs and direct surgery are not perfect. Direct surgery is the only method that ensures total removal of the AVM. The problems the surgeon confronts in extended AVMs and brainstem AVMs are not always amenable to direct surgical intervention. As for endovascular surgery, it remains to be seen.

The object of my presentation is to show you our experience with direct surgery. There are several patients with AVMs who were operated on in the Burdenko Institute using endovascular techniques. The results of those interventions are for another discussion.

Dr. Berenstein: Did you do any of them in combination?

Dr. Eliava: Yes.

Dr. Berenstein: In other words if you operated on an AVM that had been previously embolized, did it seem as though there was less chance of bleeding, less chance of harming the brain?

Dr. Eliava: Yes.

Dr. Berenstein: I think the AVM is definitely a lesion that is better treated by a combination of techniques.

Dr. Eliava: In the department of Dr. Stein I saw patients with AVMs where a combination of endovascular and direct surgical intervention was used. Now I can

realize better than before the advantages of this combination. I think that in the future it will be interesting to use this combination as much as possible. You are quite right.

Dr. Fox: The AVMs you showed in the thalamus seemed all to be fed by choroidal vessels of the posterior thalamus, meaning that they were really within the ventricle and associated with just the superficial parts of the superior posterior thalamus. Did you have any that included thalamoperforators or lenticulostriates going posteriorly as additional feeders, and have you been able to remove those? Similarly, the caudate ones you showed were fed by lenticulostriates, but being caudate and localized they were also superficial. Do you have any that go deeper as well, that you have been able to remove without much deficit?

Dr. Eliava: We are well aware, all of us, that it is impossible at the time of surgery to see all the minute feeders of AVMs. Therefore when you remove the AVM from this region, as a rule they have an additional small supply, perhaps branches of the posterolateral choroidal artery or mediolateral choroidal artery that are difficult to demonstrate angiographically. When you remove the AVM you must coagulate and divide these arteries.

Dr. Fox: The reason I am asking is—correctly or incorrectly—we believe that if we see that the feeding artery the big feeding vessels are choroidal; then the AVM is easy to remove without ensuing neurological deficit. However, once there is a large feeder from below, the AVM is no longer easy to remove without incurring a deficit. I was wondering if you have a better experience with more success?

Dr. Eliava: You are quite right because this posterior group of perforating arteries, the thalamoperforators, are important and must be preserved. I think those arteries supply the mesencephalon, and all the distal segments of this artery supply this AVM. Therefore when you coagulate this artery, you coagulate only distal segments, and the coagulation of the distal segments is not so important.

Dr Fox: Dr. Drake has said that if there is a big one coming up from the bottom, even if it is a superior thalamic AVM, it cannot be controlled. If it gets away, it shrinks, causing a disaster.

Dr. Berenstein: Why not embolize that one?

Anterior Choroidal Artery

Dr. Viñuela: Concerning your conclusions about the anatomy of the anterior choroidal artery: How many specimens did you dissect?

Dr. Eliava: Ten specimens.

Dr. Viñuela: How many variations did you find? The reason I am asking is that you have stated an important conclusion that does not go along with another microsurgical study of the anterior choroidal. This is an important anatomical variation in the anterior choroidal and the posterior communicating arteries. Sometimes dominant perforators arise and sometimes not. Sometimes one perforator divides into several branches, sometimes it does not. We go into the anterior choroidal artery all the time now, and I have not embolized it because of my concern for those perforators.

Dr. Eliava: All perforating arteries arise from the proximal segment. They arise only from the proximal segment or from the supraclinoid segments of the carotid artery. The distal segment of the anterior choroidal artery supplies only the choroid

plexus. If you clip the artery as close as possible to the choroid plexus it causes no damage.

Dr. Berenstein: There is only one variation, and that is when the anterior choroidal artery embryologically takes over the posterior cerebral artery territory. It is later that it steals the posterior cerebral territory.

Dr. Eliava: Yes, you are correct.

Dr. Berenstein: So the only thing of which you must be careful is if the anterior choroidal artery on the angiogram does not supply the temporal lobe and the temporal portion of the posterior cerebral artery. If that is the case, there is a typical curve on the angiogram—that is, as typical as they come—where the vessel goes in exactly as you have described it microanatomically. I made the point also of following the vessel to its ependymal portion. If Dr. Yasargil is right and I think you mentioned it also, then most AVMs are not in the parenchyma. Therefore it is would be logical that the vessels entering the AVM—the thalamic vessels and the choroidal vessels —are not actually in the brain and serving the parenchyma. Surgically you often have to go into the brain to remove these vessels but perhaps in reality they are extraparenchymal.

Dr. Viñuela: The reason I am asking is that nothing is ever 100% true in medicine. I had a patient with a distal anterior choroidal aneurysm, very distal, very small, a tiny berry aneurysm that hemorrhaged three times.

Dr. Berenstein: Toward the ventricle?

Dr. Viñuela: No, into the temporal lobe, producing a large temporal lobe hematoma. We went in and put a drop of IVCA, just one drop, and occluded the aneurysm. The patient developed a hemiplegia. It was not expected.

Dr. Eliava: I would like to emphasize one point. When we first started doing surgery on deep-seated AVMs—and that was not long ago—we came to learn that it was not effective. We operated on six patients with AVMs located in the hippocampal gyrus, and in all of these cases when the anterior choroidal artery was clipped the patients had a marked hemifacial syndrome. There is only one explanation. When we clipped the anterior choroidal artery we used the routine approach, visualized the supraclinoid segment, and clipped the proximal segment, not the distal segment. Even now, we cannot say that in all cases if you just clip the distal segment there will not be a deficit. Certainly there should be exceptions because of branching, anastomoses, and collateral supply. Sometimes it is dangerous, and sometimes there are not adverse sequelae.

Dr. Stein: Did you have a retrograde thrombosis. Did you obtain another angiogram on that patient?

Dr. Viñuela: It was technically a simple case, and the final angiogram, which was done while the patient was developing the hemiplegia, showed the proximal portion to be open.

Dr. Mohr: I would like to make two points regarding the choroidal territory. The first is that through a simple mistake, I think, Hannah Dimasio (who drew the CT map used by many neurologists) attributed the anterior choroidal artery to an arterial supply to the lateral wall of the lateral ventricles, which it never has, as far as anybody who has investigated the subject knows. Based on her CT maps, many well-intentioned neurologists have been trying to create syndromes of the anterior choroidal artery. If some defenses must be made for your behavioral schemes, it would be good to you set them aside, because the point of these syndromic analyses

is that conventional lenticulostriate infarction syndromes have now been mistaken completely for anterior choroidal syndromes based on the erroneous CT anatomy map created by Dimasio.

My other point is that in our stroke data bank, which is an 1800-case study, the most intense plegias for the smallest lesions have been below the level of the thalamus in the lateral peduncle, which maps in an unusual way in many CT scans depending on the angle. These lesions are really supralateral infarctions above the peduncle and below the capsule. They are proximal choroidal territory infarctions that are difficult to see on CT scanning and even on MRI are only a thin rim along the side of the midbrain.

Dr. Viñuela: Deep hemiplegia?

Dr. Mohr: Very dense. When the internal capsule becomes the peduncle, that little strip of tissue is actually supplied by tiny perforators that arise from the anterior portion of the anterior choroidal artery. To our group this is routine information, but to many neurologists it is confusing. They are looking at Dimasio's map and getting the wrong answers.

Dr. Eliava: I would like to add an important point. You have taken into consideration not only the distribution of branches of the anterior choroidal artery but also the interarterial anastomoses. I am not speaking about cortical anastomoses but about the deep-seated, deeply located anastomoses between arteries. In the patient whose distal segment was occluded perhaps there was a lack of adequate anastomosis. Perhaps it is an unpredictable circumstance unless we are able to detect these anastomoses angiographically.

We have investigated anastomoses between the superior cerebellar and the posterior cerebral arteries particularly when we are dealing with a patient with a posterior fossa AVM. We have a patient with an AVM located in the mid-line structures of the posterior fossa in the cerebellum. This patient had been operated on many years previously with successful clipping of both superior cerebellar arteries. Control angiography demonstrated no filling of the AVM. The patient returned to our clinic 5 years later with a recurrent hemorrhage. Angiography demonstrated refilling of the same AVM. We attempted to determine the source of this filling, and it turned out to be an anastomosis between the superior cerebellar and posterior cerebral arteries. Therefore we know the site of this anastomosis.

Dr. Berenstein: Not in nonoperated patients. Your patient probably also had a dural supply to the AVM that he never had before.

Dr. Eliava: Yes.

Dr. Berenstein: It was the surgery, I think. Perhaps it was similar to the surgery the Japanese perform for moyamoya disease, where the dura is cut. This is a secondary angiogenetic type of anastomosis. It does not exist in the nonviolated anatomy, at least I think it does not exist. However, in operated patients I can see exactly what you are talking about, and it can happen from the superficial temporal artery to the brain in AVMs. We manage it. We see meningiomas that recur at the site of previous craniotomy where the superficial temporal artery supplies the normal cerebral arteries and the tumor as well.

Dr. Eliava: Yes, I agree and emphasize that this anastomosis is located in the quadrigeminal plate. It has two, three, or maybe four branches and the diameter of the anastomosis may be 1.2 mm, so it is quite large. It must be taken into consideration.

Sector Anopia and the Vascular Supply to the Lateral Geniculate Body

Dr. Mohr: One other point regarding the visual fields. Our case published in 1971 is the only instance I know of infarction of the lateral geniculate body related to a posterior cerebral artery occlusion documented on serial brain sections. There was involvement of the posterolateral choroidal as well as the posterior cerebral stem. In this case the back third of the lateral geniculate body was found to be infarcted for more than 100 μm of its length, and the patient had a permanent quadrantanopsia with middle sector anopia. Frisen, a Norwegian, has been interested in the visual field disturbances due to alleged lateral geniculate infarcts, but there are no autopsy studies. There are five cases of lateral geniculate atrophy reported in the ophthalmology literature following enucleation of the globe, but no one knows the reliability of the vascular supply to the lateral geniculate body. The literature reports that the anterior choroidal supply is one part, the posterior cerebral another one-third, and the posterolateral choroidal another one-third. I believe this is unknown—not only unknown but probably wrong in every respect.

Dr. Viñuela: The first branch of the posterior cerebral artery is the so-called artery of the quadrigeminal plate, an artery that is never seen angiographically. We have seen it twice in association with an AVM. It goes from the P_1 portion all the way into the perimesencephalic cistern medial to posterior cerebral artery and supplies the lateral geniculate ganglion. I suggest that those cases with a posterior cerebral artery anastomosis close to the basilar tip and the posterior cerebral will demonstrate this artery to the lateral geniculate ganglion.

Dr. Mohr: It is possible through quantitative visual field testing to pursue the question of the sector anopia. No matter what the arterial anatomy, everyone agrees today that the existence of a sector anopia is thought to be diagnostic of a lateral geniculate infarction because it cannot occur in the optic radiations, and it is a defect in which the hours from 2 to 4 are missing from the face of a clock. Lateral geniculate infarcts with a quadrantanopsia, which is a common finding after a posterior cerebral territory infarction, are distinguished by a missing segment from 12 to 3 on the face of a clock. If the visual defect includes not only the quadrant, but 1 hour on the clock below 3 or 1 hour on the clock above 3 and the presence of that intermediate 2 to 4 o'clock piece, there is a degree of certitude that the lateral geniculate body has been involved.

Memory Disturbances with Unilateral Hippocampal Lesions

Dr. Mohr: The behavioral defects observed are likely due to infarction of the fibria of the hippocampus in the dominant hemisphere, which in our infarct cases has produced a spectacular short-term acute memory disturbance. This phenomenon is not accepted in neurosurgical circles because most neurosurgeons still rely on the reports concerning hippocampal removal during the 1950s in which it was said that bilateral lesions had to occur for the acute memory syndromes to develop. This is false. Unilateral syndromes or infarctions in the back third of the fimbria are more than enough, and if the lesion passes under the splenium of the corpus callosum into the first third just beyond the trigone, stunning total alexia can be added to the clinical picture. These people generally do not know anything is wrong; so unless they

are tested, they think everything is fine. If they work on farms, no one notices it; but if they work as a stockbroker, everyone knows the same day and the memory disturbance that occurs acutely persists for at least a year and a half.

Dr. Eliava: We consider, in most cases, this increase of neuropsychological signs to be a consequence of two injuries: section or resection of the temporal cortex in combination with removal of the AVM. When we remove AVMs using the supratentorial interhemispheric approach or via the transsylvian fissure approach we do not encounter such marked deteriorations.

Dr. Mohr: I think that it is possibly because you do not remove the fimbria, the fornix, and the mesial occipitotemporal region at the same time—just as a guess.

Dr. Emily Friedman: Dr. Mohr brought up something that is important to emphasize: that it is poorly documented in the literature that a unilateral dominant hippocampal lesion can result in profound memory loss. Some of the work with Korsakoff syndrome has suggested that some unilateral lesions may be symptomatic. This point is important to evaluate in terms of anterior, middle, and posterior hippocampal lesions. It appears from your statistics that the posterior third lesions are the ones with neuropsychological sequelae. I believe this is a significant contribution and should be published.

Dr. Mohr: It would be of value to bring it to the attention of the neurosurgical community.

Dr. Fox: If you are going to write it up as a package for this area, it would be interesting to distinguish dominant and nondominant hemisphere lesions and other aspects of the details of these cases because the posterior third of the hippocampus should be correlated as to dominance and memory loss with Amytal testing prior to surgical or endovascular treatment.

Dr. Friedman: Particularly if you have MRI evidence that the opposite hippocampus, particularly the nondominant one, is intact.

Dr. Mohr: This forum is an ideal opportunity to present these data because the presence of the lesion demands surgical or endovascular intervention. Like the early surgery done for intractable epilepsy, removal of these portions of the brain is considered necessary to save life and preserve health. Hence the secondary neurological consequences—important to us but unimportant to society—can be reported without fear of anybody claiming you did something wrong. It is important to have this information published because we do not know the lesion size that triggers these defects and whether they deficits will be short or long term. We know that they are not "complications."

Dr. Berenstein: We have experienced a similar situation with embolization in exactly that area and severe postembolization memory deficit without other serious neurological disturbance that probably contributed to the patient taking his own life.

Dr. Eliava: The surgical treatment of deep-seated AVMs is the perfect model to evaluate all these neuropsychological signs because if you take only one fact into consideration it is normal brain with an anomaly of vessels, nothing else, and the damage is brought about during its removal. The damage to certain structures can be evaluated with pre- and postoperative neuropsychological testing. Damage caused by endovascular occlusion is different because you always occlude the vessel, and you have tried to take into consideration the system—the brain. When you damage certain structures in normal brain it is not the same as occluding the feeding artery to that area. I believe the best way to evaluate this problem is by direct surgical intervention.

Dr. Mohr: It is important that you put the outcome in two categories: The expected and the unavoidable. It is the same as going through a wall to get into somebody's house. Complications can be addressed, studied, understood, and reduced, in contrast to expected consequences, which are beyond immediate control. If you link the two together as complications that is exactly what the metaanalysis people want to see. They would say, if you cannot do it safely, don't do it at all.

Dr. Berenstein: You bring up a good point because we have always included a hemianopsia due to mesial occipital infarction as a complication. As Dr. Mohr has indicated, though, it is an unfortunate, but expected, result.

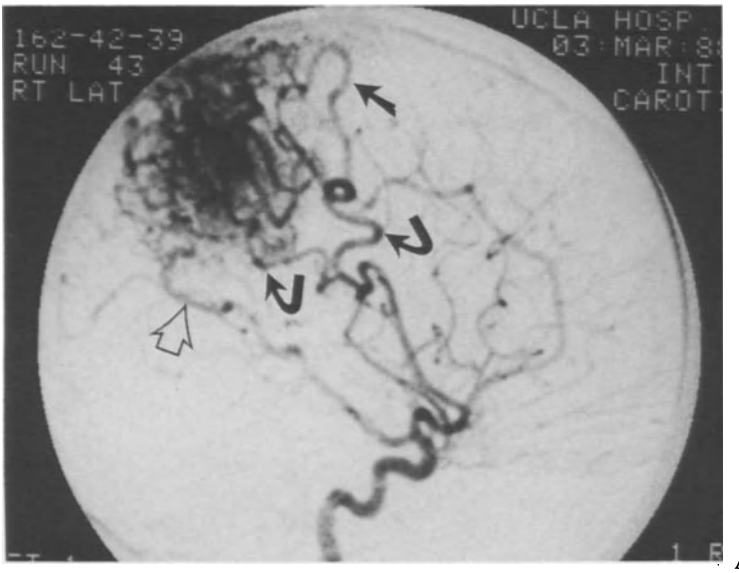
CHAPTER 19

Technical Advances in Endovascular Therapy of Brain Arteriovenous Malformations

Fernando V. Viñuela, J. Dion, G. Duckwiler, P. Lylyk, Allan J. Fox, D. Pelz, and Gerard M. Debrun

Endovascular therapy of intracranial vascular diseases—arteriovenous malformations (AVMs), aneurysms, fistulas, tumors—is a natural extension of techniques of cerebral angiography. The development of microcatheters with or without calibrated leak balloons in their tips allows safe navigation beyond the circle of Willis and catheterization of cortical or deep-seated arteries of the brain.[1] it is also possible to use the intracranial venous route and reach the venous sinuses or even the vein of Galen using a transfemoral technique. The latter technique is applied for embolization of AVMs involving the dural sinuses (especially transverse and cavernous sinuses[2]) or vein of Galen aneurysms in neonates.[3] Various microcatheters are now available that allow safe navigation beyond the circle of Willis if used judiciously. We have catheterized 850 arterial feeders in 228 brain AVMs (Fig. 19.1). No technical or clinical complications were observed in the last 347 superselective catheterizations of brain cortical or deep AVM feeders larger than 2 mm in diameter. Superselective angiography and Amytal testing of arterial feeders of AVMs located in eloquent areas of the brain may be performed on an outpatient basis. This superselective morphological and functional assessment of an AVM provides important information not available with standard cerebral angiography. For brain AVMs that appear to involve the motor cortex, this anatomical and functional localization is compared to localization techniques using somatosensory evoked potentials and intraoperative electrocorticography in an awake patient.[4] The preliminary use of magnetoencephalography to localize the speech cortex has shown some potential, and it appears to be more useful for preoperative localization of the Wernicke area.[5]

Preoperative and intraoperative functional evaluation of the brain with an AVM has shown that not infrequently the presence of an AVM produces a substantial anatomical shift of functional cortex that is difficult to depict with standard techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and standard cerebral angiography. Ojemann described a wide variation in anatomical localization of functional areas of the brain in patients with epilepsy using intraoperative electrocorticography.[6] Figure 19.2 exemplifies the unpredictable shift of the language cortex in a



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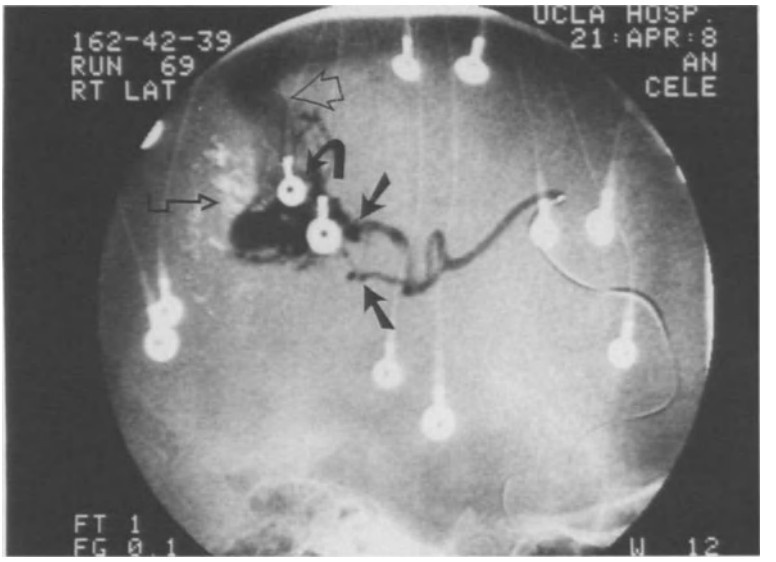

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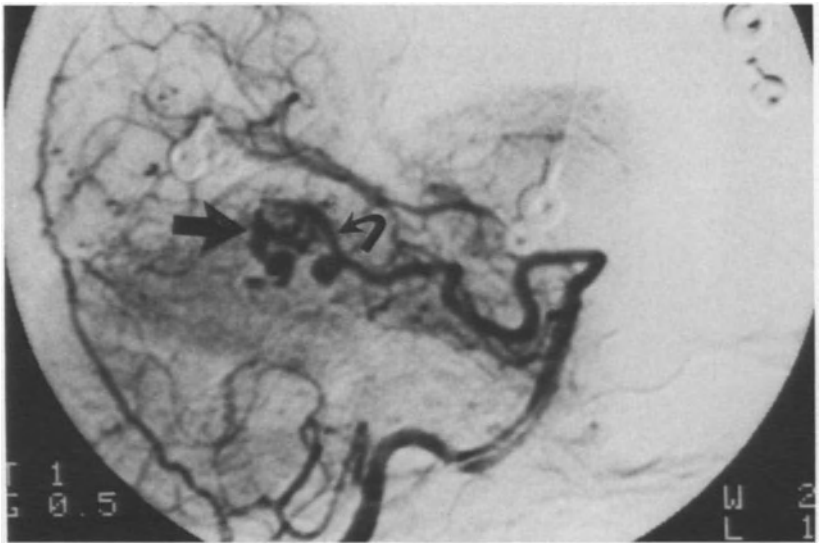
Figure 19.1. Superselective angiography. (**A**) Right internal carotid angiogram shows a large posterior parietal AVM supplied by anterior cerebral (straight arrow), middle cerebral (curved arrows), and posterior cerebral (open arrow) feeders. (**B**) Superselective right pericallosal angiogram shows the anterior cerebral feeders (straight arrows), nidus (curved arrow), and draining vein (open arrow). Note the IBCA deposited in the AVM nidus (half-open arrow) injected in previous embolizations. (**C**) Left vertebral angiogram shows a small posterior temporal AVM (straight arrow) supplied by one posterior cerebral artery feeder (curved arrow). (**D**) Superselective right posterior cerebral artery angiogram shows the microcatheter in the basilar artery (open arrow) and in the distal posterior cerebral artery (arrowhead). The AVM nidus (curved arrow) and draining vein (triangle arrow) are well identified. Complete endovascular occlusion of this AVM was achieved.



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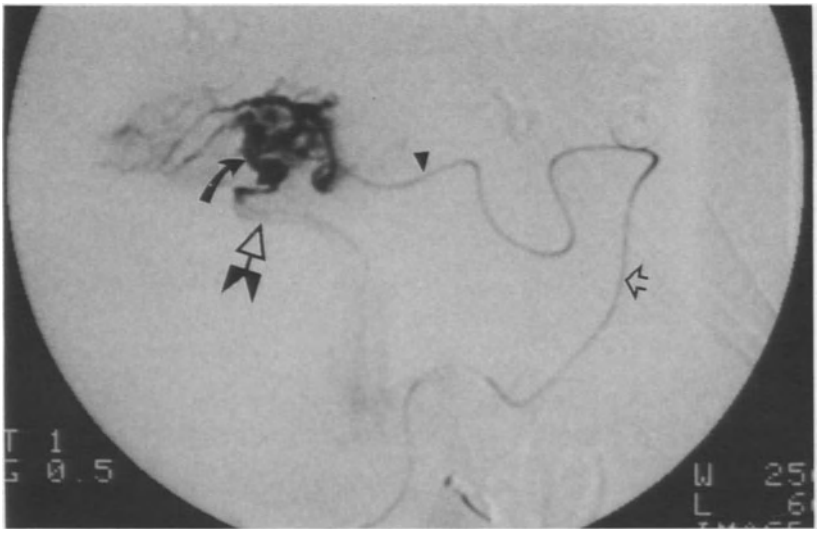

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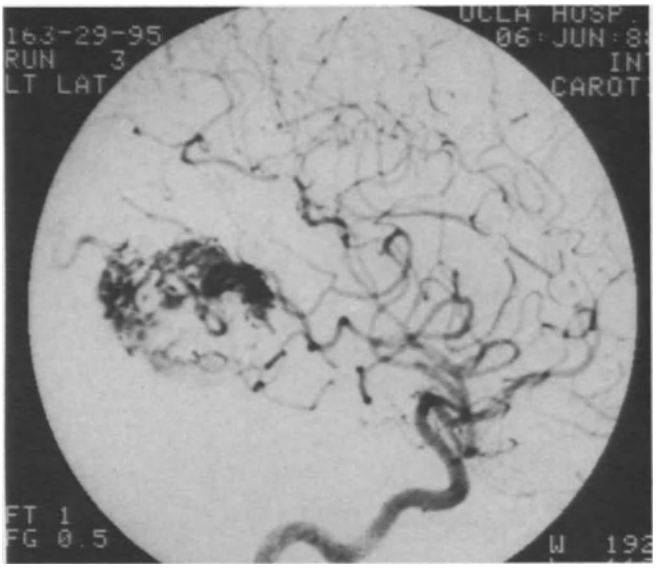

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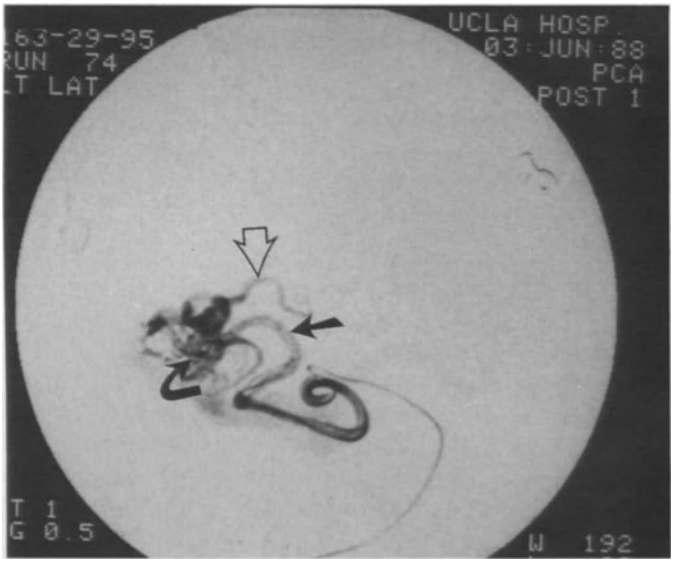

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Figure 19.2. Functional shift of language cortex. (**A**) Left internal carotid angiogram shows an AVM involving the posterosuperior aspect of the left temporal lobe just below the angular gyrus. (**B**) Superselective left posterior cerebral angiogram shows the feeder (straight arrow), AVM nidus (curved arrow), and draining vein (open arrow). This feeder was occluded with 0.2 ml of IBCA. (**C**) Superselective middle cerebral angiogram shows a normal supply to the superior temporal gyrus (straight arrow) and an artery *en passage*, giving numerous small feeders to the AVM (small arrows) and supplying a normal distal brain parenchyma (curved arrow). The injection of 30 mg of Amytal in this feeder produced depression of alpha activity in the left posterior temporal region but failed to elicit speech disturbances.

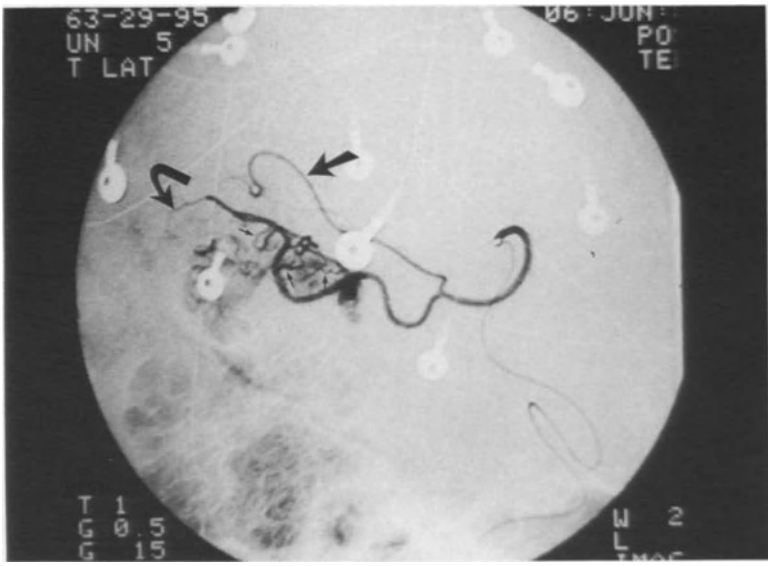

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Figure 19.2 (*continued*)

patient with a left temporal lobe AVM. MRI and standard angiography showed that the AVM involved the posterior aspect of the left temporal lobe, just below the angular gyrus. Superselective angiography of the left MCA feeders showed that the main feeders were vessels *en passage*, with multiple short claustral branches supplying the AVM nidus and an important supply to normal cortex distal to the AVM. The injection of 30 mg of Amytal in these feeders produced depression of the alpha activity of the left posterior temporal region, observed on computerized electroencephalography (EEG), but failed to elicit speech disturbances. Magnetoencephalography and intraoperative electrocorticography with the patient awake demonstrated that the speech representation had shifted superiorly and anteriorly, and it was located in the parietal lobe. This patient underwent complete surgical removal of the lesion with temporary development of mild Wernicke aphasia. The patient was completely normal 3 weeks postoperatively.

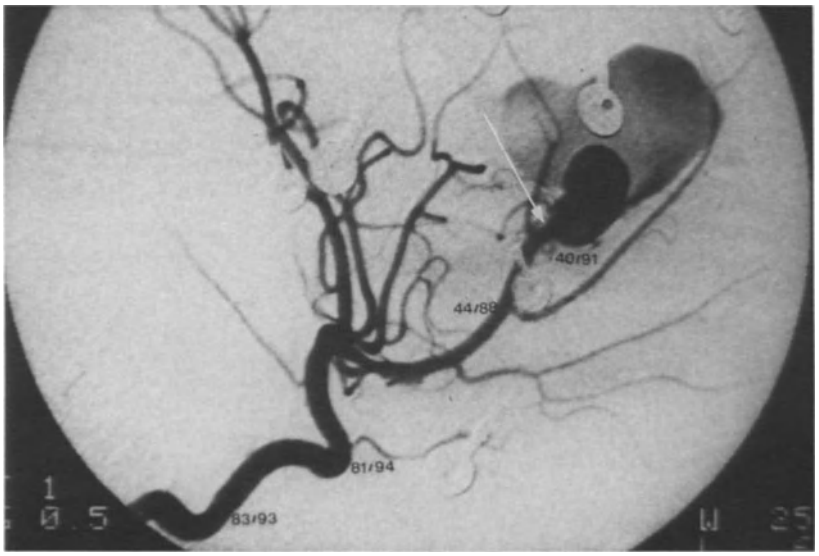
The preembolization superselective Amytal test of individual feeders of a brain AVM is an important tool to decrease iatrogenic problems.[7] The technique has been used in 247 arterial feeders. It consists in the injection of 30 mg of Amytal through the microcatheter immediately after completion of superselective angiography. For the last 93 Amytal tests there was concomitant clinical and computerized EEG brain monitoring by a team of vascular neurologists. The superselective Amytal test produced temporary depression of the alpha activity of the brain cortex in the territory corresponding to the

analyzed artery in 20 of 93 injections (23%). In 11 of these 20 cases the EEG abnormality was accompanied by a neurological deficit that cleared within a few minutes. In feeders of brain AVMs involving brain eloquent areas and in which more than one embolization was performed, the superselective Amytal test was repeated immediately before each embolization. It was shown that a previously negative Amytal test could become positive when partial occlusion of the AVM reduced the sum effect of the lesion and diverted more Amytal to surrounding normal brain cortex. Of 27 Amytal tests, only two elicited false-negative results (0.8%).

Duckwiler et al. have described the technique of intravascular pressure monitoring in arterial feeders of brain AVMs before, during and immediately after embolization.[8] This technique has been incorporated as a standard procedure for all cases of embolization of brain AVMs in our institution. Figure 19.3 is an example of postembolization intravascular pressure changes recorded with microcatheters after occlusion of a left frontal congenital arteriovenous (AV) fistula. Note that the mean pressure in the arterial feeder increased 30 mm Hg as soon as the AV fistula was occluded with a detachable balloon. Similar local and regional intravascular pressure changes have been recorded in true brain AVMs after occlusion of the nidus with various embolic materials (IBCA; PVA particles; mixture of Avitene, PVA, and 30% ethanol).

The prospective analysis and comparison of this hemodynamic information with MRI findings (development of postembolization vasogenic edema or hemorrhage) and with the clinical outcome may shed some light on the controversial postoperative and postembolization complications that have been linked to the breakthrough phenomenon. It is conceivable that some hemodynamic conditions observed in some brain AV fistulas and AVM may be prone to elicit iatrogenic changes as soon as therapy abruptly changes them. The technique of intravascular pressure monitoring may be useful for identifying these potentially risky hemodynamic conditions.

Several embolic materials may be utilized to occlude a brain AVM. The most frequently used are Silastic beads,[9] isobutyl-2-cyanoacrylate (IBCA),[10] detachable balloons,[11] microcoils, and silk. In the last 54 patients we used a mixture of Avitene, 30% ethanol, and PVA (150–250 mm in diameter).[12] The pedicles embolized with this mixture were always permanently occluded with small amounts of IBCA (0.1–0.2 ml), silk, or microcolis to improve the long-term morphological results. This maneuver appears to decrease the percentage of recanalization described when this mixture is utilized.[12] Histopathological analysis of AVM surgical specimens embolized with this mixture shows that this embolic material produces an organized thrombus within the nidus of the AVM with a mild to moderate inflammatory response in the vascular wall. No evidence of angionecrosis of the vascular wall or severe inflammatory response of the surrounding brain parenchyma was noted (Fig. 19.4).[13] In 93 of 228 patients (40%), embolization of the AVM was followed by complete surgical removal of the residual nidus (Fig. 19.5).



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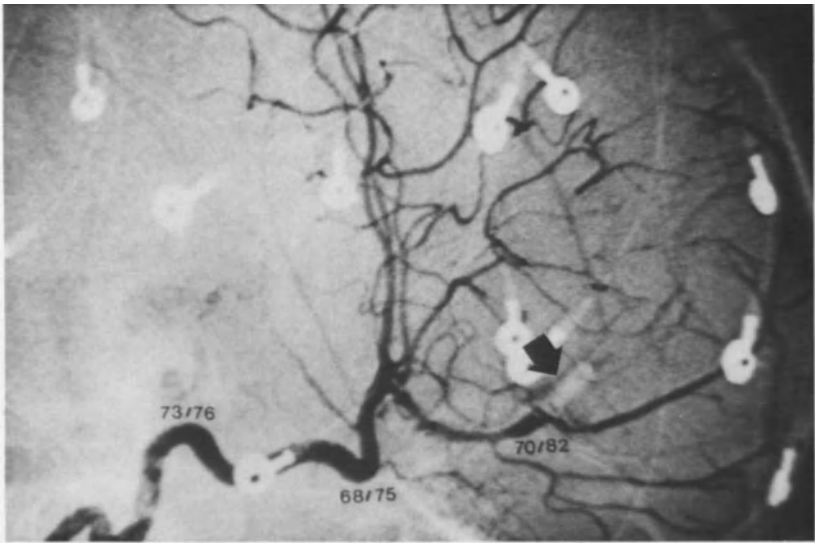

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Figure 19.3. Intravascular pressure measurements. (**A**) Left internal carotid angiogram shows an anterior cerebral artery fistula (arrow) communicating with a giant frontal varix. The pressures on the left have been measured through the microcatheter. The pressures on the right are from the introducer located in the cervical left internal carotid artery. (**B**) Postembolization left internal carotid artery angiogram shows an AV fistula occluded by a detachable balloon (arrow). Note the increase of 30 mm Hg pressure in the arterial feeder. The procedure was well tolerated by the patient, and no evidence of postembolization edema or hemorrhage was noted.

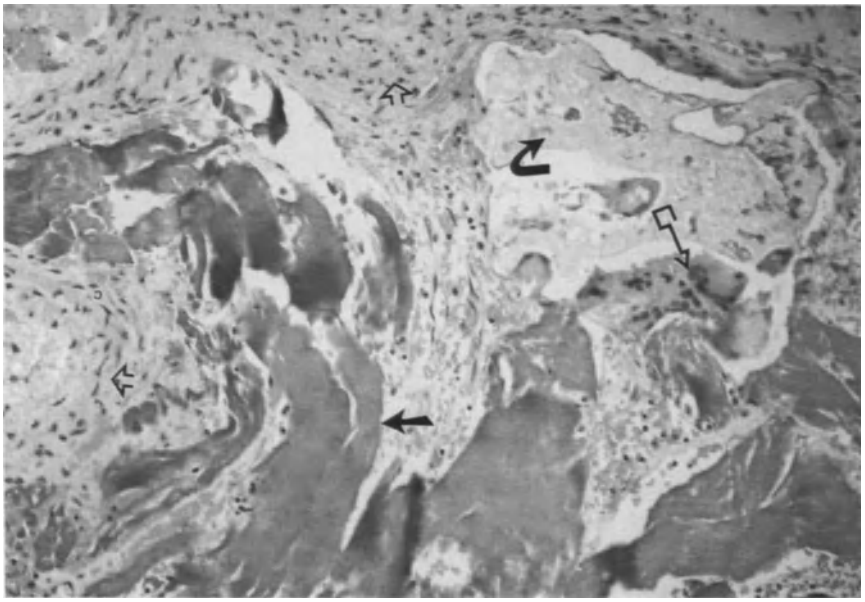
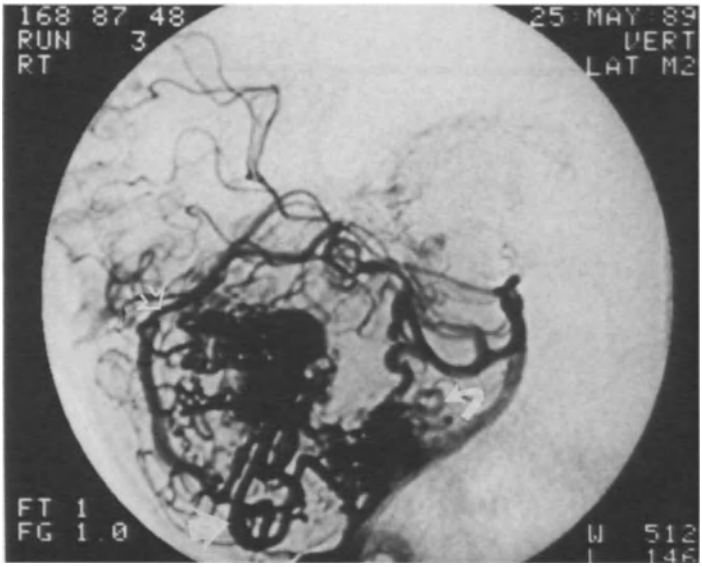


Figure 19.4. Histopathological specimen shows an AVM feeder occluded with Avitene (curved arrow) and PVA (straight arrow). Note an early organization of the thrombus (square arrow) and no significant inflammatory response in the vascular wall (open arrow).

Forty-three of these lesions had 50% to 75% occlusion of the AVM, 24 had 75% to 90% occlusion, and 19 had less than 50% presurgical obliteration of the AVM. It is advisable to wait 7 to 10 days between the last embolization and the surgical procedure. This waiting periods provide time for the surrounding brain to adjust to a new circulation, to decrease postembolization ischemia and vasogenic edema, and to allow progressive thrombosis of AVM draining veins. These local morphological modifications in and around the AVM nidus may be helpful to the neurosurgeon for the identification of a plane of cleavage between normal brain and the AVM nidus. Presurgical embolization of large or giant AVMs with multiple pedicles may be useful (decreased operating room time and blood loss) when most of the deepest feeders have been occluded (anterior cerebral, posterior cerebral, and perforating feeders), when a significant portion of the AVM nidus has been obliterated, and when thrombosis of large draining veins has occurred. The occlusion of AVM feeders alone without obliteration of the AVM nidus may not help the neurosurgeon because the endovascular occlusion of large primary feeders may promote enlargement of myriad smaller cortical and deep collaterals that may be more difficult to coagulate during surgical removal of the lesion.

Midline AVMs may present a difficult therapeutic challenge for the neuro-



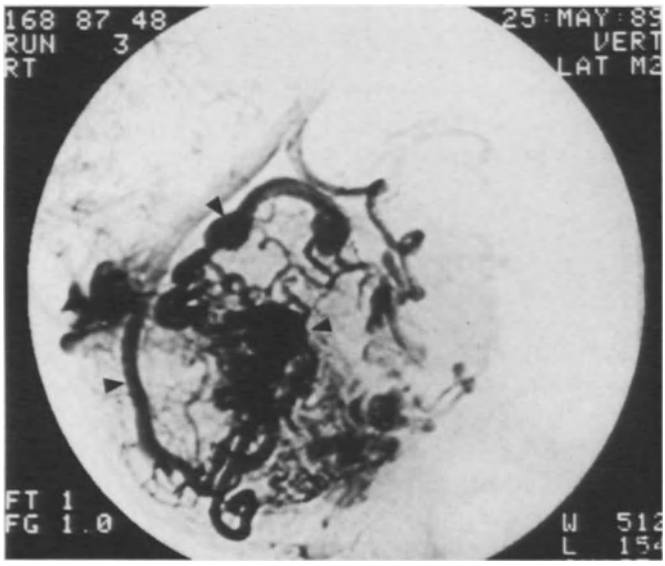
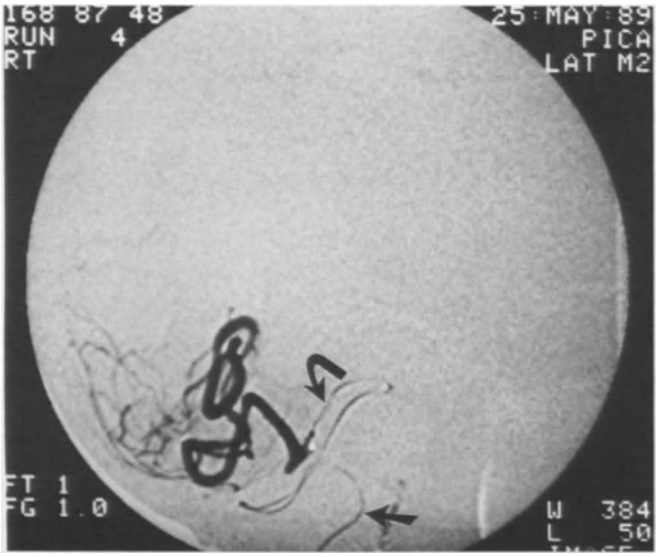


Figure 19.5. Presurgical embolization of a large posterior fossa AVM. Lateral arterial (**A**) and venous (**B**) left vertebral angiograms show a large cerebellar AVM supplied by pica (straight arrow), aica (curved arrow), and superior cerebellar (open arrow) feeders. The AVM nidus drains through dilated cerebellar cortical veins (arrowheads). (**C**) Postembolization superselective right pica angiogram shows obliteration of the AVM nidus with preservation of normal artery. Note the microcatheter in the right vertebral artery (straight arrow) and proximal right pica (curved arrow). (**D**) Postembolization left vertebral angiogram shows marked reduction in the size of the AVM nidus. Residual AVM (straight arrows) is supplied by pica (curved arrow) and superior cerebellar (arrowhead) feeders. Surgical removal of the residual AVM was performed 1 week after embolization.



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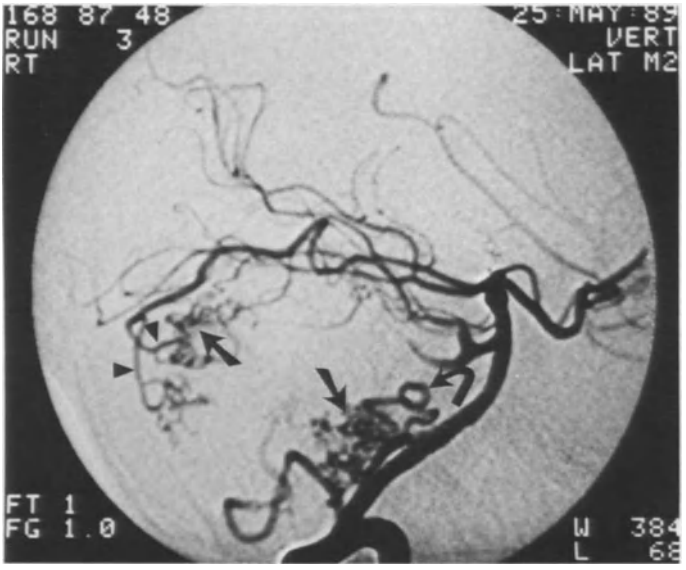


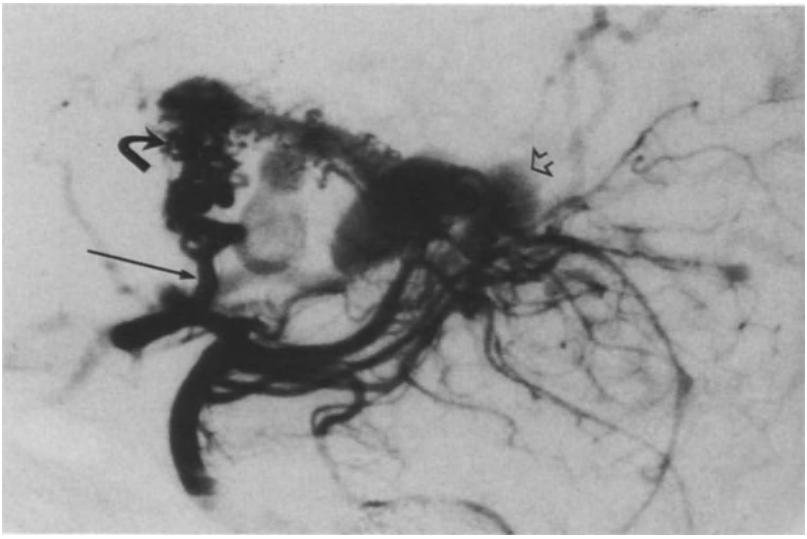
D

Figure 19.5 (*continued*)

surgeon. They include AVMs of the corpus callosum, mesiotemporal lobe, incisura, thalamus, basal ganglia, diencephalon, and mesencephalon.[14] Some of these AVMs involve essential anatomical structures, and they may be difficult to remove without producing a severe neurological deficit. In cases amenable to surgical removal, the neurosurgeon finds that a significant blood supply to the lesion arises from feeders too deep to be clipped before the AVM nidus is resected. These deep-seated feeders may be obliterated using endovascular embolization techniques if they are more than 2 mm in diameter (Fig. 19.6). Embolization of deep-seated lesions may be followed by radiotherapy of the remaining AVM nidus when surgical excision of the lesion cannot be performed without severe neurological dysfunction.

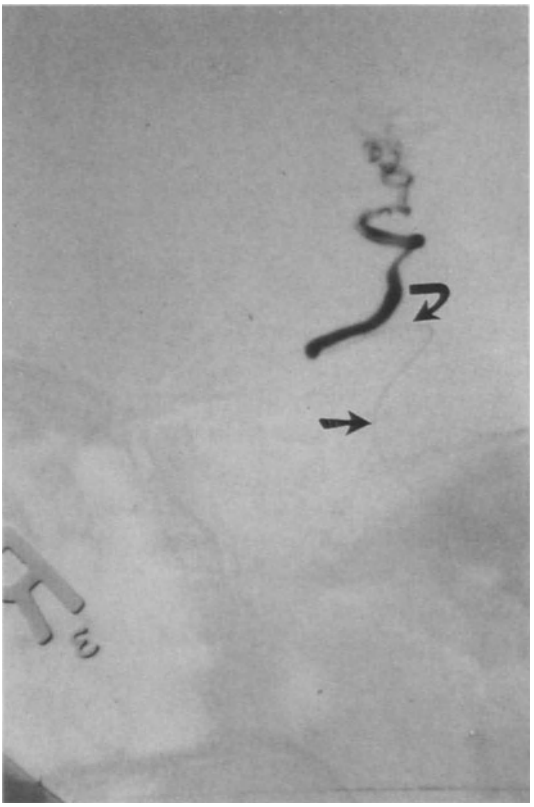
A similar endovascular-neurosurgical approach can be used for large posterior fossa cerebellar AVMs. The presurgical embolization of superior cerebellar, anterior inferior (AICA) and posterior inferior (PICA) cerebellar artery feeders with marked occlusion of the AVM nidus may be of great help to achieve complete surgical removal of the lesion with low morbidity and mortality.

Table 19.1 describes immediate and long-term morbidity of endovascular



A

Figure 19.6. Embolization of perforators. (**A**) Left vertebral angiogram shows the anterior thalamus perforator (straight arrow) supplying an AVM in the cistern of the vellum interpositum (curved arrow). The AVM drains into a thrombosed vein of Galen (open arrow). (**B**) Superselective angiogram of thalamoperforator performed through the basilar (straight arrow) and posterior communicating (curved arrow) arteries. The AVM was successfully removed after embolization of several lenticulostriate and thalamic perforating feeders.



B

Figure 19.6 (*continued*)

embolization of 228 brain AVMs. It includes embolization and postembolization surgical morbidity. Pre- and immediately postembolization subarachnoid hemorrhage (SAH) occurred in nine patients (3.9%), intracerebral hematoma in six patients (2.6%), long-term mild neurological deficit in 18 patients (7.8%), moderate neurological deficit in three patients (1.3%), and severe neurological dysfunction in six patients (2.6%).

Table 19.2 summarizes mortality in these 228 patients treated with embolization alone or a combination of embolization, surgery, and radiotherapy. Six deaths occurred during or immediately after an embolization procedure (2.6%). In four of these six cases (1.8%) rupture of an artery by a inflatable calibrated leak balloon could be identified as the source of the hemorrhage. In two of those six cases (0.9%), the sudden occlusion of a large fistula associated with an AVM nidus could have produced a rapid increase in pressure in the AVM nidus with its subsequent rupture. Three deaths were related to postembolization surgery (1.3%). They include one case of intra-

Table 19.1. Brain AVMs: Morbidity ($n = 228$)

	No. of patients	
Problem	Immediate	Long term
Hemiparesis		
Mild	12 (5.2%)	8 (3.5%)
Moderate	10 (4.3%)	1 (0.4%)
Severe	7 (3%)	2 (0.87%)
Sensory deficit	3 (1.3%)	1 (0.4%)
Aphasia		
Mild	3 (1.3%)	3 (1.3%)
Moderate	5 (2.1%)	1 (0.4%)
Severe	2 (0.87%)	2 (0.87%)
Gait ataxia		
Mild	1 (0.4%)	2 (0.87%)
Moderate	2 (0.87%)	1 (0.4%)
Severe	2 (0.87%)	2 (0.87%)
Memory deficit		
Mild	2 (0.87%)	3 (1.3%)
Moderate	2 (0.87%)	1 (0.4%)
Visual field		
Hemianopia	7 (3%)	5 (2.1%)
Quandrantopsia	3 (1.3%)	4 (1.75%)

Table 19.2. Brain AVMs: mortality ($n = 228$)

Cause	No.	%
Related to embolization	6	2.63
First 128 cases	5	3.90
Next 100 cases	1	1.00
Related to surgery	3	1.30
Delayed hemorrhage	4	1.75

operative hemorrhage, one case of postsurgical massive pulmonary thromboembolism, and one case of postoperative lung abscess formation and septicemia).

Four deaths occurred 6 months or more after embolization, all related to a fatal intracranial hemorrhage (1.8%). In one of these cases approximately 90% of the AVM nidus had been obliterated using IBCA. Despite this anatomical result, the patient had a fatal intracranial hemorrhage 9 months after embolization. Two of these four patients had large basal ganglia AVMs, and only 50% or less of the AVM had been obliterated by endovascular techniques. In one case the residual AVM was associated with an

intracranial aneurysm, and it was not possible to know the cause of the terminal intracranial hemorrhage.

Summary

Recent technical advances in the development of microcatheters allows safer intracranial navigation beyond the circle of Willis. The techniques of superselective angiography and Amytal tests of arterial feeders of brain AVMs involving eloquent areas can be performed on an outpatient basis. This invaluable morphological and functional information is not available on a standard cerebral angiogram, CT, or MRI; and it may assume a fundamental role in the final therapeutic decision taken by the neurovascular team.

The functional evaluation of the brain using preembolization localization of the central sulcus with somatosensory evoked potentials, superselective Amytal tests, magnetoencephalography, and intraoperative electrocorticography showing the presence of an AVM may produce an unpredictable and significant shift of brain eloquent areas such as the motor or speech cortex. Presurgical embolization of large or giant AVMs appears to be a useful technique when a large portion of the AVM nidus has been occluded, when the largest and deepest feeders have been obliterated, and when thrombosis of the largest cortical or deep draining veins has occurred. It is essential to develop new embolic materials that allow better control of their delivery and consistent long-term obliteration of the AVM nidus. The mixture of Avitene, 30% ethanol, and PVA appears to be suitable as a presurgical embolization agent, but it has been shown that it does not have satisfactory long-term results. IBCA still appears to be the agent that achieves the best long-term morphological results when it has been deposited in the nidus of the AVM.

The development of more controllable microcatheters, the functional information obtained by the superselective Amytal test with concomitant EEG and clinical brain monitoring, the combination of embolic materials that may be used in individual arterial feeders depending on their hemodynamic characteristics, and the increasing experience of the endovascular team appear to be the most influential factors that have contributed to the improvement of the morphological results and the reduced morbidity and mortality in the last 100 cases of this series compared with the first 128 cases.

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Discussion

Monitoring Cerebrocortical Function During Embolization

Dr. Viñuela: We are in the process of amassing functional information about AVMs before, during, and after embolization. We are going to complement this functional information with a local injection of xenon in the various feeders in order to assess the flow before and after embolization. We expect that this information will provide a perspective relevant to a functional evaluation of a given AVM. It should help us avoid reacting after the fact and, instead, enable us to predict, before initiating treatment, which AVM is hazardous and which carries a risk of morbidity during embolization.

Dr. Berenstein: How many participants in this group of interventional neuroradiologists are monitoring cortical and brainstem function using such techniques? The answer is probably no one.

Dr. Moret: In the presence of an AVM the area of functional brain tissue may be shifted away from the AVM. We use the Amytal test.

Dr. Fox: When we inject Amytal into a feeding vessel of an AVM we always worry that the sump effect of the AVM will take most of it and there will be a false-negative reading. Have you examined the adjacent normal middle cerebral artery branches to prove that the motor area is nearby as a positive test rather than the negative test of not finding an effect in a given feeder?

Dr. Viñuela: When you do superselective angiography you are going into the areas that are supposed to be involved and you are going to do an Amytal test. You are asking if we put a catheter into a normal vessel with a normal caliber. The answer is that from our experience with the "stress technique" in AVMs near or in the motor or language cortex—and that experience is now substantial—it permits us to minimize, but not eliminate, the possibility of a false-negative result.

Dr. Fox: I understand that part. In effect we have been doing it as well, and probably our colleagues are doing just that. I think what is special is your integrated and learned assessment of where the functional cortical areas are located. However, some of your procedures are done on an outpatient basis; and if you are injecting only some of the feeders and the AVMs are a fair distance away, you are not performing the same kind of detailed study as you are with the staged procedures.

Dr. Viñuela: The point is that I am ethically compelled to analyze the area because it is the area on which the surgeon is going to operate. If it is two gyri behind, you might ask what does it matter? If it is two gyri behind and you want to take the risk of producing ischemia in that area, of course it matters. I am not going to act on any area with an interventional technique in which we believe eloquent function is present.

Dr. Fox: What I understand from your presentation is that the ultimate study you are performing is the staged clinical Amytal test. The other tests you are doing are neat and fancy, but they are not the ones on which you base your final decision.

Dr. Viñuela: The Amytal test is one part of the functional analysis. Electrical activity of the brain forms another part of the analysis by virtue of the electrocortical marking. The endovascular neuroradiologist does not make the final decision alone. All this information is presented to the group for discussion. In a year or two we will be able to tell you whether our functional evaluation was worthwhile or electrocortical monitoring was better.

Dr. Taveras: Was it not positive often enough in the examples you showed here? In

other words, despite the fact that you were injecting a feeder, the test was still positive often enough.

Dr. Viñuela: If you inject 30 ml of Amytal into a given feeder, even with the sump effect the Amytal test is positive. It is positive by electrocortical mapping. The alpha activity of the brain is highly sensitive and reacts dramatically. It often correlates well with function. We feel confident with the watchful "hawk eye" of the neurologist, who tells us whether we can or cannot embolize a given AVM. He is obsessive in depicting those early changes seen in the alpha activity of an electrocortical map. We have markedly improved the outcome and decreased the morbidity of our procedures in this manner.

Radiosurgery for AVMs

Dr. Apuzzo: A key issue in neurosurgery overall is finding a place for radiosurgery in the management of AVMs. In this context a second key issue relates to the interaction between interventionalists, neurosurgeons, and radiosurgeons. You showed a case of an individual who had subtotal occlusion of an AVM with a residual lenticular-shaped component of that lesion. Dr. Viñuela, what is the confidence factor in radiosurgery targeting for a given AVM? If I were going to target that lesion, recognizing that it is a difficult target to begin with because of its lentiform shape, would you be confident in telling me that I should just target that particular portion of the lesion keeping in mind that there is an 80% to 85% certainty of occlusion within a 2-year period. The key issue from the radiosurgical standpoint is that subtotal occlusion is as good as none, so then what do you target?

Dr. Viñuela: Perhaps I did not explain myself clearly. The angiogram I showed is the final result of endovascular therapy. It was decided that because of the deep location, the distribution of the AVM, and the necessity of traversing a great deal of normal brain parenchyma to reach it that surgical excision would be difficult and carried a significant risk of morbidity. It was also thought that endovascular obliteration of the anterior choroidal artery similarly carried a high risk of incurring a deficit. The patient, a girl, was neurologically intact, and it was decided to send her for radiosurgery, which was performed. At 6 months I was informed that there were no significant changes, so we are continuing to follow the patient.

Dr. Apuzzo: Forgive me for pressing the point, but it is a key point. When you target a lesion for radiosurgery, the radiosurgeon has the ability to target a lentiform portion of a larger lesion. Therefore the key question that this group might answer from pathological studies on AVMs and from following patients whose lesions are deemed inoperable or those that were treated with radiosurgery is the degree of confidence one can have in the "blind" portion of the angiogram: There *is* a "blind" portion of the AVM that looks clean on angiography. Is it indeed clean, or should the radiosurgeon treat the larger area?

Dr. Viñuela: That is exactly what happened in this case. The patient had an angiogram 1 month later, which is standard procedure. The angiogram showed the same thing—there was no recanalization. They had targeted the vertebral portion only.

Dr. Apuzzo: It is an important case from which to derive information. There must be data from inoperable cases on which radiosurgery was not performed.

Dr. Viñuela: This case was unique because the radiosurgery relied on the angiographic findings to target those areas. That is why the radiosurgeon is so obsessed about saying what happens if it recanalizes.

Dr. Apuzzo: Because of that situation Dr. Heishima is doing our preoperative AVMs. Currently what we target is the area that remains after embolization. We do not target a larger area.

Dr. Debrun: This key issue was addressed at the meeting in Charlottesville, Virginia by Dr. Steiner. I was surprised to see that many people were speaking of the association of embolization and radiosurgery when they were performing the embolization with particles, PVA, and 30% Isonat, and irradiating the patient. We have shown that with embolization using particles (Isonate) there is almost always recanalization. If we are to consider the association of embolization and radiosurgery, we should use more effective embolizing material, such as a glue, and try to block as much as we can of the nidus and then wait, probably 1 to 2 months at least, before offering radiosurgery to be certain that this portion of the nidus is effectively embolized.

Dr. Berenstein: I agree with Dr. Debrun that one should not use PVA if one is contemplating radiosurgery.

Dr. Fox: A case was presented at the Val D'Isère meeting in which IBCA and embolization had been done on an AVM in Sweden. We might criticize how much was injected, but the angiogram at the end of the procedure showed almost all of the AVM not filling. The small portion remaining was treated with radiosurgery. At follow-up, the portion that had received radiotherapy had disappeared, but parts of the rest were seen again. This situation is the challenge of IBCA embolization. Some of the results are excellent at follow-up, and others demonstrate refilling. Just because we use glue does not guarantee that the AVM will not refill at some later time.

Dr. Berenstein: It is not the glue; it is how you use it. Indian researchers have reported that IBCA use is associated with recanalization, and so many believe that IBCA is useless. If you use 0.3 to 0.2 ml I agree it acts like a particle. We have shown on many occasions with coils, glue, and Ivalon that what brings about recanalization is autologous blood that becomes mixed with the embolic material. It is not the glue that recanalizes. The case you mentioned from Sweden was the result of a fragmented push technique, as were all the cases from India. Dr. Pile-Spellman said that the injection has to be a continuous column. It has to be a true cast. Dr. Steiner has done 70 to 75 cases for us, and I agree with Dr. Debrun that you do have to wait because even the best of us gets a column that is not perfect. It is critically important to obtain a column of embolic material that is perfect so it does not recanalize. Vinters reported that glue was present outside the lumen of the vessels. He was misreading the pathology because it was actually autologous blood clot mixed with glue where the autologous clot created a new endothelium. Cross sections of the specimen make it appear that the glue is outside the new endothelium. When you have a continuous column and a good catheter tip, there is no recanalization. Of course no procedure is 100% successful. This point, however, is key, particularly if radiosurgery is contemplated. If you are going to do a preoperative embolization you can use coils, silicon spheres, or Ivalon; they all seem to work.

Neuropsychological Testing of Patients with AVMs

Dr. Eliava: Would you perform neuropsychological investigations before or after surgery?

Dr. Viñuela: Neuropsychological testing is done in all of our patients.

Dr. Eliava: It is my opinion that we have to take into consideration the entire cerebral system when attempting to compare brain function in a patient with an AVM with that of a normal individual. We have had numerous patients who after

resection of an AVM located in the motor area had an excellent recovery of motor function, which should not be expected after resection of normal motor cortex without a vascular malformation. It is difficult to find a neurosurgeon who can accurately explain the phenomenon of recovery of function, especially motor disorders, after removal of the AVM.

Neuropsychological testing demonstrates some of the dysfunctions accompanying an AVM that are more persistent than motor dysfunction. Therefore a thorough neuropsychological examination must be included in the analysis of results of surgical resection of AVMs. If I may exemplify this with a short anecdote: A 16-year-old boy was admitted to our institute after two seizures and was found to have a large AVM located in the central motor area. The parents of this youngster compelled Professor Filatov to proceed with a surgical excision after all the surgical risks were presented in a detailed manner. Following the operation his recovery was uneventful, and he was discharged with no evidence of motor difficulties. No one had a complete explanation for this recovery, and it implies that there is a significant difference in function of the brain in the region of an AVM.

Dr. Stein: I would like to make a few summary comments at this juncture. Dr. Mohr has followed all of our patients, many of whom have undergone embolization. I think that your studies of cortical function with Amytal are interesting, and they help to correlate the work of Dr. Ojemann and others. Your technique represents an ingenious way to measure the pressures during these procedures. Quite frankly I think we are confusing neurophysiological problems with flow dynamics. I do not consider the potential for neurophysiological disturbances in these patients to be particularly significant, but I do consider the circulatory dynamic changes that occur after removal of an AVM to be important. Let me explain that statement further. As regards Amytal testing, if you are injecting only into the AVM, which is the target of surgical excision or endovascular obliteration, in and of itself it is a nonmetabolic unit. That is why the veins that emerge from the lesion are red. There are no metabolic activities within the confines of most AVMs. They are relatively discrete entities and well marginated, so infusing Amytal into them per se without having it diffuse into the surrounding brain tissue should produce no change in neurological function. I think that is what you were referring to. Those with a congenital AVM have disruption of the cerebral function that should exist in the area peripheral to the lesion. What may be happening in some of those cases is that the Amytal diffuses out before it gets to the AVM, and the results of the test thus relate to the brain structures surrounding the lesion. I can remove an AVM from any part of the brain without permanent neurological deficit so long as it is marginated and I can control the vascular changes. That statement, however, implies a lot of "ifs": *if* I can get the exposure and *if* I can control the vascular changes both during and after the surgery. There are tremendous changes in the arterial perfusion of the surrounding brain after sudden interruption of a large fistula.

An issue that has not been addressed by investigators is what happens to the cortical veins. At one moment they are carrying high flow under high pressure, and then suddenly that flow drops to zero in a vessel that is too large for even zero flow. There must then be a spreading cortical vein thrombosis after removal of most large fistulas.

I am intrigued by the circulatory dynamics, and it is those parameters that we should measure and analyze. This is one area where embolization has helped me a great deal, especially with large fistulas. I have learned to produce the circulatory changes gradually—first during one embolization, then during a second emboliza-

tion, and perhaps even a third—and then by surgical excision so the insult does not occur as suddenly.

There are two components in the embolization process worth addressing. The first is blocking of the interior of the malformation, which the liquids accomplish satisfactorily; and the second is blocking of the major arterial channels at the margins of the AVM, which perhaps is better accomplished by coils and balloons.

In terms of preventing a perfusion pressure problem, blocking the main feeder artery is most important. In terms of making surgery easier, occlusion of the interstices of the malformation is most important. Therefore the embolization process is a twofold procedure depending, of course, on the materials being used. When we use coils along they serve to block the major feeders, but they do nothing for the interior of the malformation. When we use pellets or slurries the interior of the malformation is blocked, which brings up my final point.

What are perceived as angiographic occlusions are not necessarily anatomical occlusions. These data are derived from operating on patients who have recently undergone embolization where a good portion of the malformation is angiographically occult and not visualized. When we operate on those lesions there is still blood flow present. It may not be enough to demonstrate angiographically, but it is there. The idea of irradiating the portion of the AVM that remains visible after embolization makes no sense because probably that part of the angiographically occult AVM is still active. If they are seen to be active at surgery after embolization but not seen to be active angiographically, it is irrelevant whether you believe they will or will not recanalize: One must accept the fact that they will progress.

The point is what you as interventional neuroradiologists see is not what we surgeons see. When we operate on an AVM that appears to be obliterated, we still have to remove the entire area of the AVM. I submit that it is impossible for the radiotherapist or radiosurgeon to irradiate the entire lesion because it is too large an area.

Dr. Berenstein: The experience you talk about may be controversial. I disagree with you on only one point—what you say about the particles, the silicone spheres. There are many surgeons who operate on patients with a good casting of the nidus using even as much as 3 ml per pedicle.

Dr. Stein: What substance is being used for the obliteration is not the argument. It is the point that what you see as being obliterated angiographically is in fact not anatomically obliterated. It may appear obliterated on an angiogram, but I can tell you unequivocally when we operate on it we can see that it is not. Its vascularity is certainly reduced enormously, but it is not totally obliterated.

Dr. Apuzzo: One other point along those lines has to do with radiosurgery per se. There have been a number of cases that have been deemed angiographically clean but that seem to have bled from the point where radiosurgery was performed. These cases were mentioned in the San Francisco experience and occurred more than 2 years after the radiosurgery.

Dr. Viñuela: I must disagree. If we have standardized cerebral angiography at the present time, if we do a full angiographic analysis with every single feeder or potential feeder of the AVM injected and we do not see the AVM, I contend from my experience following those patients with intraoperative angiography that those lesions do not bleed.

Dr. Stein: Try cutting into them.

Dr. Viñuela: I do the intraoperative angiography, so I have been in the operating room. They do not bleed. If you are saying that we removed 95% or 98% and left a small channel that we did not see on angiography, you must be referring to the

quality of the angiography. We use superselective angiography and have zero angiographic findings. I would be willing to bet anything that the AVM is obliterated.

Dr. Stein: Maybe if the angiography is done superselectively you are correct. We have not yet done that.

Dr. Berenstein: We just embolized a malformation and referred the patient to Dr. Malis. He cut into the lesion, and there was no bleeding at all.

When at angiographic follow-up at 6 months we see a cast of bucrylate in a part of the nidus that we consider to be completely obliterated, with no filling in the region of the cast, we proceed with radiosurgery on the part of the lesion believed to be active. I believe, Dr. Stein, that you have the experiences you mentioned because you operate too soon after embolization.

Dr. Debrun: I agree. You were too close temporally to the embolization.

Dr. Fox: If we had two different embolization results—one that shows a full column that is filled and one that shows a bunch of little things—the angiograms at the end of the procedure in both cases look the same. However, if we had the most perfect angiogram one could imagine—one where there are multiple small shots, collateral feeders coming around—but the veins do not seem to fill in the angiographic series until the venous phase or even later, the angiographic interpretation would be imperfect and we would not be able distinguish those two from the angiogram. At follow-up a distinction can be made, and what Dr. Viñuela and I and our group called recanalization on the follow-up angiograms was not recanalization at all. I think it was just better filling of what was there all along. We just never saw it. If you operate a couple of days after particulate embolization, you miss the chance of seeing the different outcomes.

Occult AVMs

Dr. Apuzzo: Where do occult AVMs fit into this picture?

Dr. Berenstein: What is an occult AVM?

Dr. Apuzzo: The patient bleeds from an AVM, and the AVM is found at surgery, but the angiogram is negative.

Dr. Berenstein: You are right on target. Those lesions are small, and the hematoma may compress the nidus such that it is not visible angiographically.

Dr. Apuzzo: We either aspirate that type of case, or the clot disappears spontaneously. An angiogram is repeated, and again nothing is seen. We have seen patients who have been subjected to multiple angiograms and who have had multiple hemorrhages. Surgery has revealed an AVM in the wall of the clot. Angiography is limited to a certain extent in defining the microvasculature of an AVM.

En Passage Arteries in AVMs

Dr. Taveras: Do you believe that every artery entering the malformation feeds only the malformation, or is it possible that some of the branches might be feeding the adjacent brain? I believe the latter.

Dr. Stein: This subject is an entity unto itself. It speaks to arteries *en passage*, which situation indeed characterizes many of these arteries. In fact, Dr. Yasargil said that he never interrupts an artery larger that 2 mm because those arteries are going around the AVM. That takes a special skill, and in most situations we end up clipping arteries that are in the 2 to 3 mm range. Sometimes it is difficult for us and for the interven-

tional neuroradiologist to spare the arteries *en passage* and still achieve effective reduction of the AVM.

It appears that some of these so-called major arteries in the vicinity of an AVM, such as a large lenticulostriate artery or a suprasylvian middle cerebral vessel, that otherwise would be important are dedicated to the AVM. They have high flow, are larger than normal, and when you cut them off the proximal pressures are so increased that they open up collaterals. Most of these patients are young, so they do not suffer from occlusion of these otherwise important major arteries, which would be the case in a normal individual. For example, large lenticulostriate arteries entering the AVM (even those that have small aneurysms on them) have been embolized by Dr. Hilal without evidence of capsular infarction and a definitely occluded artery.

Dr. Taveras: Is it because they are going into the malformation?

Dr. Stein: Yes. They are dedicated to the AVM and are not important in some instances to normal brain. However, the surgeon is not always able to distinguish the ones important to the brain from those that are not.

In addition, if we occlude a major artery at the margin of the AVM and look at it under the operating microscope, we see branches going into the normal cortex and perfusing normal cortex. This is one of the large, specifically dilated arteries. An angiogram is performed 1 to 2 weeks later, and that artery is seen to be, occluded 3 to 4 cm back from where the clip was placed even though you know it has been supplying the brain and the patient has no neurological deficit. We consider that type an unusual dedicated artery.

Dr. Berenstein: There are short anastomotic arteries and long anastomotic arches. They do exist. Another element, namely the ischemic break, is a factor. Certain angiogenetic factors can produce sprouting and nonsprouting angiogenesis; and perhaps hormonal factors play a role. What we see angiographically is not all AVM; some of the "AVM" probably represents collateral blood vessels.

Dr. Stein: We have seen several such cases. In one case we embolized the lesion and did a one-stage operation. We cut the dura all the way around the surface of the AVM to the draining vein. We then performed a partial cut around the AVM and closed the wound, planning to come back another day; we resutured the dura and waited 3 weeks. At reoperation the dura had vascularized to the AVM, a fact that was proved histologically. One could see the new vessels. Dr. Hilal performed a simple embolization. At the time of operation I was amazed at the number of small cortical vessels going to the margin of the AVM.

Dr. Berenstein: Was there a proximal occlusion in that case?

Dr. Stein: Thee was a major occlusion with the AVM, but the appearance of collateral ingrowth was enormous. There must be an angiogenesis factor.

Dr. Berenstein: Do you remember a case you did in Boston that showed just the opposite? There was a multifocal AVM. You took care of the major fistula, and the rest of the AVM regressed. That case implies that not all of the vessels that appear to be angiographically abnormal are in fact part of the AVM. When evaluating the anatomy of AVMs one cannot always tell which vessels belong to the AVM. There are times when I look at an aneurysm and am not sure if it belongs to the AVM or to the collaterals. We too have seen regression of AVMs, just as Dr. Stein has noted, so I believe there are factors present that elude our understanding at present.

Dr. Viñuela: There is an angiographic interpretation of regrowth of AVMs, suggesting that it is not really regrowth but, in fact, may be angiogenesis.

IV. FUTURE CONSIDERATIONS

CHAPTER 20

Determining the Feasibility of Creating a Statistically Significant Cooperative Study of Arteriovenous Malformations

J.P. Mohr

Efforts to estimate the impact of intervention on the natural course of disease has finally reached even arteriovenous malformations (AVMs). Here, however, the attempt to estimate the effects of therapy is confounded by the small database, the great difficulty obtaining natural history data, a history that spans decades of risk, the nonuniformity of the disorder (which in the case of AVMs may well represent a family of conditions rather than a single one), and finally and not least the variable outcome of surgery and interventional radiology, which appear to depend heavily on the skills of the management team as much or more than do many other conditions.

Until the 1930s AVMs were scarcely identified during life. During the last few years the sensitivity of neuroradiological imaging tools has greatly increased their rate of discovery. Because most of the reported cases of AVM come from the experience of large centers with special interest in surgical therapy the exact natural history data are unclear. The largest series report of the incidence of AVMs contains 549 cases among 6368 subarachnoid hemorrhages (SAHs) (8.6%). It has long been known that SAH accounts for roughly 10% of strokes and that AVMs make up approximately 1% of all strokes. These figures are reflected in another population-based prospective study of stroke done during the census year 1980, carried out by me and colleagues in southern Alabama, in which an eligible population of 100,000 was studied over a period of 3 years. Nine AVMs occurred among 494 new cases of stroke, yielding an incidence of 1.8%.

Few studies have appeared dealing with the natural history of unruptured AVMs. They contain a mixture of asymptomatic and symptomatic cases with varying presentations, with nonuniform decisions about who is operated. Estimations of the risk of initial hemorrhage vary from 1% to as high as 4% per annum and for rebleeding as high as 17% during the first year, settling down to 3% after 10 years, with a 29% risk of death by 20 years after the diagnosis.

Less is known concerning possible changes in the AVM over time and the effect such changes have on the prognosis. It is not even known whether or which forms of AVM are static anomalies, which grow, and if the risk of hemorrhage is related to such events.

Estimating the efficacy of embolization or surgery as the therapy for AVM would be difficult to test in a clinical trial. Fox, Pelz, and Viñuela attempted to determine whether a clinical trial of the efficacy of embolization is feasible. Assuming an annual risk of first hemorrhage of 1% to 2% and an annual rehemorrhage rate of 3% to 4%, they contrasted their experience at Western Ontario with 111 cases and found a mortality rate of 4.5% and permanent morbidity of 12.6%. By assuming a combined morbidity-mortality of 10% with therapy and a hemorrhage risk of 4%, and assuming that therapy would reduce the bleeding rate by 50%, they calculated that 5250 cases followed for a mean of 10 years would be needed to conduct a trial to compare therapy with natural history. Such a project would exceed the known frequency of AVMs manyfold, making any such study a practical impossibility.

Others might disagree as to the risks of embolization cited above, and each group is inclined to argue that the risk is lower in their institution. However, another variable confounds the estimation of outcome: the continuing changes in technique. These changes make it difficult to compare results among centers and even in the same center over time. The material used for embolization has evolved over the years from pieces of fascia and dura, to barium-impregnated Gelfoam, to barium-impregnated Silastic spheres, to polyvinyl alcohol powders, to several forms of polymerizing substances such as silicone and bucrylate, and most recently to detachable balloons, platinum coils, and even glues that remain flexible. Add to this situation the possibility that the patient may have been exposed to one of several forms of radiation followed by surgical intervention, and it requires little imagination to determine that a given form of therapy would be almost impossible to compare against another.

There is a general, but untested, agreement that obliteration of the AVM rids the patient of the major risks of death from the lesion. The management issue is not whether the smaller lesions can become totally obliterated; they are successfully reduced by irradiation, surgery, and even in some instances embolization alone. The issue is, instead, that the most common AVMs are large, cannot be successfully obliterated by embolization or irradiation, and are associated with high morbidity and technical difficulty for their total surgical removal.

A proposal was put forward at the meeting represented in this book that we devise a uniform method of data collection in order to form a data bank so we can determine at least the spectrum of the cases being treated. It is hoped a data bank would permit early detection of complications of the newer forms of therapy. In answer to this proposal: First, it will be necessary to show that a data bank can demonstrate some uniformity among cases in the hope of discovering the variables associated with AVMs that are relevant to outcome. At present, the size, number of feeders, evidence of growth, and prior hemorrhage are among the items thought to be important, but

none has been demonstrated in enough cases to estimate the risk of complications save evidence of symptomatic hemorrhage.

Once a stable database can be developed, the feasibility of a clinical trial can be tested. The data collection forms suitable for such a study were briefly discussed at the meeting with plans to circulate them for general review.

CHAPTER 21

Proposed Potential Standards of Training in Interventional Neuroradiology

Norman E. Leeds

A new grouping consisting of neuroradiologists from Maine to Maryland—The Eastern Society of Neuroradiology—has been formed and its first meeting completed. It was held the weekend before the meeting represented in this book in view of the outstanding talent invited to this conference and the importance of interventional neuroradiology. This planning allowed the conference participants to present their work also to their neuroradiological peers.

Neuroradiology and neurosurgery have been entwined in the United States because of the interdependence on each other. The neuroradiologist working in close cooperation with neurosurgeons developed the imaging information required to reach clinical decisions about determining the best therapeutic methods. Neuroradiologists refined and developed techniques to improve sensitivity, specificity, and accuracy of diagnostic imaging while neurosurgical techniques were also improving (e.g., microscopy, microtechniques, lasers, and various pharmaceuticals to extend and refined surgical applications).

The interest of radiologists in entering the field of neuroradiology was enhanced by the interaction and close cooperation between the radiologist and neurosurgeon to provide the best quality of patient care. This close cooperation between the two specialties has taken a new turn with the growth and development of interventional neuroradiology. Luessenhop, a neurosurgeon, advocated the use of material injected through a catheter to treat arteriovenous malformations (AVMs). During the 1960s the diagnosis of spinal AVMs by angiography and treatment with endovascular material was advocated in some cases.

Endovascular therapy of AVMs and other lesions continues to develop. Dr. Serbinenko, in Moscow, introduced the balloon catheter with balloon release, which revolutionized diagnosis and treatment of vascular brain lesions. Dr. Debrun introduced methods learned from Dr. Serbinenko to the West. Refinements in catheter balloons and intravascular materials led to the growth of inteventional neuroradiology. Dr. Scheglov in Kiev, a neurosurgeon, pioneered the use of endovascular balloons to treat intracranial aneurysms. Many of the interventional neuroradiologists at this conference have visited, worked with, or plan to visit Dr. Scheglov.

Proposal

The need to develop standards for training in interventional neuroradiology has become a necessity. With discussions between the various interventional neuroradiologists, members of the interventional and Intersociety Liaison Committee, as well as the neurosurgical community, a constructive and positive dialogue has developed to create standards of training in interventional neuroradiology, so proper training is given to individuals interested in this subspecialty. It is agreed by all groups that interventional neuroradiological procedures should continue to be part of neuroradiology. However, mechanisms should be developed to permit individuals coming from a radiological or neurosurgical background to be properly trained in the radiological performance of endovascular procedures, and the prerequisite clinical background to care for these patients to meet the guidelines and standards in place for interventional procedures. Individuals with radiological training should be board-certified and have training in neuroradiology, and appropriate clinical training.

Neuroradiologists have varied levels of expertise in the performance of interventional procedures. It has resulted in two levels of expertise. Some neuroradiologists have had significant experience in a variety of interventional procedures developed before formal training programs existed. These individuals should be categorized as being at one of two levels of expertise, as should be defined in current programs: level 1, those who perform interventional procedures such as external carotid artery embolization for the management of epistaxis or preoperative embolizations of tumors; and level 2, those who have had previous experience or received training in balloon catheter technology (occlusive balloon catheters used to determine tolerance to carotid occlusion or vertebral artery occlusion; detachable balloon technology for the treatment of arteriovenous fistulas). The more advanced endovascular procedures, which involve the intracerebral and spinal cord circulation, can be reserved for those individuals who have received formal training in interventional neuroradiology or who have significant prior experience with sufficient expertise in the performance of such procedures.

It is believed by all members of both committees and both specialties that the first responsibility is the quality of patient care. Therefore it is important in the current environment to properly train individuals for the benefit of patient care and to extend the usefulness of interventional techniques.

Individuals coming from a radiological background, in addition to training in interventional techniques, should receive exposure to the pre- and postoperative care of patients with neurological diseases. Knowledge of the medical management of the patient with subarachnoid hemorrhage and stroke is necessary to provide appropriate care for these complex cases. It is important that neuroradiologists be capable of dealing with the presenting symptoms or complications that may arise as a consequence of the diseases being treated by endovascular techniques or the occasional complications

that develop as a result of treatment. This training can place the interventional neuroradiologist on an equal footing with clinical colleagues. Therefore clinical expertise should become a necessary component of neuroradiological training in interventional procedures. The increased importance of endovascular techniques has attracted the attention of the neurosurgical community. Their interest in the management of cerebrovascular disease has been further advanced by the possibility of endovascular management of cerebral aneurysms. In addition, neurosurgeons have become aware of the potentials that exist in the role of functional mapping and the future possibilities of endovascular techniques to accomplish it. Therefore they have expressed considerable interest in the potential participation in this type of procedure.

The neurosurgical leadership had demonstrated a high degree of responsibility, as revealed by the letter sent by the American Association of Neurological Surgeons to all members, in which they emphasize the need for proper training prior to attempting to perform endovascular procedures. Therefore it is thought that if properly motivated individuals of the neurosurgical community are interested in endovascular procedures the proper training should be available to them. The neurosurgical leadership is desirous of working in concert with neuroradiology rather than taking their own course as have the cardiologists and vascular surgeons.

It is the joint opinion of the Intersociety Liaison Committee and the Interventional Committee that a cordial and constructive approach should be taken that would be advantageous to the patient as well as to other interested parties. The problems that have arisen between the vascular radiology community and the cardiologists and peripheral vascular surgeons should not be repeated. The neurosurgical community has demonstrated their responsibility to patient care and has looked for a working relationship with us. Therefore we have pursued commitment and cooperation rather than becoming adversaries. It is our strong feeling that no action on the part of neuroradiology should send the wrong signal to our neurosurgical colleagues, namely that they should pursue their own course, the significance of which is patient referral and patient management in the community and the hospital environment. Opening pathways for neurosurgeons to perform interventional neuroradiology with appropriate and acceptable training guidelines will provide high quality patient care. The standards of training for interventional neuroradiology that have been developed by the Interliasion Committee and Interventional Committee are available upon request and should serve as a guideline for training of neurosurgeons. The standards of training are available from: Dr. Alexander Berenstein, c/o NYU Medical Center, 560 First Ave., New York, NY 10016, USA (phone: (212) 263–6325).

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