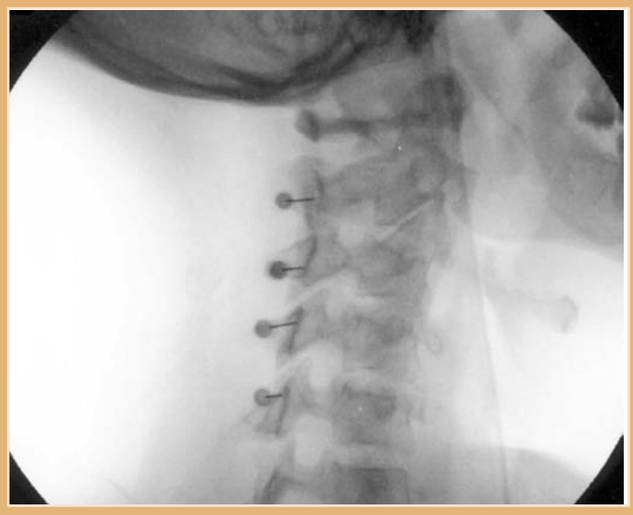
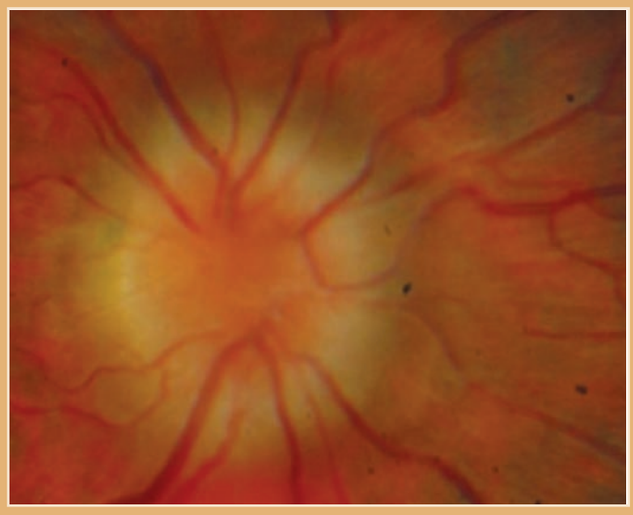
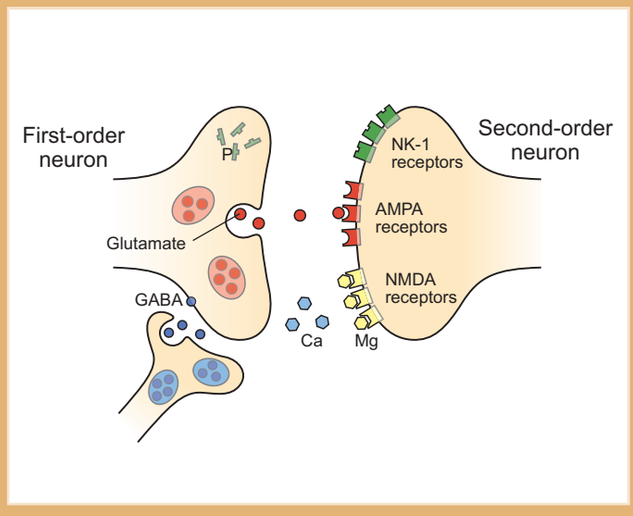
An Atlas of Investigation and Management

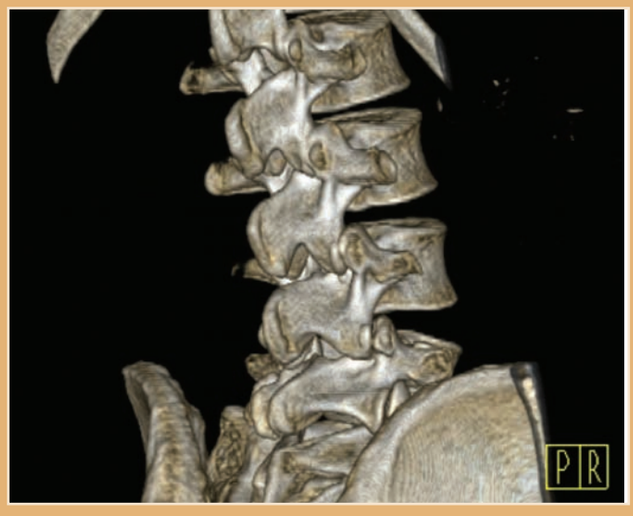
CHRONIC PAIN

Dawn A Marcus • Doris K Cope • Atul Deodhar • Richard Payne









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Contents

Preface

Chronic pain affects nearly one in every four adults worldwide, with pain one of the most common symptoms resulting in medical consultation. Patients typically describe a complex pattern of discomfort, disability, and distress, with pain affecting physical, social, and psychological functioning. Clinicians must efficiently condense widely varied symptomatic descriptions into characteristic patterns to permit accurate diagnosis and implement effective treatment. *Chronic Pain: An Atlas of Investigation and Management* provides an up-to-date, comprehensive resource for the busy healthcare provider, offering ready access to characteristic descriptions of common pain syndromes, patient case histories, photographs, and imaging studies, and evidence-based data summaries from the latest research studies, all presented in easy-to-understand visual formats. Diagnostic and treatment algorithms included throughout provide practical tools for effectively assessing and managing patients in the busy clinical setting.

This Atlas offers a unique and broad-based perspective, drawing on the resources and extensive clinical experience of anesthesiology, internal medicine, neurology, oncology, and rheumatology. Each of the authors is a recognized authority in chronic pain management, accumulating a wealth of knowledge through direct patient care and pain research. Authors address both nonmalignant chronic pain syndromes and cancer pain, with an additional chapter focused on important end-of-life pain issues. Pain assessment and management is comprehensively addressed by including common syndromes from most body regions and inclusion of medication, nonmedication, and interventional therapy options for both nonmalignant and malignant chronic pain.

Chronic Pain: An Atlas of Investigation and Management draws on decades of medical practice with chronic pain patients from each of the contributing authors, ensuring that the recommendations and patient tools have proven value in actual clinical practice.

Dawn A. Marcus, MD

Abbreviations

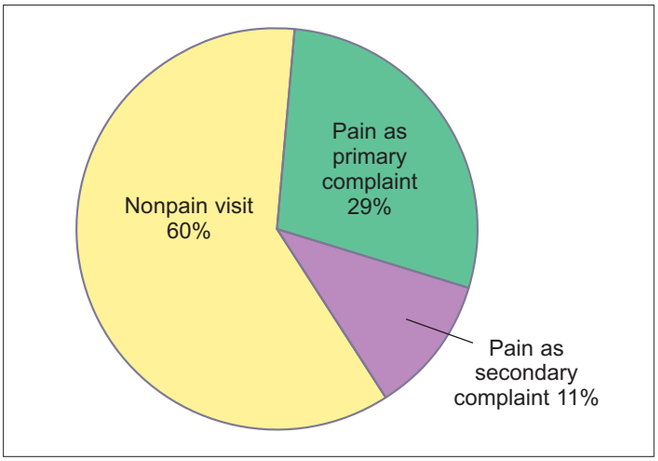
ADL activities of daily living
AMPA α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid
BBB blood–brain barrier
BTP break-through pain
CGRP calcitonin gene-related peptide
CMC carpometacarpal
CNS central nervous system
CRP C-reactive protein
CRPS complex regional pain syndrome
CT computed tomography
DHE dihydroergotamine
DIP distal interphalangeal
DMARD disease-modifying antirheumatic drug
EMG electromyography
ESR erythrocyte sedimentation rate
FDA Food and Drug Administration
GABA gamma aminobutyric acid
HIV human immunodeficiency virus
IBS irritable bowel syndrome
MCP metacarpophalangeal
MMP matrix metalloprotease
MRI magnetic resonance imaging
MTX methotrexate
NK-1 neurokinin-1
NMDA N-methyl D-aspartate
NSAID nonsteroidal anti-inflammatory drug
OA osteoarthritis
PHN postherpetic neuralgia
PIP proximal interphalangeal
PMN polymorphonuclear leukocyte
RA rheumatoid arthritis
ROM range of movement
RSD reflex sympathetic dystrophy
SNRI serotonin and norepinephrine reuptake inhibitor
SSRI selective serotonin reuptake inhibitor
TCA tricyclic antidepressant
UBO unidentified bright object
WBC white blood cell

Chapter 1

Definition and classification of chronic pain

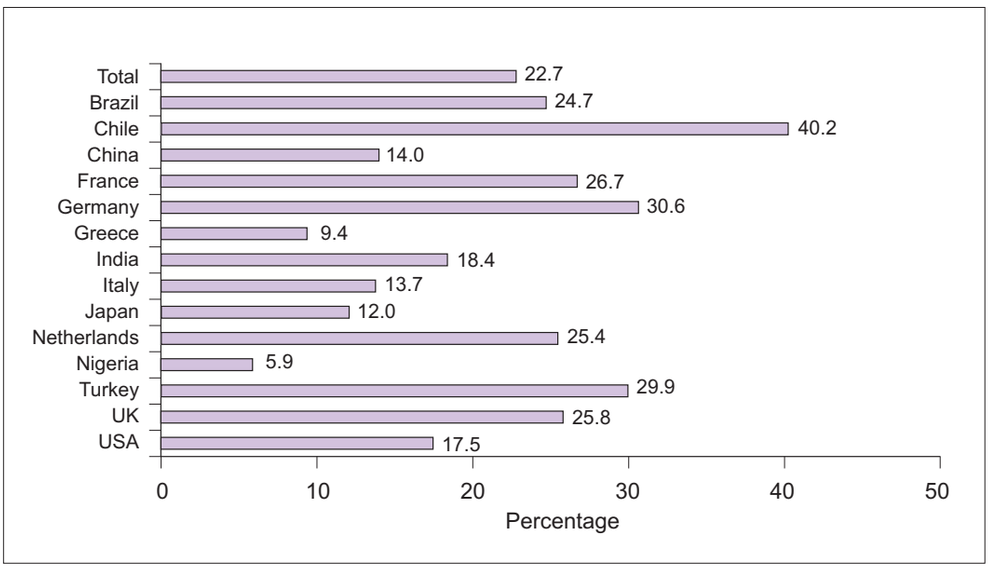
Introduction

Chronic pain is one of the most common conditions seen in primary care practices, accounting for 40% of office visits (**1.1**)[1]. Data from the World Health Organization identified the worldwide prevalence of significant, persistent pain at about 23% (**1.2**)[2]. The three most common pain locations were back pain (53%), headache (48%), and joint pain (46%). When re-evaluated after 12 months, pain complaints persisted in 49% of patients with baseline pain worldwide. In addition, 70% of persistent pain patients are managed by their primary care physician, while only 2% see a pain management specialist[3].



1.1 Percentage of primary care practice visits for pain. (Based on Mäntyselkä P, *et al*., 2001[1].)

1.2 This survey of primary care patients in 14 countries identified the prevalence of persistent pain, defined as pain occurring on most days for at least 6 months. The pain also needed to be significant enough to result in presentation to a healthcare provider, use of medication, or significant interference with activities. (Based on Gureje O, *et al*., 2001[2].)



Case presentation

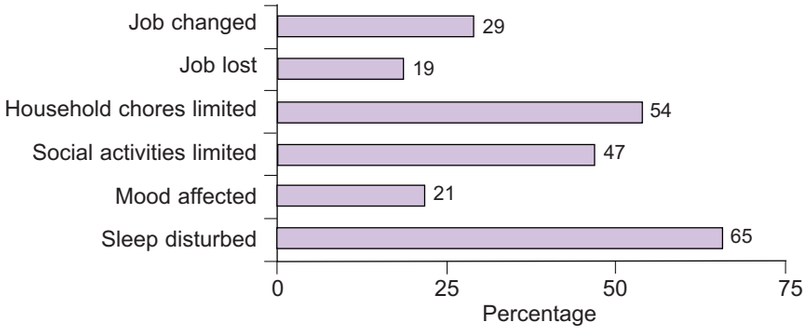
A 53-year-old hospital custodian/caretaker complained of low back pain shooting down his left leg after completing a typical day of work. Neurological evaluation showed marked muscle spasm of the paravertebral muscles, extreme pain with straight leg raise testing, and numbness over the lateral left calf. A magnetic resonance imaging (MRI) scan confirmed the clinical suspicion of an L5 radiculopathy from a pinched nerve in the spine. Failing to get relief from conservative treatment of bed rest, steroids, and analgesics, he underwent uncomplicated surgical discectomy. Postoperatively, straight leg raise testing normalized and numbness resolved. The patient, however, continued to report persistent, disabling pain at visits 3 and 6 months after surgery. Repeat MRI scan showed good relief of previous neural compression. One year postoperatively, he had still not returned to work and was seeking permanent disability.

This patient typifies many features of chronic pain, which often persists despite seemingly successful correction of underlying pathology and healing. Medical staff, family members, and even patients sometimes begin to wonder if their pain complaints can be real when physical examinations, X-rays, MRI scans, and other tests fail to reveal any ongoing pathology. Through careful investigations with animal models of pain, researchers have demonstrated the physiological basis of persistent, chronic pain.

Persistent pain often leads to functional disturbance, depression, and sleep impairment (**1.3**). A survey of people with at least moderately severe chronic pain in Europe and Israel found that, on average, 7.8 work days were lost during the preceding 6 months due to pain[3]. Economic costs are also substantial for chronic pain patients (**1.4**)[4].

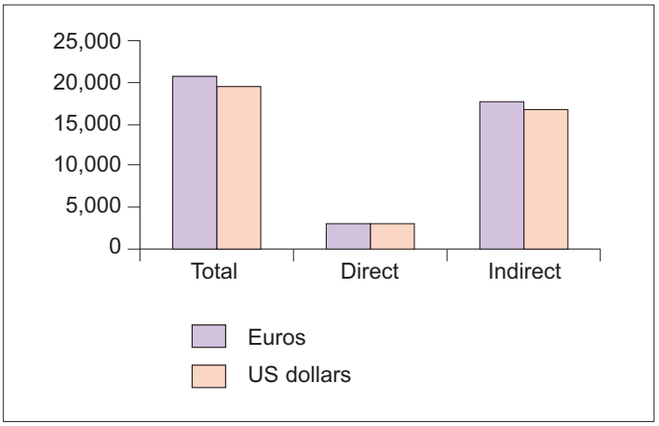
Chronic pain is also common and related to significant impact in pediatric patients. A survey of children aged 0–18 in the Netherlands identified chronic pain in 25%, with pain occurring more frequently in older children and adolescents (**1.5**)[5]. About one in three children with chronic pain have very frequent and intense pain[5]. Children having frequent pain are more likely to miss school more often than children with infrequent pain (41% *vs*. 14%, $P<0.001$)[6]. The most common pain areas reported in children and adolescents are: head, abdomen, limbs, and back[7]. Chronic pain in children persists for 1 year in 48% and for 2 years in 30%[8]. Costs are also high for children with pain. In a European study, mean 12-month costs for adolescent pain were £8,027 (over $13,000) (£4,431 in direct costs and £3,596 in indirect costs, including £600 for additional educational services)[9].

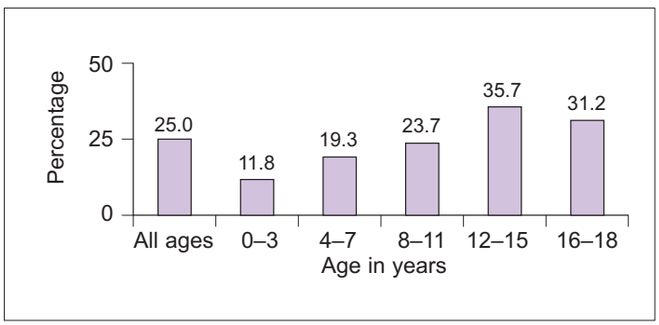
Despite the important impact and disability associated with chronic pain, patients often believe that their doctors are uninterested in addressing pain complaints (*Table 1.1*). About one in three people with chronic pain are not currently receiving treatment, often due to perceptions that their healthcare providers cannot help, they should just live with their pain, or treatments will not be tolerated[3].



1.3 Impact of chronic pain. A community-based survey of people in 15 European countries and Israel identified at least moderately severe chronic pain lasting at least 6 months in 19%. Among those who were employed full- or part-time, nearly one in three changed their job or job duties due to pain, while one in five lost a job. Nearly half of all people with chronic pain reported disturbances in household and social activities. One in five reported developing depression and the majority had disturbed sleep. (Based on Breivik H, *et al*., 2006[3].)

1.4 Annual per-patient costs from chronic low back pain. Annual 2002 costs for chronic low back pain were estimated by evaluating patients in 14 centres in Sweden. The majority of pain-related costs were indirect, with work absence having the major impact. About 60% of employed patients with low back pain missed at least 1 day of work during the preceding 3 months, with an average work loss of 33 out of 60 possible work days. (Based on Ekman M, *et al.*, 2005[4].)





1.5 Chronic pain (pain for >3 months) prevalence in children and adolescents. (Based on Perquin CW, *et al.*, 2000[5].)

Table 1.1 Percentage of patients reporting beliefs about doctors' attitudes toward chronic pain

- My doctor does not think my pain is a problem – 20%
- My doctor never asks about my pain – 22%
- I don't get enough time to talk to my doctor about pain – 23%
- No one believes my pain is as bad as it is – 29%
- My doctor would rather treat an illness than my pain – 43%

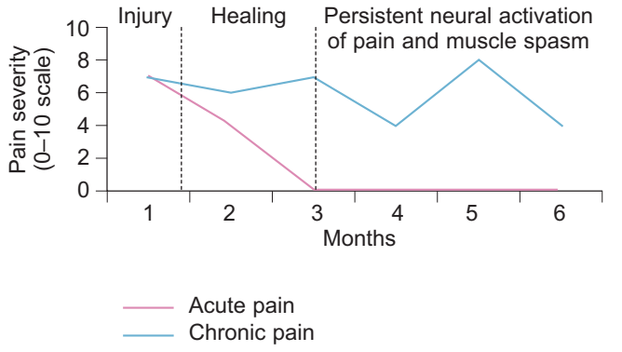
(Adapted from Breivik H, *et al.*, 2006[3])

Definition of acute versus chronic pain

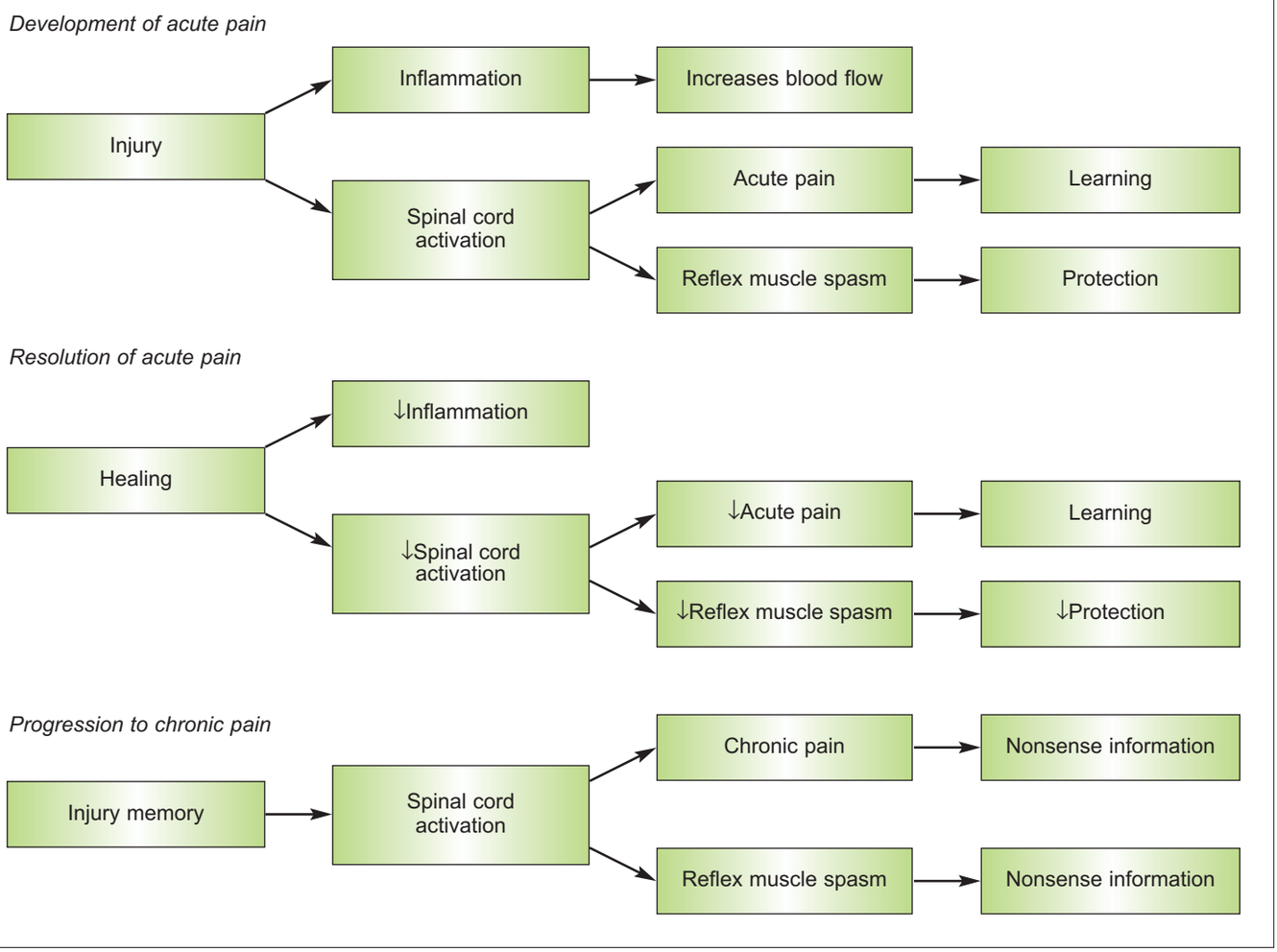
Daily life frequently results in experiences of mild pain – stubbing a toe, twisting an ankle, bumping the 'funny bone'. These episodes of new-onset pain are termed acute pain. In most cases, acute pain resolves quickly. With more severe injuries, acute pain can persist for several months, resolving during the healing process. The duration of healing depends on the amount of blood flow to various tissues (*Table 1.2*). After an injury without an ongoing degenerative condition, healing is expected to be completed within 3 months. When pain persists beyond the time of healing or longer than 3 months, this is termed chronic pain (**1.6**)[10]. Chronic pain can continue without the occurrence of ongoing degenerative illness or additional injury.

Table 1.2 Time to achieve normal healing

Organ type	*Time to complete healing*
Skin	3–7 days
Bones	6 weeks
Tendons and ligaments	3 months



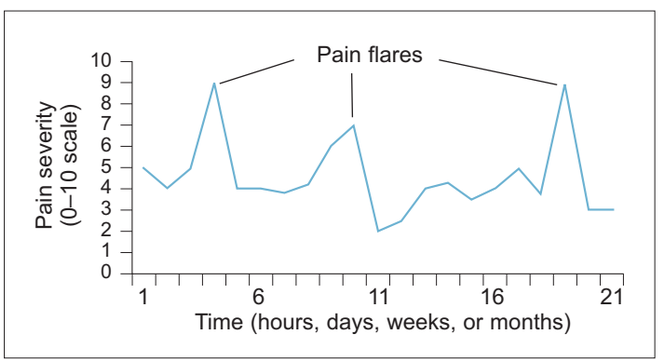
1.6 Acute versus chronic pain. Pain often occurs with trauma or illness, generally decreasing during the period of healing. Acute pain usually resolves within 3 months. Chronic pain persists after healing is completed, due to continued activation of neural pain pathways and muscle spasm. (Based on Marcus DA, 2005[10].)



1.7 Physiology of acute and chronic pain. Acute pain is associated with inflammation that brings repair cells to the site of injury and activation of spinal pathways that send instructive pain messages to encourage future injury avoidance and provide protective muscle spasm, like a natural splint. During the subsequent weeks or months of healing, inflammation typically resolves and fewer impulses are sent from the spine to register as pain or trigger muscle spasm. When pain persists beyond the period of healing, the memory of the initial injury results in persistent neural messages for pain and muscle spasm. (Based on Marcus DA, 2005[10].)

Acute pain is an important experience, motivating the injured person to rest and recuperate during the critical healing period. Increased blood flow and protective muscle spasm assist in speeding recovery. Acute pain also provides learning opportunities so that future injury can be avoided (**1.7**). In some cases, pain persists after healing is completed. This persistent or chronic pain provides patients with false signals about injury and encourages excessive activity restriction.

Patients experiencing chronic pain typically notice fluctuations in their pain severity (**1.8**). In some cases, pain remains at a moderate level for weeks and then increases to severe pain or a pain flare lasting several days to weeks. In other patients, pain severity may fluctuate between mild, moderate, and severe several times daily. Flares in pain may occur in response to medication withdrawal, stress, increased activity, sleep disturbance, additional injury, or the natural physiology of the pain response. Short-lived pain flares are often well managed with nonpharmacological techniques, such as physical therapy modalities, stretching exercises, relaxation, and distraction techniques. Long-lasting flares, continuing for more than 1 day, often require medication or interventional therapies.



1.8 Typical pattern of chronic pain. (Based on Marcus DA, 2005[10].)

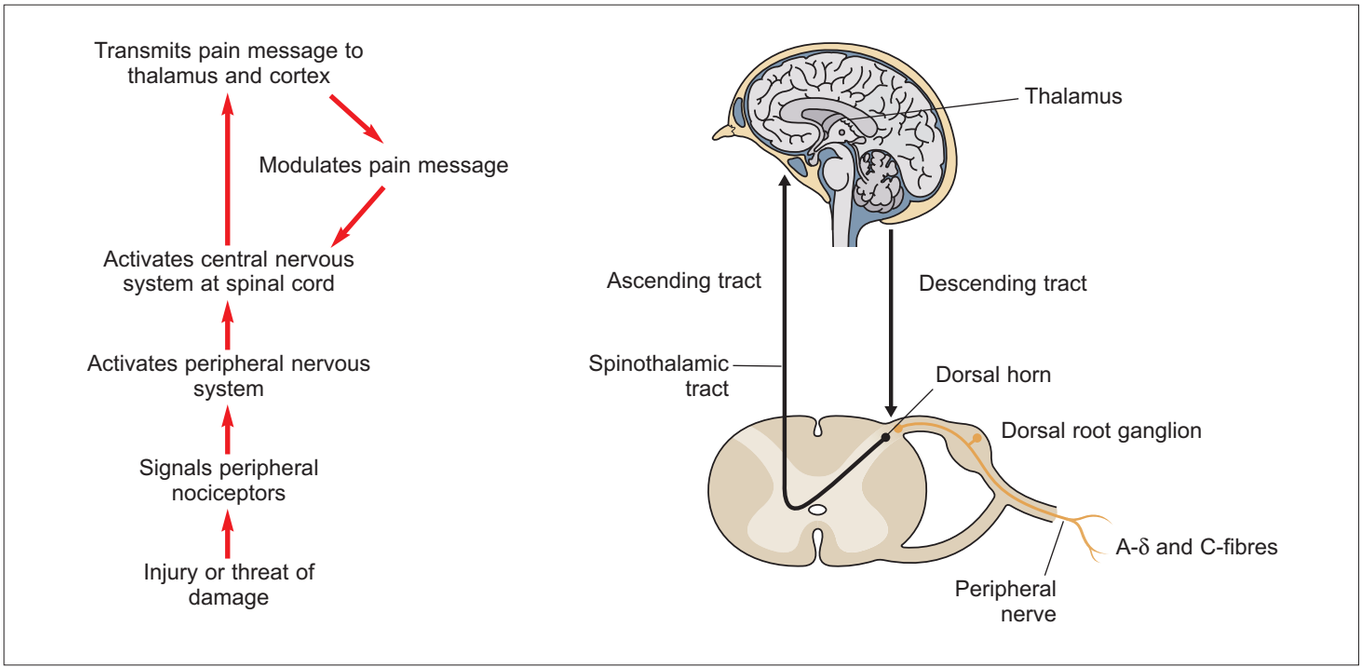
Pathophysiology of pain

Nerves can be divided based on their size, speed of conduction (depending on degree of myelination), and type of messages transmitted (*Table 1.3*). Large, fast conducting A-β fibres send nonpainful sensory messages and may help block pain signals. For example, pain can be temporarily relieved by lightly stroking the painful area. The thinly myelinated A-δ and unmyelinated C-fibres send pain impulses and are called nociceptors. Based on conduction speed, sharp pain will be conducted more quickly than dull pain. Nociceptors differ from neurons sending nonpainful touch signals by having a slower speed of signal conduction and an inability to adapt to repeated activation. Although repetitive touch signals will result in reduced nerve firing or desensitization, persistent pain messages result in continued nerve discharges and sensitization.

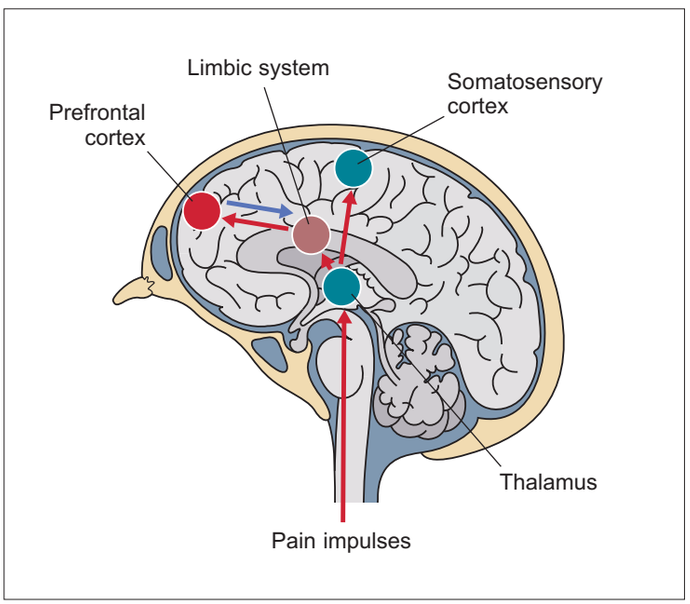
Noxious signals are transmitted via free nerve endings to the spinal cord and subsequently to the brain (**1.9**). A variety of neurotransmitters are important for relaying pain messages, including substance P, glutamate, and calcitonin gene-related peptide. Descending pathways from the brain help modulate pain activity via serotonin, norepinephrine, and opioid release. Pain perception is also modulated by important cerebral influences on the limbic system (**1.10**). This may explain how psychological techniques, like cognitive restructuring and stress management, can effectively reduce chronic pain complaints.

Table 1.3 Characteristics of pain-modulating neurons

Neuron type	*Size*	*Average conduction speed*	*Adaptability*	*Signal*
A-β	Large – 8 μm	Fast – 50 m/sec	Yes	Touch, proprioception, inhibit pain
A-δ	Small – 1 μm	Moderate – 10 m/sec	No	Sharp pain
C	Small – 1 μm	Slow – 1 m/sec	No	Dull pain



1.9 Peripheral pain messages activate central structures in the spinal dorsal horn. A-δ and C-fibres transmit peripheral pain signals to the dorsal spinal root, which sends messages to the superficial dorsal horn. Connections from lamina 1 convey pain signals to the substantia gelatinosa, where pain messages are modulated via intermediate neurons and signals from descending neural tracts travelling in the dorsolateral funiculus. Activation of descending pathways helps explain how pain can be lessened with distraction or on the battlefield. Second-order neurons then cross the spinal cord and travel to the thalamus via the lateral spinothalamic tract. Third-order neurons from the thalamus signal the somatosensory cortex, resulting in the conscious perception of pain.



1.10 Central modulating influences on pain perception (adapted from Robert Bennett, MD). After pain impulses travel to the thalamic nuclei, pain perception is influenced by signals from the limbic system and prefrontal cortex. These cortical influences help explain the modulating role that memory and learning have on pain perception.

Central sensitization model of chronic pain

When pain symptoms persist beyond the healing period, pain is often perpetuated by activation of the central nervous system (CNS) (*Table 1.4*). Under normal conditions, presynaptic neural input from one neuron produces a predictable and comparable signal output after postsynaptic activation (**1.11**). When nerves become sensitized in the dorsal horn in chronic pain patients, postsynaptic signal output exceeds presynaptic input from peripheral nociceptors, resulting in a reduced pain threshold and the spread of pain beyond the area of the original injury.

Several experimental models of chronic pain have been developed in animals subjected to peripheral nerve injury. These models effectively describe changes that occur in patients with neuropathic pain and may also explain changes occurring in other chronic pain conditions. Similar to humans with chronic pain, animals exposed to peripheral nerve injury likewise develop hyperalgesia, allodynia to cold and mechanical stimulation, and pain behaviours (favouring or gnawing at the injured leg) (**1.12**)[11]. This heightened pain response persists for about 2 months in rats experiencing chronic constriction injury with ligatures loosely tied about the proximal sciatic nerve and up to 7 months after partial sciatic nerve ligation with a tight ligature. These experimental models may be likened to humans who experience nerve trauma or compression (e.g. postoperative pain, carpal tunnel syndrome, or a herniated disc). Even after surgery to repair damage or relieve constriction, chronic pain, hyperalgesia, and allodynia often persist.

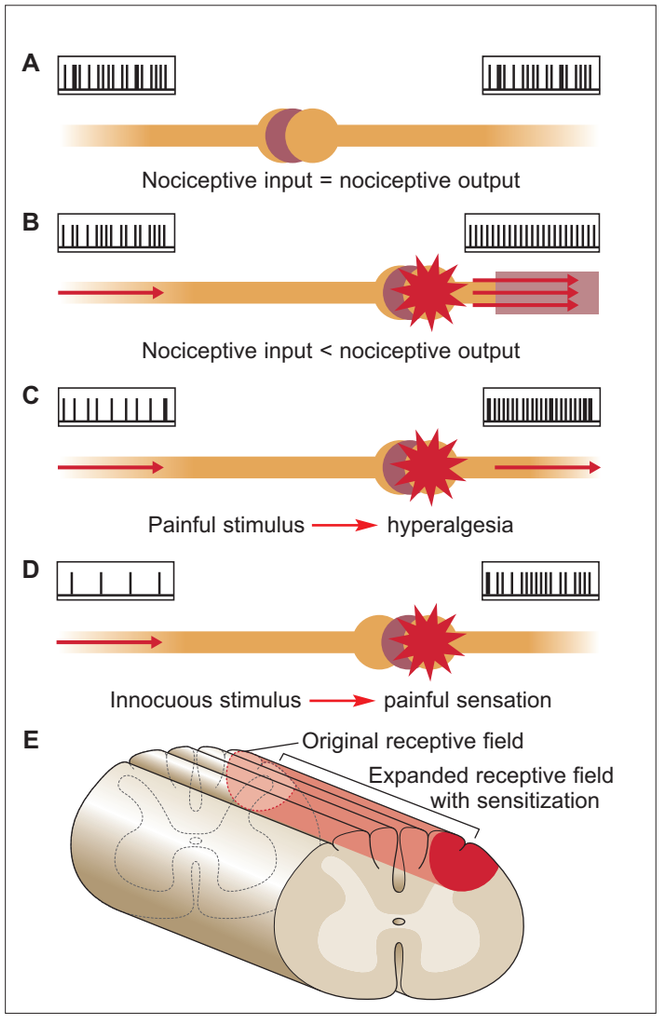
Neural sensitization has been studied most thoroughly in the dorsal horn of the spinal cord, using the rodent models described above. Changes occur in neurotransmitter activity at both pre- and postsynaptic sites in the dorsal horn where first-order peripheral nerve terminals activate second-order

Table 1.4 Triad of sensitized pain

1 Hyperalgesia: amplified response to painful stimulus

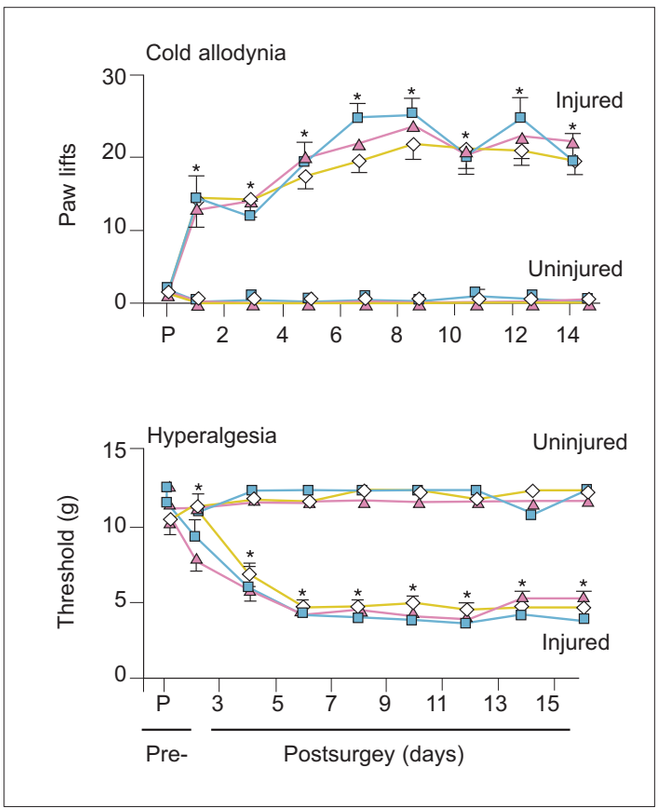
2 Allodynia: pain perception to nonpainful stimulus

3 Receptive field expansion: spread of pain beyond area of original injury

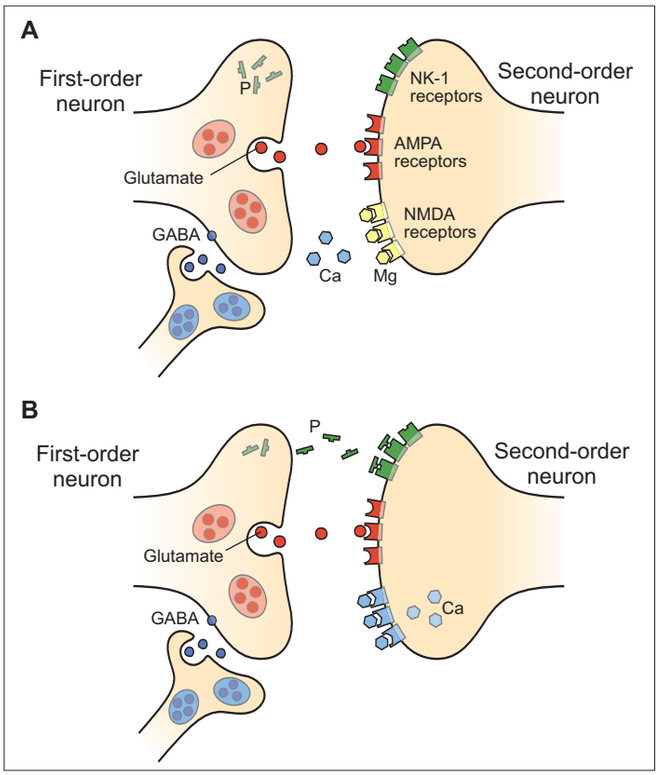


1.11 Neural processing under normal and chronic pain conditions (adapted from Robert Bennett, MD). This series of drawings depicts changes in nerve signalling with chronic pain exposure. The vertical bars represent action potentials. **A**: Normal processing, with the signals generated from pain input corresponding to the amount of pain generation output. With repeated pain signalling, the dorsal horn becomes sensitized, forming the basis of neural wind-up (**B**). Wind-up is mediated by glutamate-dependent N-methyl D-aspartate (NMDA) receptor activation. With sensitization, pain output signals exceed what would be predicted based on the number of input action potentials. Persistent dorsal horn sensitization leads to amplified pain sensitivity and the triad of chronic pain: hyperalgesia (**C**), allodynia (**D**), and pain expansion (**E**).

central neurons in the spinal cord (**1.13**). Alterations in the ability of glutamate to activate N-methyl D-aspartate (NMDA) receptors with repetitive peripheral nerve activation result in postsynaptic calcium influx and a cascade of events that results in excessive pain signalling from the second-order neuron. Changes in pre- and postsynaptic transmission provide possible sites for medication intervention with drugs designed to decrease excitatory activity by blocking NMDA receptors, calcium channels, or glutamate, or increasing GABA inhibitory drive.

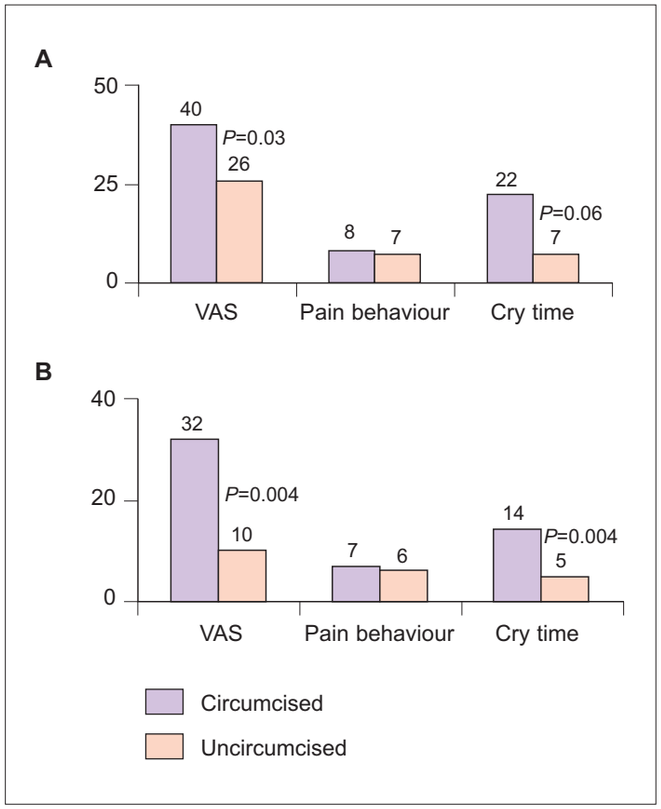


1.12 Sensory dysfunction induced by peripheral nerve injury. Sensation was tested in rats before (Pre-: P) and every other day after sciatic nerve chronic constriction injury. Withdrawal from cold stimulation was tested on odd days and touch response was tested on even days. Rats exposed to peripheral nerve injury experienced an increase in pain response to placing their feet on an ice plate (cold allodynia, top) and a reduced threshold for perceiving light touch as pain (hyperalgesia, bottom) after 3–5 days. There were no changes in the uninjured rats. (* Denotes significant change from preinjury level, $P<0.05$.) (Based on Keay KA, *et al.*, 2004[11].)



1.13 Pre- and postsynaptic changes after peripheral nerve stimulation. These diagrams represent the synapse between first-order (peripheral) neurons and second-order neurons in the dorsal horn. N-methyl D-aspartate (NMDA) receptors are located throughout the central nervous system and normally are involved with removing dying neurons. **A**: Under normal circumstances, NMDA receptors are blocked by magnesium, preventing activation by glutamate. The presynaptic release of glutamate normally activates nonpain α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptors. In addition, inhibitory gamma aminobutyric acid (GABA) normally prevents excessive release of glutamate and substance P. **B**: After peripheral nerve injury, GABA activity decreases and excessive activation of AMPA receptors by glutamate and neurokinin-1 (NK-1) receptors by substance P results in loss of NMDA-receptor magnesium blockade, allowing glutamate to bind to NMDA receptors. This results in an influx of calcium into the postsynaptic neuron. After calcium enters the postsynaptic cell, there is further activation of NMDA receptors, more calcium influx, and increased presynaptic release of substance P, resulting in wind-up, signalling a stronger pain message than would have been sent by the original peripheral nerve impulse. Ca: calcium; Mg: magnesium.

The ability of pain exposures to change subsequent sensitivity to pain in humans has been demonstrated in two important studies investigating the role of perinatal circumcision pain on later sensitivity to routine vaccinations[12,13]. Response to vaccination given at 4–6 months was compared in boys who had (N=30) and had not (N=12) been circumcised as newborns[12]. Demographics were similar between groups. Pain reactions were significantly higher among boys who had been circumcised (**1.14A**). Previously circumcised babies were also less responsive to premedication before vaccination with local anesthetic (**1.14B**). In a second study, boys circumcised after pretreatment with 5% topical lidocaine–prilocaine had a significantly lower response to vaccination than boys circumcised with no anesthesia ($P<0.05$)[13]. These data support the theory that painful peripheral stimulation can produce long-lasting changes in central pain processing mechanisms.



1.14 Response to routine vaccination 4–6 months after circumcision. Visual analogue scale (VAS) ranged from 0 (no pain) to 100 (worst possible pain). Pain behaviour was rated from 0 (no pain) to 10 (worst possible pain) based on scores for face, cry, and body movements. Cry time was recorded in seconds. **A**: Vaccination response in all babies (N=42). **B**: Vaccination response after pretreatment with local anesthetic (N=24). (Based on Taddio A, *et al.*, 1995[12].)

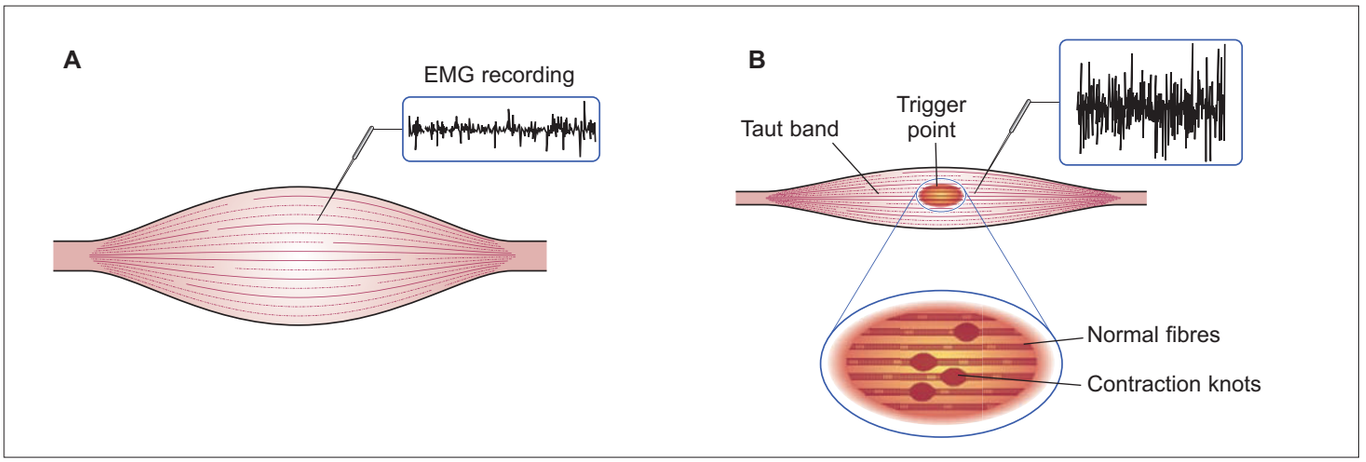
Understanding myofascial pain

Muscle spasm and hurting frequently accompany chronic pain and may be either the primary pain generator or a secondary pain contributor. The protective muscle spasm that occurs with an acute injury can persist as a nonproductive, persistent muscle spasm and tenderness. In addition, changes in normal movement patterns due to pain and deconditioning from excessively rested muscles can further aggravate muscle spasm. Patients often develop co-contraction of complementary muscles, e.g. muscle flexors and extensors. This co-contraction results in restricted active movement and increased pain.

Muscle or myofascial pain is characterized by areas of involuntarily contracted muscle (*Table 1.5*). These contracted areas result in focal tenderness and shortened muscles, with reduced range of motion and muscle strength (**1.15**). Palpation may also result in predictable pain referral patterns, which will be described for common myofascial pain conditions in subsequent chapters.

Table 1.5 Hallmarks of myofascial pain

- Taut muscle band
  - Contracted cord of muscle fibres
- Local twitch response
  - Plucking band or inserting needle into band causes involuntary muscle contraction
- Trigger points
  - Palpating taut band results in local tenderness (*latent trigger point*) or referred pain (*active trigger point*)



1.15 Myofascial pain physiology (adapted from Robert Bennett, MD). Myofascial pain develops when muscles experience localized contraction. A taut band with contraction knots is typically palpable on physical examination. Taut bands have spontaneous electrical activity, with increased signals detected with electromyographic (EMG) testing. **A**: Normal muscle; **B**: muscle with myofascial pain.

Chronic pain assessment

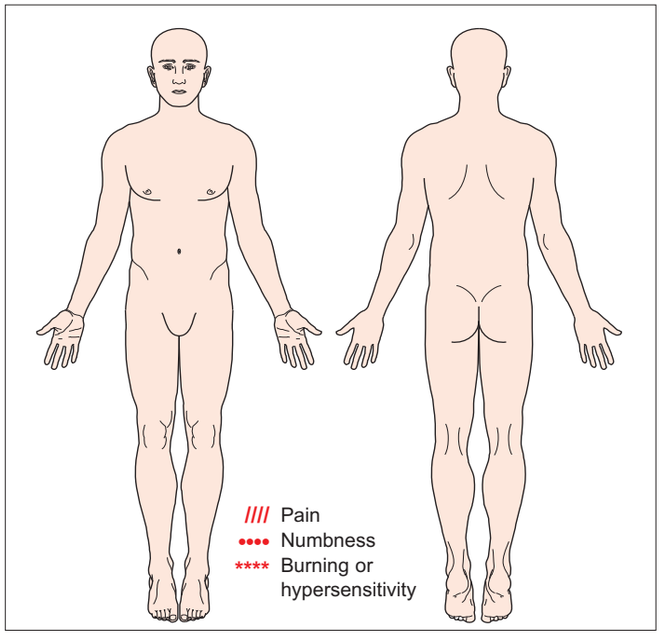
All patients should be asked to complete a basic pain assessment, including both qualitative and quantitative pain assessment measures. The most efficient method for patients to describe their pain location and quality is through the use of a pain drawing (**1.16**). Familiarity with pain drawings allows the practitioner to assess patients with pain complaints rapidly. These drawings can be particularly helpful for patients with complicated pain syndromes. Patients often focus on their most severe or newest ache when verbally describing their pain. Understanding the full scope of their pain involvement allows the diagnosis of pain conditions that affect more widespread areas, such as fibromyalgia and rheumatoid arthritis. In addition, pain drawings can also help show common pain referral patterns from neuropathic or radicular pain, as well as myofascial pain. Completed pain drawings will accompany patient case reports in subsequent chapters.

Pain severity can be quantified using a numeric rating scale, visual analogue scale, or descriptive scale (**1.17**). In clinical practice, the numeric rating scale is usually the easiest for patients to understand and doctors to interpret quickly. Numeric pain ratings of 5 or higher correlate with substantial pain-related interference and disability[14]. In patients with nonmalignant chronic pain, a score of ≥5 correlates with moderate pain and interference, while scores of ≥7–8 denote severe pain and interference. Among patients with cancer-related pain, a score of >4 similarly corresponds to moderate pain and >7 severe pain[15].

Pain severity and interference can also be quantified at initial screening and in post-treatment assessments using validated screening tools, such as the Profile of Chronic Pain: Screen, a 15-item questionnaire that patients can complete in about 5 minutes (**1.18**). This tool characterizes pain severity, functional impact, and emotional distress.

Patients reporting chronic pain require a comprehensive evaluation of both their pain complaint and general medical condition. Reviewing a pain drawing, pain severity assessment using the numeric rating scale, and the Profile of Chronic Pain: Screen helps clarify pain complaints. A detailed history and physical examination help differentiate among possible diagnoses and the need for additional laboratory or radiographic testing (**1.19**).

1.16 Pain drawing recording sheet. Patients are instructed to shade all painful areas. Patients are instructed to shade all painful areas using the following key: //// for pain; :::: for numbness; **** for burning. (Based on Marcus DA, 2005[10].)



A
Patients rate pain severity from 0 (no pain) to 10 (unbearable pain).

Circle the number that indicates your pain severity:

0 1 2 3 4 5 6 7 8 9 10
No pain Unbearable pain

B
Patients mark their pain severity on a 100 mm line. Pain severity is measured in mm from zero (no pain) to 100 mm (worst pain imaginable).

Mark your pain severity along this line:

No pain ———————————————————— Worst pain imaginable

C
Patients choose descriptors about pain from: none, mild, moderate, severe.

Circle the term that indicates your pain severity:

None Mild Moderate Severe

1.17 Pain severity assessment measures. **A**: Numeric rating scale; **B**: visual analogue scale; **C**: descriptive scale.

Patient name: **Date:**

Circle an answer for each question.

A Pain severity

1 How often do you get pain?

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

2 How severe is your average level of pain? (0 = very little pain, 9 = unbearable pain)

0 1 2 3 4 5 6 7 8 9

3 How often do you get 1 hour of severe pain?

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

4 How severe is your most severe level of pain? (0 = very little pain, 9 = unbearable pain)

0 1 2 3 4 5 6 7 8 9

B Pain interference: rate how often your pain interferes with each of the following:

1 Enjoyable activities

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

2 Home responsibilities

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

3 Relationships

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

4 Personal goals

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

5 Self-care

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

6 Thinking clearly, problem-solving, concentrating, or remembering

0 – Never
1 – Less than once per month
2 – Once per month
3 – Twice per month
4 – Once per week
5 – Several times weekly
6 – Daily

C Emotional burden (0 = never, 5 = extremely often)

1 How often does your pain make you *sad or depressed*?
0 1 2 3 4 5

2 How often does your pain make you *tense, anxious, or jittery*?
0 1 2 3 4 5

3 How often does your pain make you *angry*?
0 1 2 3 4 5

4 How often does your pain make you *isolated or lonely*?
0 1 2 3 4 5

5 How often does your pain *reduce your ability to enjoy your life*?
0 1 2 3 4 5

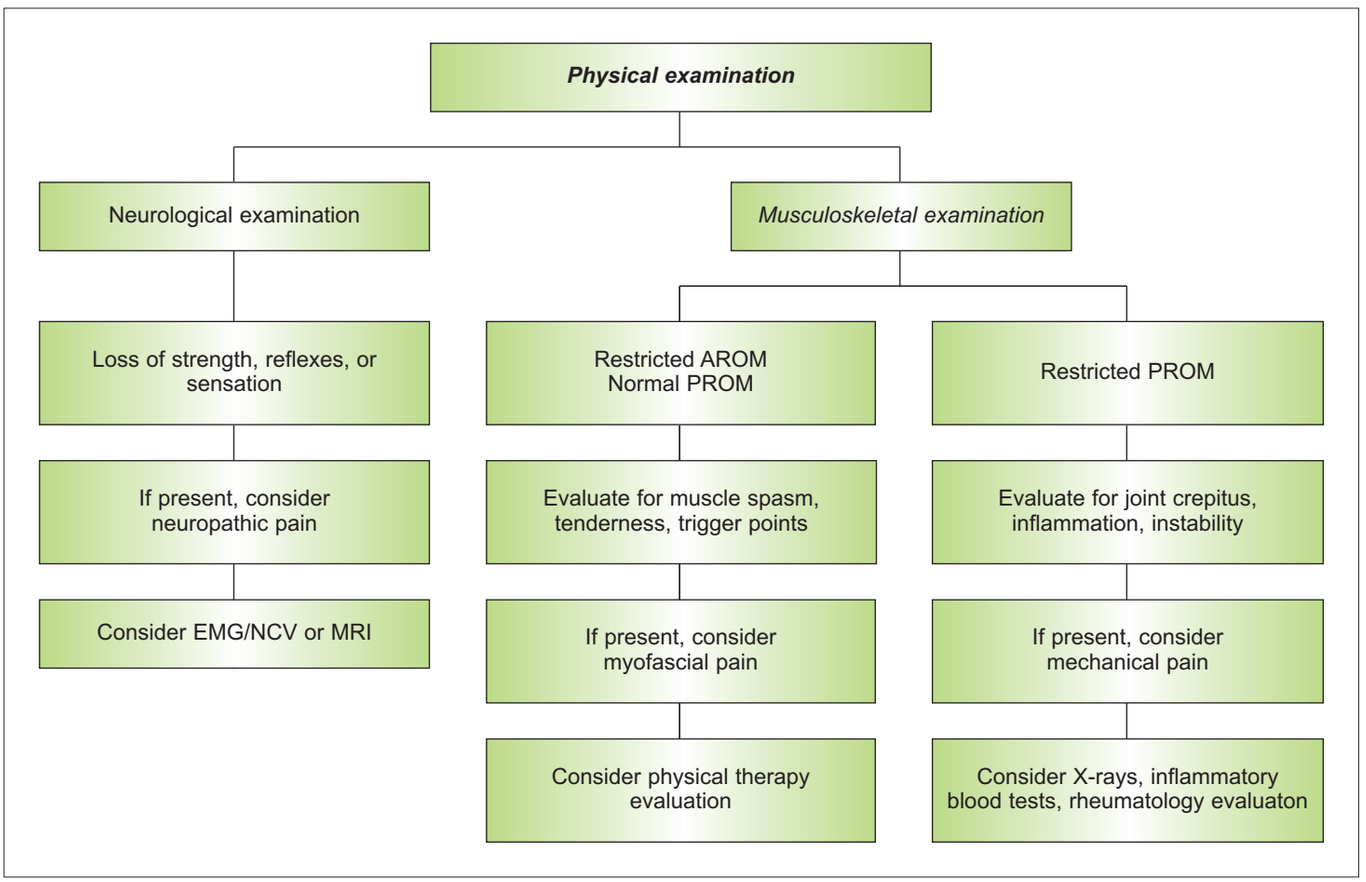
Patient name:	**Date:**
Average pain severity (0–10)	
Primary pain location	
History	
Pain precipitants	Events that preceded pain onset:
	Current pain triggers:
Active medical conditions	
Complete review of systems	
Physical examination	
Neurological screen	Gait: Strength: Reflexes: Sensation:
Musculoskeletal examination	Posture: Muscle tenderness/spasm: Active ROM: Passive ROM:
General medical examination	
Supplemental testing	
Blood work for systemic illness or inflammatory disease	
X-rays for bony abnormalities	
MRI for neurological conditions	
EMG/NCV for peripheral nerve disease	
Differential diagnosis	

1.19 Chronic pain assessment. EMG/NCV: Electromyography/nerve conduction velocity; MRI: magnetic resonance imaging; ROM: range of motion. Active ROM is performed by asking the patient to move joints through full range. Passive ROM is performed by asking the patient to relax; the examiner then moves the relaxed joint through the full range.

1.18 (opposite) Profile of Chronic Pain: Screen questionnaire. This validated pain assessment questionnaire addresses pain severity, interference, and emotional burden. Scores are calculated for each category by adding response scores. Possible score ranges are: 0–30 for severity, 0–36 for interference, and 0–25 for emotional burden. Based on a United States national nonpain sample, norms for males are about 11 for pain severity, 3.5 for interference, and 3 for emotional burden. Norms for females are about 13 for pain severity, 5 for interference, and 5 for emotional burden. (Based on Ruehlman LS, *et al*., 2005[16].)

Differentiating among pain diagnoses

In general, chronic pain can be divided into several categories, including myofascial, mechanical, and neuropathic pain. Pain characteristics and physical examination findings can distinguish among pain categories (**1.20**). In some cases, patients may have contributions from several pain categories, such as migraine plus myofascial pain or neuropathic plus mechanical pain. Pain descriptions, like burning, cold, and numb, are often associated with neuropathic pain. Pain location along typical nerve distribution patterns can also help identify neuropathic pain. Myofascial pain is often quite severe and typically associated with restricted active motion. Characteristic muscle tenderness and pain referral patterns help identify myofascial pain. Mechanical pain is characterized by restrictions in joint movement when isolated from muscle contraction. In some cases, a physical therapy assessment is necessary to identify mechanical dysfunction in patients who are unable to relax muscles successfully for passive range of motion testing. Typically, patients with mechanical pain will experience pain reproduction or aggravation with movement of involved joints.



1.20 Pain assessment algorithm. AROM: active range of motion; EMG/NCV: electromyography/nerve conduction velocity; MRI: magnetic resonance imaging; PROM: passive range of motion. In general, patients with myofascial pain have limited AROM due to muscle cocontraction. Think muscular dysfunction when PROM exceeds AROM. If patients successfully reduce muscle contraction and relax joints for PROM testing, restrictions usually represent a mechanical dysfunction.

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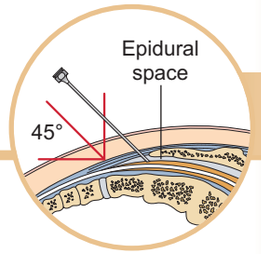


Chapter 2

Chronic pain management strategies

Introduction

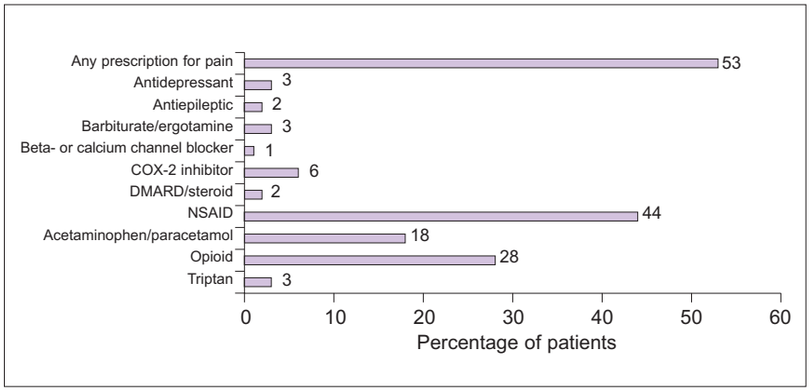
Chronic pain is typically treated with a combination of medication and nonmedication therapies. While patients often initially want to focus treatment around medications, inclusion of nonmedication therapies generally offers the best long-term benefit. A large population survey found that 45% of patients reported their pain medications were very effective and an additional 41% felt their prescriptions were somewhat effective[1]. Although medications were often helpful, 64% noted that at times their medications were not adequate to control their pain. These data suggest that, while medications are an important component of pain management, medications should be used in a comprehensive treatment programme, including additional nonmedication therapies to maximize treatment outcome.

Medication therapies

Pain medications include a wide assortment of therapies (*Table 2.1*). While simple and opioid analgesics were designed to reduce pain severity, other medications developed to treat alternative medical conditions may also offer analgesic properties, including medications designed to reduce mood disturbance, epilepsy, and elevated blood pressure. The majority of people with chronic pain use prescription medications, especially analgesics (**2.1**)[1].

Table 2.1 Pain medications

- Simple, nonopioid analgesics
  - Acetaminophen/paracetamol
  - Nonsteroidal anti-inflammatory drugs
- Adjuvant analgesics
  - Antidepressants
  - Neurostabilizing antiepileptics
  - Antispasmodics
  - Alpha-2 agonists
  - Topical agents (lidocaine, capsaicin)
- Opioid analgesics
  - Immediate-release
  - Extended-release



2.1 Common prescription medications for chronic pain. Among people with moderate or severe chronic pain in Europe and Israel, 53% reported currently using a prescription medication for pain. The most commonly used medication group was nonsteroidal anti-inflammatory drugs (NSAIDs). Some of the reported medications would be used for specific pain conditions, like beta- and calcium channel blockers or triptans for chronic headache and disease-modifying antirheumatic drugs (DMARDs) for rheumatoid arthritis. (Based on Breivik H, *et al.*, 2006[1].)

Adjuvant therapies are most commonly used to treat neuropathic pain and chronic headache.

A large, systematic review of outpatient chronic pain management analysed data from the existing literature to identify the number of patients needed to be treated to achieve an effective response from an assortment of medication therapies (*Table 2.2*)[2]. None of these individual therapies was effective for most patients. These data show that a variety of therapies may be effective for chronic pain, but the individual patient will probably need to try several therapies before finding one that works well for him or her.

Mechanism of action of pain medications

Analgesics and adjuvant therapies influence both peripheral and central pain mechanisms (**2.2**, *Table 2.3*). Acute injuries result in an abnormal accumulation of sodium channels in affected nerves, leading to increased nerve firing and reduced threshold for depolarization. This sensitization of peripheral nerves enhances pain signalling. Once peripheral nerves are activated, changes in neuronal calcium levels and upregulation of NMDA receptors increase excitability of spinal neurons, resulting in central sensitization of pain pathways. Pain medications work by reducing peripheral or central sensitization or enhancing activity of descending inhibitory pathways from the brain. Serotonergic pathways from the periaqueductal gray and

Table 2.2 Number-needed-to-treat (NNT) for efficacy of pain medications

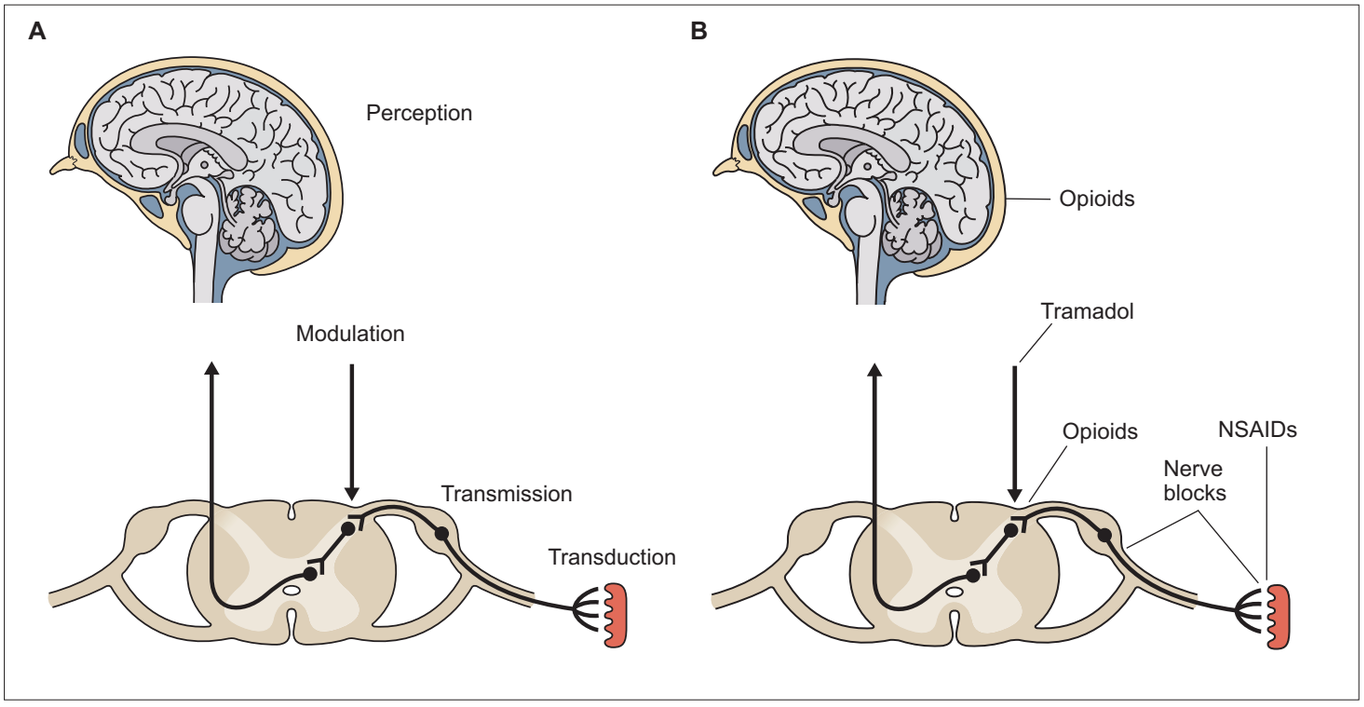
Medication	*NNT*
Minor analgesics	
Acetaminophen/paracetamol	2.9
Ibuprofen	2.0
Tramadol	8.2
Propoxyphene	7.5
Topical NSAIDs	3.0
Topical capsaicin	3.9
Antidepressants	3.0
Antiepileptics	2.5

Treatment efficacy was determined by a literature review of randomized, controlled clinical trials. NNT was defined as the number of patients needed to be treated to result in 1 patient with moderate–severe pain achieving >50% pain relief compared with placebo. NNT values between 2 and 4 were considered to indicate effective treatment. (Based on McQuay HJ, *et al*., 1997[2].)

Table 2.3 Mechanisms of pain medications

Pain function	*Neural mechanism*	*Medications*
Peripheral sensitization	Sodium channels	Antiepileptics (carbamazepine, oxcarbazepine, phenytoin, topiramate)
		Local anesthetics
		Tricyclic antidepressants
Central sensitization	Intracellular calcium	Antiepileptics (gabapentin, oxcarbazepine)
	NMDA receptor	Ketamine
		Dextromethorphan
Descending inhibition	Serotonin receptors	Antidepressants (tricyclics, SSRIs, SNRIs)
	Norepinephrine receptors	Tramadol
	Opioid receptors	Opioids

NMDA: N-methyl-D-aspartate; SNRI: serotonin and norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor



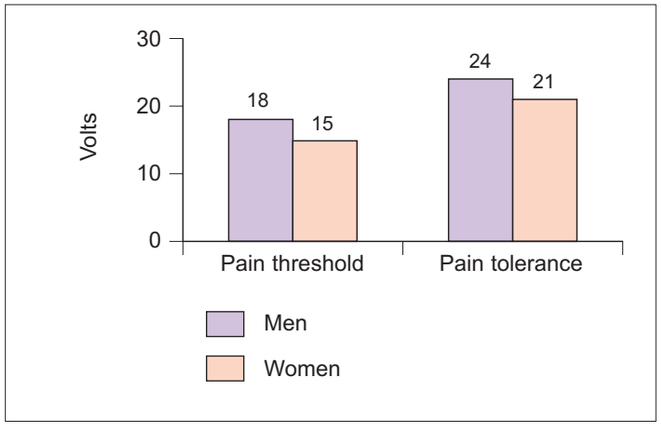
2.2 Mechanism of common analgesics. Myelinated A-δ fibres and unmyelinated C-fibres preferentially respond to noxious stimuli, sending impulses to the dorsal horn, where they synapse in outer laminae before crossing to ascend in the spinothalamic tract (**A**). Signals from the spinothalamic tract terminate in the thalamus, resulting in activation of the somatosensory cortex and limbic systems. Analgesics reduce pain transmission by influencing peripheral pain transduction and transmission or modulating central mechanisms in the brain or spinal cord (**B**).

noradrenergic pathways from the locus ceruleus dampen pain transmission by inhibiting pain pathways in the spinal cord, through interactions on inhibitory interneurons.

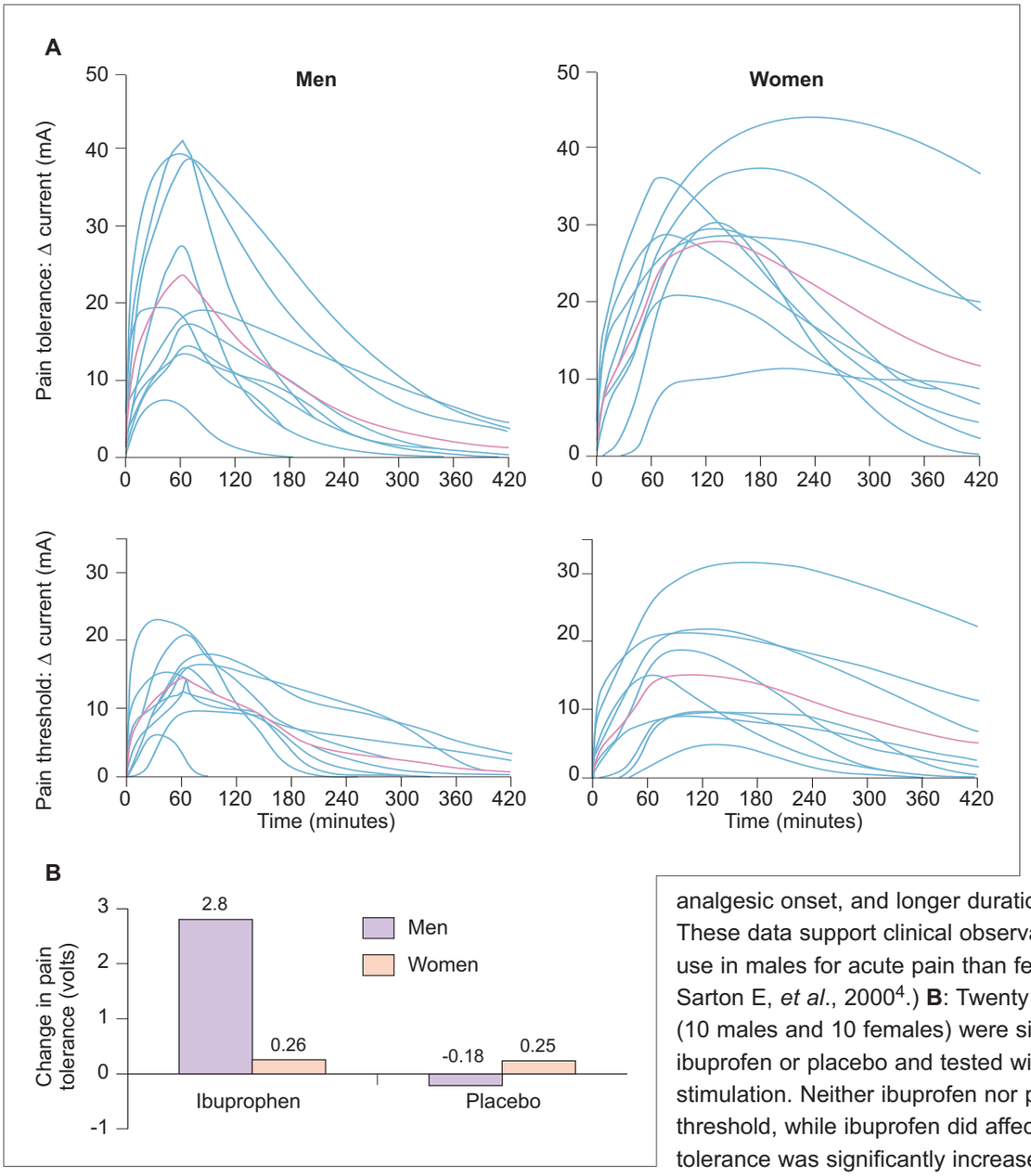
Gender and ethnic influences on medication efficacy

Women are more sensitive to pain than men (**2.3**)[3]. Furthermore, analgesic response varies by gender. Although men experience a greater early effect from opioids, the overall analgesic response is greater and more persistent in women (**2.4**)[4]. Nonsteroidal anti-inflammatory analgesia, alternatively, is superior in men[3]. Gender differences in pain perception and treatment response may be at least partially explained by the important role of estrogen as a pain modulator.

Pain sensitivity and treatment effectiveness are also influenced by ethnicity. Although pain threshold is similar among ethnic groups, studies consistently show a lower pain



2.3 Pain sensitivity by gender. The ability to perceive electrical stimulation as pain (threshold) and greatest tolerable level (tolerance) were tested in 20 healthy adults. Both pain threshold and tolerance were significantly higher in men ($P<0.05$). (Based on Walker JS, Carmody JJ, 1998[3].)

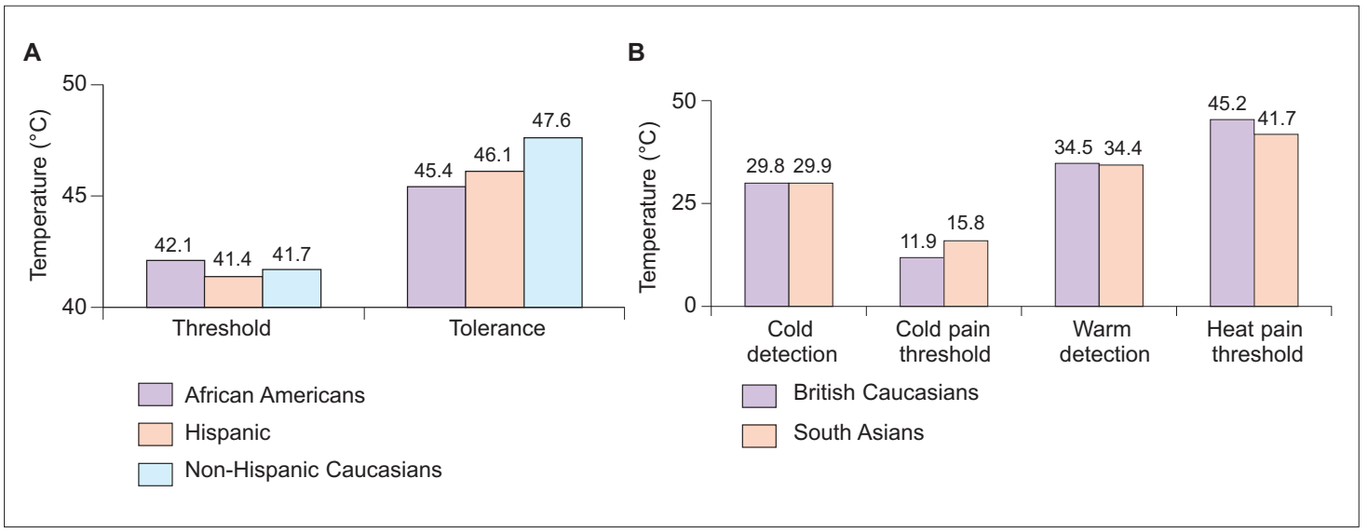


2.4 Analgesic response by gender. **A**: The effect of a single dose of intravenous morphine was tested in healthy adults (10 males and 10 females). The graphs show individual (blue lines) and mean (red lines) responses to electrical current stimulation. Baseline currents were similar between genders for pain threshold and tolerance. While concentrations of morphine and its metabolites were similar between genders, women demonstrated greater overall morphine potency, slower speed of analgesic onset, and longer duration of analgesic effect. These data support clinical observations of higher opioid use in males for acute pain than females. (Based on Sarton E, *et al*., 2000[4].) **B**: Twenty healthy adults (10 males and 10 females) were similarly treated with ibuprofen or placebo and tested with electrical stimulation. Neither ibuprofen nor placebo affected pain threshold, while ibuprofen did affect pain tolerance. Pain tolerance was significantly increased with ibuprofen in men ($P<0.05$) and not different between ibuprofen and placebo in women. (Based on Walker JS, Carmody JJ, 1998[3].)

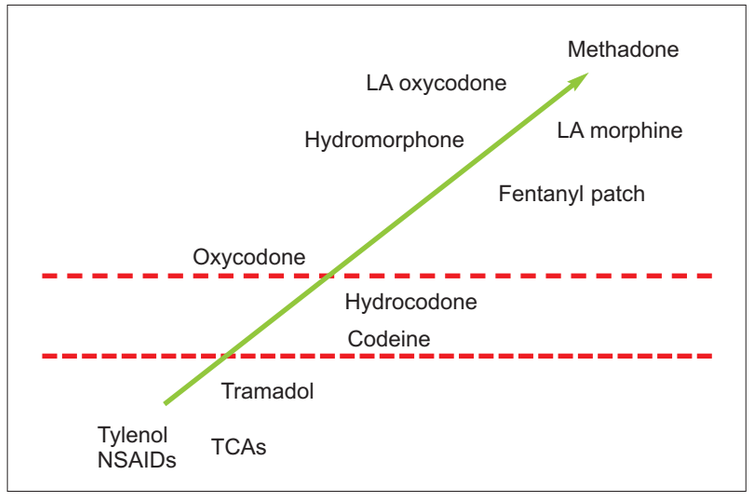
tolerance and greater perception of pain stimuli as unpleasant in African Americans and Hispanics compared with Caucasians (**2.5**)[5–8]. Reduced pain tolerance to experimental pain in African Americans supports findings in a population of chronic pain patients that showed similar pain intensity but increased perception of pain unpleasantness in African Americans compared with Caucasians[9]. Asians similarly demonstrate increased sensitivity to pain[10].

Analgesics

Short-acting analgesics may be used to treat intermittent, severe pain flares, while long-acting or sustained analgesics and adjuvant therapies are effective for reducing persistent disabling pain. Opioids provide stronger analgesic potency for noninflammatory pain than nonopioid analgesics, like nonsteroidal anti-inflammatory drugs (NSAIDs), without risk from prostaglandin-related effects (**2.6**)[11]. About 30% of primary care patients prescribed opioids for chronic pain,



2.5 Differences in pain response by race. **A**: Experimental pain testing was completed in healthy adults representing three ethnic groups: African American (N=63), Hispanic Americans (N=61), and non-Hispanic Caucasian Americans (N=82). Demographic factors were considered as covariates in analyses. There were no differences in pain threshold for heat or cold pain among genders (not shown). Both heat and cold pain tolerance, however, were similar for African Americans and Hispanics and significantly lower in both ethnic groups compared with non-Hispanic Caucasians (P<0.05). (Based on Rahim-Williams FB, *et al*., 2007[8].) **B**: In a similar study, pain testing was performed in 40 healthy adults: 20 British Caucasians and 20 South Asians from India, Pakistan, and Bangladesh. Perception of cold and warm was similar between ethnicities, while pain thresholds were lower among Asians. Differences between Caucasians and Asians were significant for heat pain threshold (P=0.006) and showed a trend toward significance for cold pain threshold (P=0.057). (Based on Watson PJ, *et al*., 2005[10].)



2.6 Analgesic potency ladder. This analgesic potency ladder is based on the World Health Organization (WHO) 3-step analgesic ladder. The WHO recommends matching analgesic potency with pain severity. Patients with mild pain are initially treated with therapies within the first rung of the ladder, including nonopioid analgesics and adjuvant therapy. Treatment for patients with moderate severity pain should include the addition of weak opioids, with strong opioids reserved for patients with severe pain. The effectiveness of this approach was validated in a 10-year prospective study with cancer pain patients. Although 3 in 4 patients required weak or strong opioids, pain relief was shown to be equally effective in each step of the ladder when therapy was initiated with analgesic potency matched to pain severity. LA: long-acting; NSAID: nonsteroidal anti-inflammatory drug; TCA: tricyclic antidepressant.

however, demonstrate medication misuse or abuse, including reporting lost/stolen prescriptions, obtaining opioids from secondary sources, and repeatedly requesting early refills[12]. While opioids are most effective in reducing non-neuropathic pain, they may also be used for disabling neuropathic pain, although pain reduction may be less and dose requirements may be higher (**2.7**)[13,14].

Antidepressants

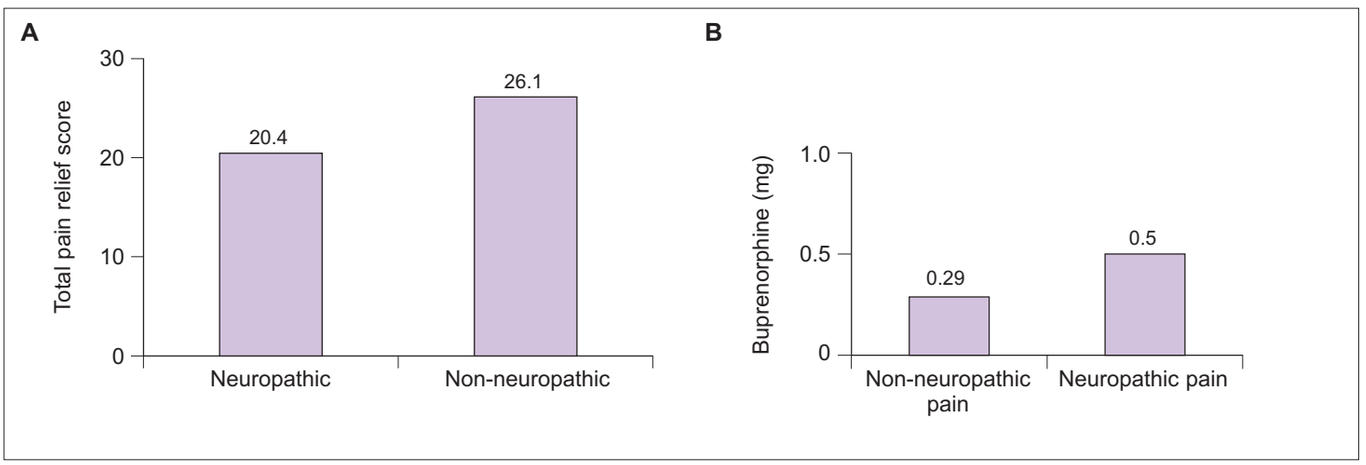
In addition to mood-enhancing properties, antidepressants offer potent analgesic effects. A variety of neural mechanisms explain the analgesic properties of antidepressants (*Table 2.4*)[15]. Antidepressants may be effectively used to treated chronic pain and frequently comorbid disturbances in mood and sleep.

Analgesic properties of antidepressants, however, are independent of their mood-relieving qualities, with analgesia occurring in patients without comorbid depression. Among different classes of antidepressants, tricyclics have the most potent analgesic effects (**2.8**)[16]. Among the newer antidepressants, serotonin and noradrenergic reuptake inhibitors, such as venlafaxine and nefazodone, and noradrenergic and specific serotonergic antidepressants, such as mirtazapine, offer the most promise for providing analgesia. Both of these classes of antidepressants affect α_2-adrenergic receptors and κ_1,κ_3, δ-opioid receptors, which may contribute to their analgesic properties[15].

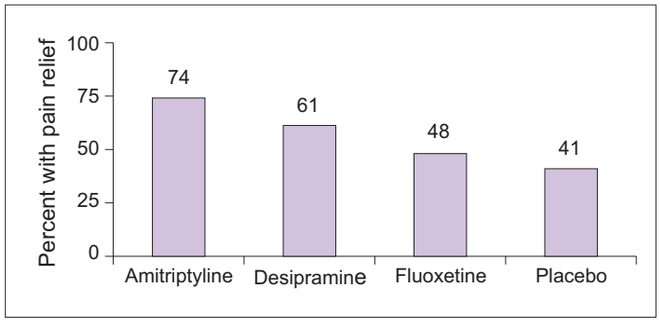
Table 2.4 Analgesic effects from antidepressants

- Presynaptic effects
  - Inhibition of noradrenaline reuptake
  - Inhibition of serotonin reuptake
- Postsynaptic
  - Block α-adrenergic receptors
  - Block histamine receptors
  - Block cholinergic receptors
- Induce opioid release
- NMDA antagonism
- N-type calcium channel blockade

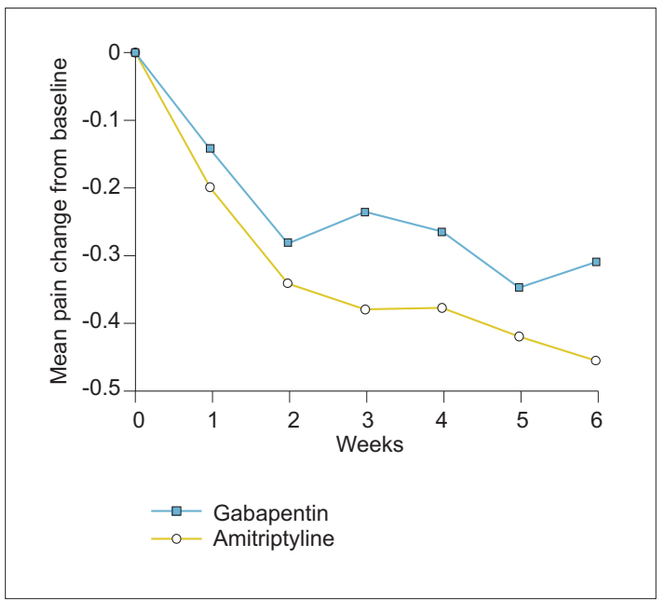
NMDA: N-methyl-D-aspartate



2.7 Opioid efficacy for neuropathic pain. Opioids may be effectively used to reduce neuropathic pain. Total pain relief was evaluated in 4 single-dose studies in which 168 patients received doses of opioid (**A**). Pain relief occurred with both groups, although relief was significantly better in patients with non-neuropathic pain (P=0.02). (Based on Cherny NI, *et al.*, 1994[13].) In a second study (**B**), the dosage of opioid buprenorphine necessary to reduce pain by at least 50% was compared in 21 patients who were treated for non-neuropathic postoperative thoracic surgery pain and 1 month later for post-thoracotomy neuropathic pain. While pain reduction was successfully achieved for both acute non-neuropathic pain and subsequent neuropathic pain, the opioid dosage required to achieve similar pain relief was significantly higher for the neuropathic pain (P<0.001). (Based on Benedetti F, *et al.*, 1998[14].)



2.8 Effects of antidepressants on diabetic neuropathy pain. Fifty-seven patients (59% male; median age = 58 years) with painful diabetic neuropathy were randomized to treatment with amitriptyline, despiramine, fluoxetine, or placebo in two double-blind studies. Mean daily doses were 105 mg amitriptyline, 111 mg despiramine, and 40 mg fluoxetine. The graph shows the percentage of patients receiving each treatment who experienced moderate or better pain relief. Pain relief was superior to placebo for both tricyclic antidepressants (P<0.05) but not fluoxetine. There were no significant differences in efficacy between the two tricyclics. (Based on Max MB, *et al*., 1992[16].)



2.9 Antiepileptics for neuropathic pain. In a controlled, pilot study, 25 patients with diabetic neuropathy were randomized to treatment with gabapentin (mean dosage = 1,565 mg daily) or amitriptyline (mean dosage = 59 mg daily). At least moderate pain relief was experienced by 52% with gabapentin and 67% with amitriptyline. The graph shows changes in pain severity from baseline for patients completing the full 6 weeks of treatment. A reduction of 0.35 represents a decrease from moderate to mild pain. There were no significant differences in pain reduction between gabapentin and amitriptyline. These data support that both tricyclic antidepressants and antiepileptics can be effective therapies for neuropathic pain. (Based on Morello CM, *et al*., 1999[17].)

Neurostabilizing antiepileptics

Antiepileptic drugs with neurostablizing properties reduce neuronal excitability by blocking sodium and calcium channels and acting as GABA mimics. Antiepileptics, such as gabapentin, pregabalin, carbamazepine, baclofen, valproate, topiramate, and others, provide modest analgesic benefit and reduction of neuropathic pain and chronic headaches. Pain relief with antiepileptics is similar to that achieved with tricyclic antidepressants (**2.9**)[17].

Muscle relaxants

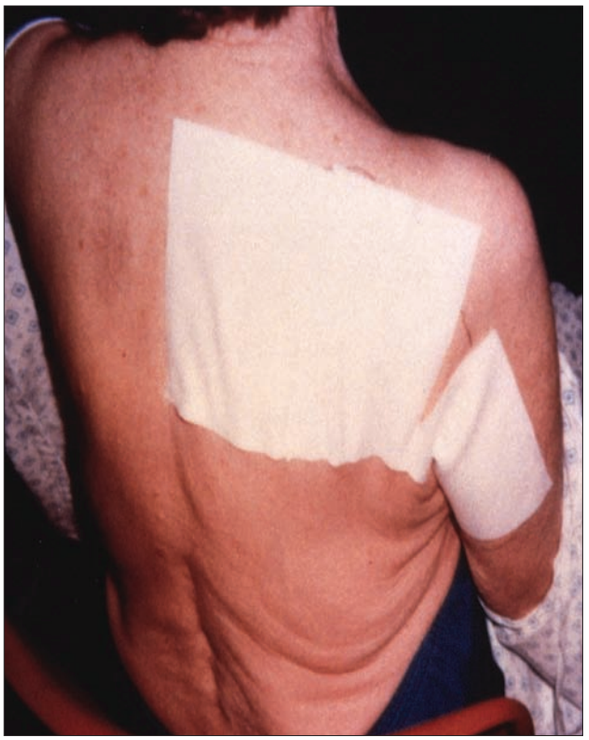
Most muscle relaxants or antispasmodic medications offer minimal long-term benefit for chronic pain. Tizanidine has been shown to reduce pain and sleep disturbance in patients with chronic headache and neuropathic pain. Tizanidine acts as an alpha 2-adrenergic receptor agonist, similar to the analgesic mechanism for clonidine.

Topical agents

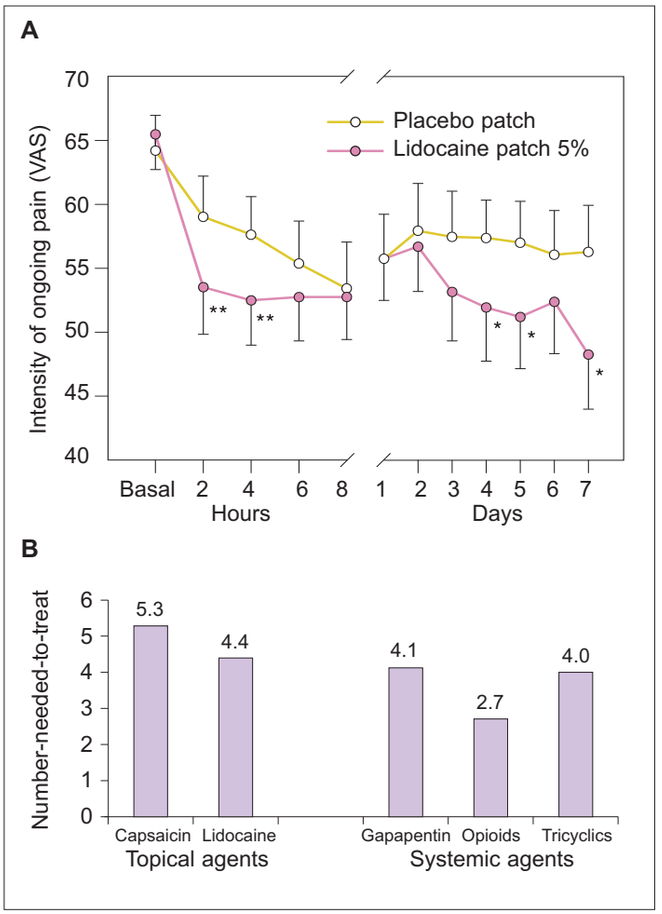
Effective topical agents for neuropathic pain include 5% lidocaine patches and capsaicin cream (**2.10**, **2.11**)[18]. In addition to reduction in neuropathic pain, these treatments also provide minimal systemic adverse effects.

Pain medications during pregnancy

Selection of medications prescribed to women capable of childbearing is influenced by medication safety during pregnancy (*Table 2.5*). Gabapentin may be used during attempted conception and early pregnancy. Because gabapentin may adversely affect development of the fetal bony



2.10 Lidocaine patches. 5% lidocaine patches are placed to cover a thoracic area of postherpetic neuralgia pain, using 2.5 patches. Patches are recommended to be used for 12 hours, followed by 12 hours without patches. Serum levels of lidocaine remain low, even with multiple patch use.



2.11 Efficacy of topical agents. Fifty-eight outpatients with chronic peripheral focal neuropathic pain syndromes in Switzerland and Germany were randomized to treatment with 5% lidocaine or placebo patches. The most common diagnoses were postherpetic neuralgia (55%) and postsurgical neuralgia (18%). Mean patient age was 63 years, with a mean pain duration of 3 years. Pain was measured using a visual analogue scale (VAS) with 0 representing no pain and 100 maximum pain. Changes in pain severity compared with baseline are shown in the graph (**A**). Differences between lidocaine and placebo were significant and favoured lidocaine during the first 4 hours after patch placement (**P<0.01) and after 4, 5, and 7 days of treatment (*P<0.05). The number of patients needing to be treated (NNT) to obtain one patient with a 50% reduction in pain was calculated at 4.4 for lidocaine patches in this study. The authors compared this to literature reports of NNT for patients with postherpetic neuralgia (**B**). (Based on Meier T, *et al.*, 2003[18].)

growth plate, it should be discontinued as pregnancy progresses. Opioids are best limited to infrequent, intermittent use. Patients who have been chronically using daily opioids during mid-to-late pregnancy must continue daily opioids because of the risks of fetal mortality and premature labour associated with intrauterine fetal opioid withdrawal[19].

Interventional therapies

Interventional therapies target neural structures believed to operate as pain generators. Therapies include reversible neural blockade with local anesthetics, neuroablation (e.g. radiofrequency neurotomy), enhancement of spinal cord stimulation, and intraspinal delivery of medications. Reduction of pain using interventional therapies facilitates other rehabilitation efforts and can significantly improve function and mood.

Table 2.5 Pain medications during pregnancy and attempted conception

	Safe (FDA risk category A or B)	*Use if benefit > risk (FDA risk category C)*	*Avoid (FDA risk category D or X)*
Prevention	Beta-blockers† Long-acting opioids* Topical lidocaine	Most SSRI antidepressants** Tricyclic antidepressants Venlafaxine Gabapentin Topiramate Lamotrigine Topical capsaicin Buproprion	Paroxetine Valproate
Flare	Acetaminophen NSAIDs 2nd trimester Opioids*	NSAIDs 1st trimester†† Triptan	Aspirin Ergotamine NSAIDs 3rd trimester

NSAID: nonsteroidal anti-inflammatory drug; SSRI: selective serotonin reuptake inhibitor

* Long-acting oxycodone is FDA category B, while other short- and long-acting opioids are category C. Clinical experience, however, suggests safe short-term use with pregnancy

** Except paroxetine, which should not be used

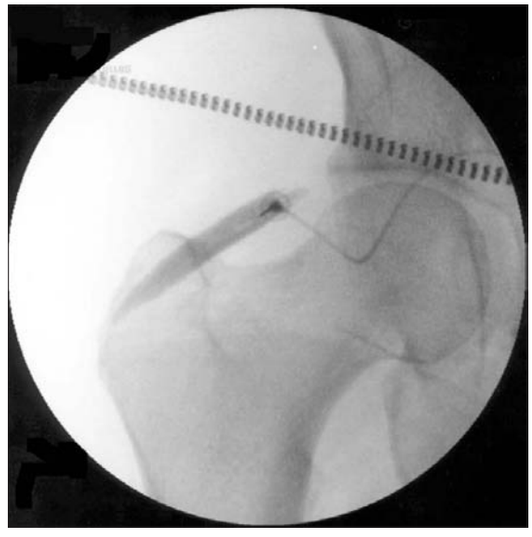
† Although technically an FDA risk category C drug, the long track record of safe use of beta-blockers, e.g. propranolol, during pregnancy suggests safety. Atenolol, however, is contraindicated during pregnancy

†† Early NSAID use has been linked to increased risk of miscarriage and is restricted in many European countries

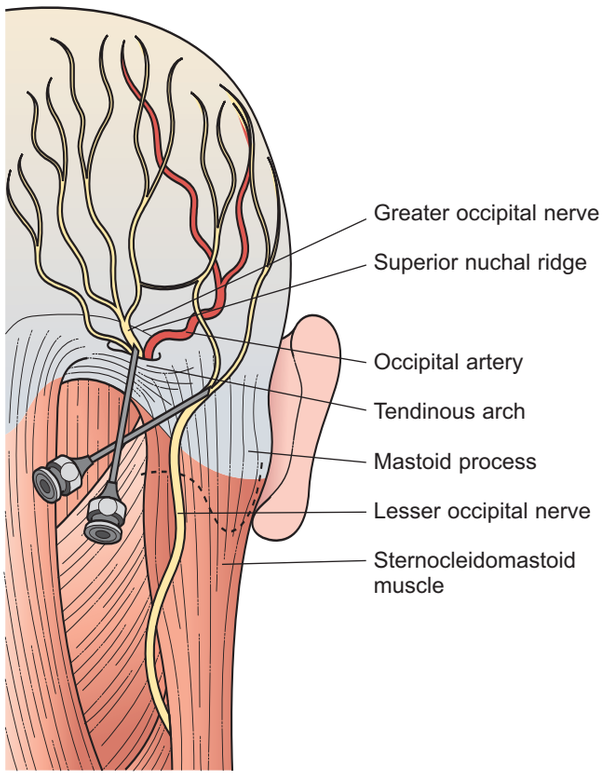
Injections

Trigger point injections for myofascial pain, peripheral blocks for mononeuropathy (such as occipital nerve blocks)[20], sympathetic blocks for sympathetically-mediated pain (such as early complex regional pain syndrome), and epidural injections for spinal pain offer temporary pain relief, typically lasting weeks to months (**2.12**–**2.14**). The facets are paired synovial joints formed by an inferior articular vertebral process above and a superior articular vertebral process below, innervated by the posterior ramus of the spinal root. Facet injections may provide temporary pain relief (**2.15**). Adding corticosteroids to injections blocks the local inflammatory response to pain while the acute pathology resolves. Local anesthestic helps relieve pain until the steroids have time to be effective.

In musculoskeletal pain, relief from injections is generally symptomatic and often transient; therefore, these therapies are best used in conjunction with additional pain-relieving therapies designed to provide more long-term benefit, such as physical therapy. In patients with sympathetically-mediated neuropathic pain (e.g. complex regional pain syndrome, postherpetic neuritis, and human immunodeficiency virus [HIV] peripheral neuropathy), a series of sympathetic nerve blocks can actually modify



2.12 Piriformis injection. Fluoroscopy is used to improve success of a variety of injections. Piriformis muscles between the sacrum and greater trochanter are frequently injected to relieve buttock pain associated with myofascial piriformis syndrome. Fluoroscopic guidance, confirming needle placement through injection of contrast dye, is often beneficial due to the small size, deep location, and close relationship to neurovascular structures of the piriformis muscle.

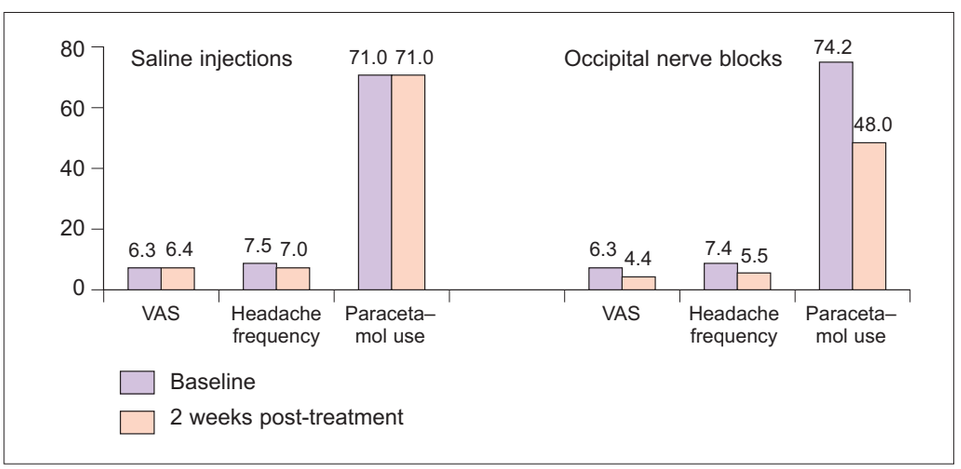


2.13 Occipital nerve block. Occipital nerve blocks are performed by inserting a needle at the base of the skull and injecting medication around the origin of the greater or lesser occipital nerve.

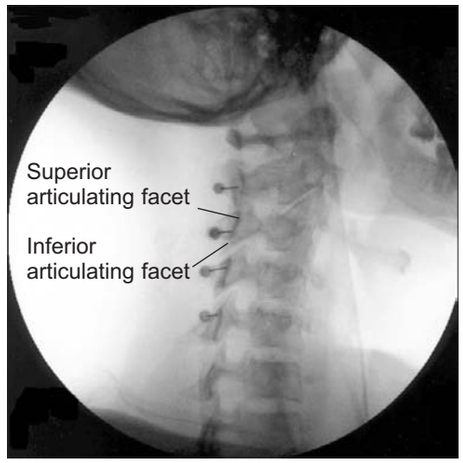
disease course, preventing the development of a chronic, severely debilitating pain syndrome.

Epidural injections include caudal, interlaminar, and transforaminal blocks (**2.16**, **2.17**). If patients achieve >50% reduction in pain for 6–8 weeks, injections may be repeated after 2 months or longer, to a maximum of 4–6 procedures within a year. A systematic literature review of epidural steroid injections for chronic spine pain provided evidence-based recommendations, with moderate to strong evidence of benefit for both short- and long-term relief in patients with either cervical or lumbar radicular pain treated with epidurals (*Table 2.6*)[23]. Epidurals are also considered routine care for lumbar stenosis not responding to conservative measures. Epidural injections have limited benefit for nonradicular and nonstenosis pain or isolated back pain.

Possible complications with epidural injections are listed in *Table 2.7*. Major complications are rare with epidurals and any complication with fluoroscopic guidance has been reported for 10% of transforaminal lumbar, 17% of interlaminar cervical, 20% of interlaminar thoracic, and 16% of caudal epidurals[23].

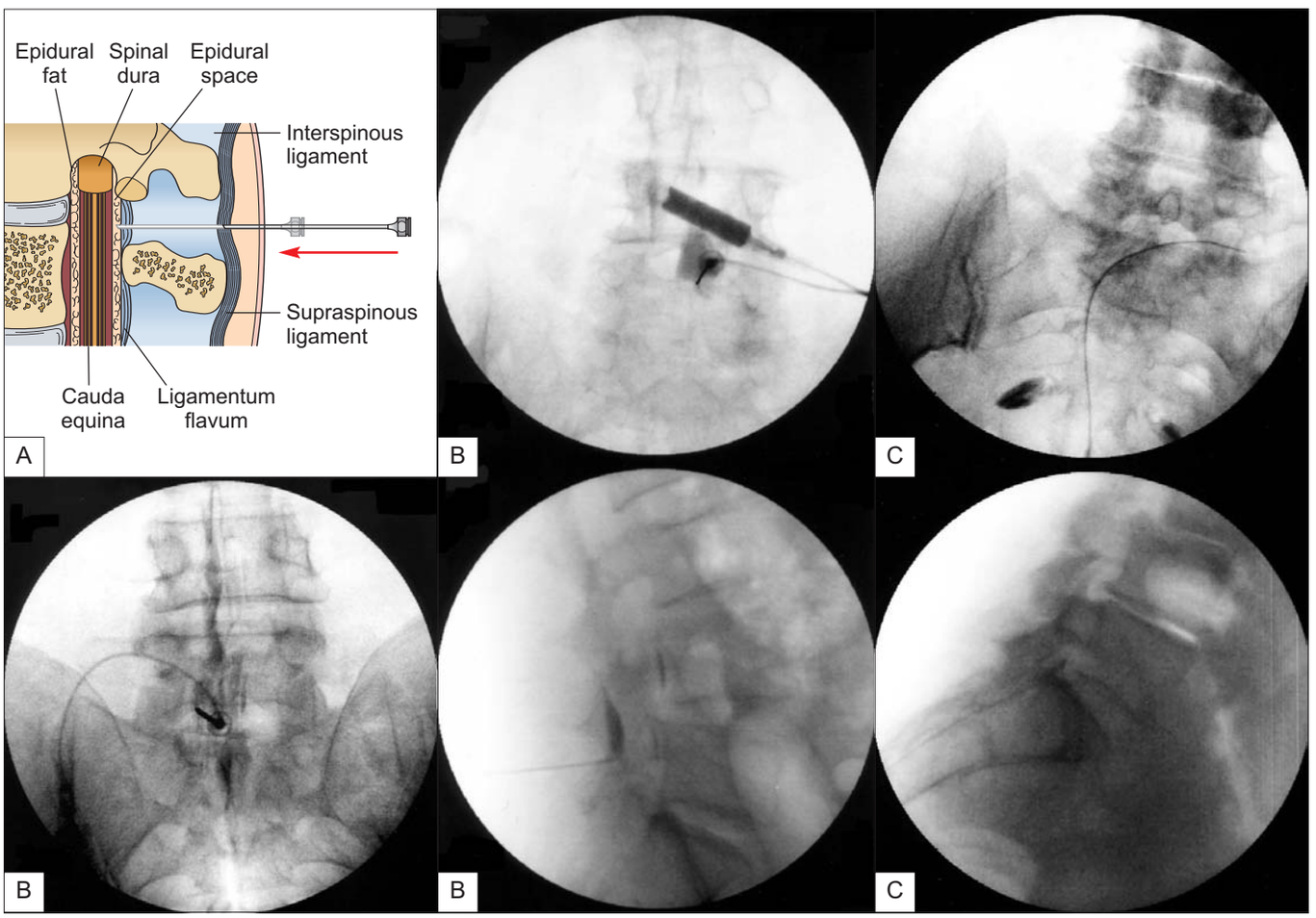


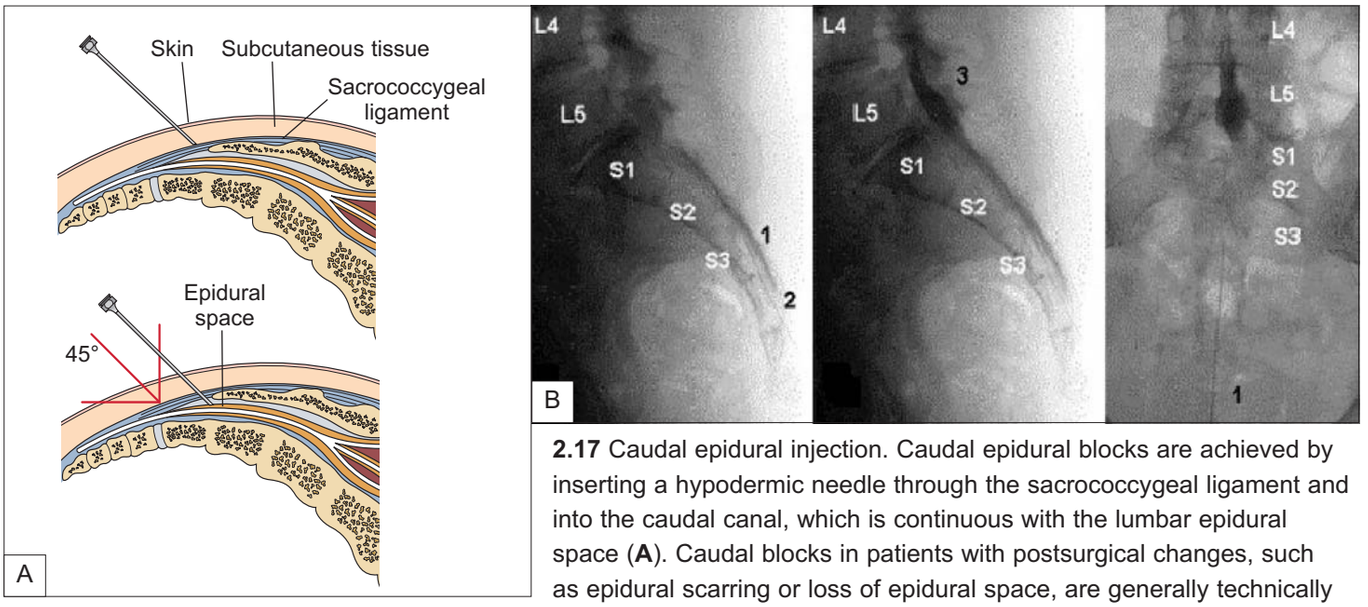
2.14 Occipital nerve block. Fifty patients with cervicogenic headache (74% female, mean age 46.5 years) were randomized to receive occipital nerve block or control saline injections. Pain severity was assessed on an 11-point scale from 0 (no pain) to 10 (excruciating pain). Headache frequency was defined as the number of headaches during 2 weeks. Paracetamol use was defined as the number of 500 mg tablets consumed during 2 weeks. Baseline headache characteristics were similar between groups. Two weeks after treatment, headaches were significantly better among patients treated with occipital nerve blocks for pain severity (P=0.0001), frequency (P=0.026), and paracetamol use (P=0.0001). Use of dextropropoxyphene, tramadol, and ketoprofen were likewise similar at baseline between groups but significantly reduced after treatment for patients receiving occipital nerve blocks ($P \leq 0.01$). (Based on Naja ZM, *et al.*, 2006[20].)



2.15 Cervical facet blocks. Facet arthropathy can be treated by fluoroscopically-guided injections into the facet joint itself or at the median branch nerve blocks. Facet joints are shown on this oblique view of the cervical spine. Cross innervation of the facets necessitates blocking multiple levels, usually one level above and one below the affected joint. Facet injections are generally reserved for the cervical or lumbar spine, as the risk of pneumothorax in the thoracic spine is substantial. If diagnostic facet blocks provide significant but temporary relief, patients may receive repeated facet blocks, radiofrequency ablation, or pulsed radiofrequency stimulation.

2.16 Lumbar epidural injection. Performing lumbar epidurals using anatomical landmarks (**A**) and perception of loss of air pressure resistance to verify location of the epidural space results in a faulty injection into soft tissues in the posterior back outside of the spinal canal in one in four attempts[21]. Utilizing fluoroscopic guidance (**B**) improves epidural injection placement accuracy, as seen with the dye column in the epidural space, and treatment success. (**C**) Epidurolysis developed by Dr. Gabor Racz is designed to dissolve scar tissue around entrapped nerves in the epidural space by inserting an epidural catheter under fluoroscopy, followed by injecting hyaluronidase and subsequently anethestic and steroid. This patient had scarring at the right L5 nerve root, with a clinical L5 radiculopathy. Pain that failed to respond to conservative measures resolved with epidurolysis.





2.17 Caudal epidural injection. Caudal epidural blocks are achieved by inserting a hypodermic needle through the sacrococcygeal ligament and into the caudal canal, which is continuous with the lumbar epidural space (**A**). Caudal blocks in patients with postsurgical changes, such as epidural scarring or loss of epidural space, are generally technically easier than lumbar epidurals, with a lower risk of inadvertent puncture of the dural sac. Fluoroscopic guidance with contrast dye confirmation ensures accurate placement (**B**). In a recent prospective study, over half of those patients treated with fluoroscopically-guided caudal epidural injections for degenerative lumbar stenosis achieved pain reduction of at least 50% and improved function (walking and standing tolerances) that were maintained for at least 1 year post-procedure[22].

Table 2.6 Evidence-based recommendations for epidural steroids for chronic spine pain

- Interlaminar epidurals
  - Moderate evidence supports short- and long-term benefits for cervical radiculopathy
  - Strong evidence for short-term benefits for lumbar radiculopathy
  - Limited evidence for long-term benefits for lumbar radiculopathy
  - Indeterminate evidence for axial spine pain or lumbar stenosis
- Transforaminal epidurals
  - Moderate evidence supports short- and long-term benefits for cervical nerve root pain
  - Strong evidence supports short-term benefits for lumbar nerve root pain
  - Moderate evidence supports long-term benefits for lumbar nerve root pain
  - Indeterminate evidence for axial spine pain and lumbar disc extrusion
- Caudal epidurals
  - Strong evidence for short-term benefits for lumbar radiculopathy and postlumbar laminectomy syndrome (failed back)
  - Moderate evidence for long-term benefits for lumbar radiculopathy and postlumbar laminectomy syndrome (failed back)
  - Moderate evidence supports short- and long-term benefits for nonradicular chronic low back pain

(Based on Abdi S, *et al.*, 2007[23])

Table 2.7 Possible complications from epidural steroid injections

- Dural puncture
- Spinal cord trauma
- Infection or abscess
- Hematoma
- Subdural injection
- Intracranial air injection
- Epidural lipomatosis
- Pneumothorax
- Nerve damage
- Headache
- Increased intracranial pressure
- Intravascular injection
- Cerebral vascular or pulmonary embolus
- Steroid effects (e.g. euphoria, increased blood sugar, hypertension)

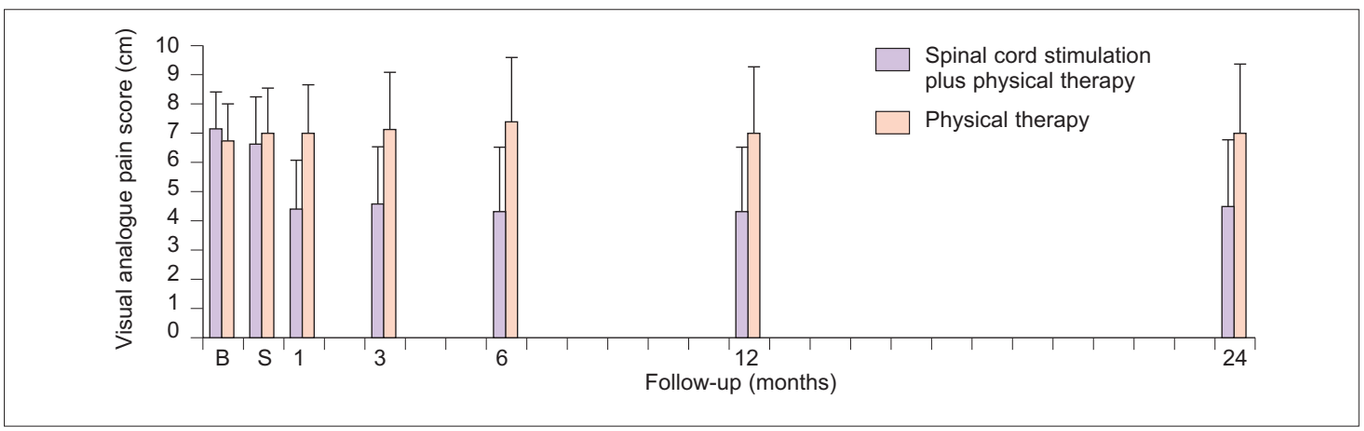
(Based on Abdi S, *et al*., 2007[23])

Spinal cord stimulation

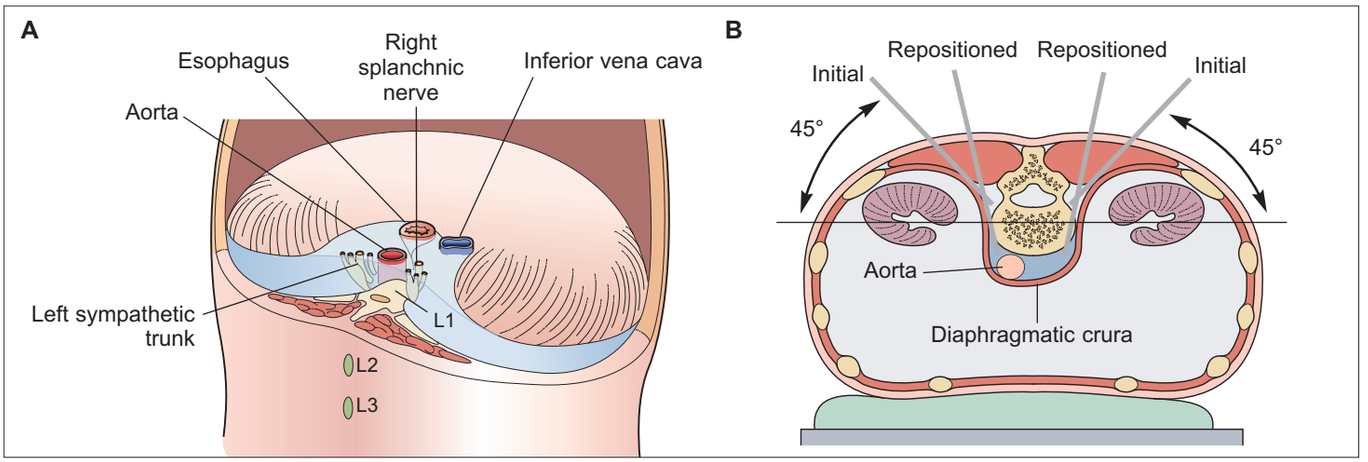
Stimulating metal contacts are placed in the dorsal epidural space and attached to a pulse generator, creating an electric field to stimulate the dorsal roots and columns. This electrical stimulation is designed to increase inhibition in the lateral spinothalamic tract and enhance antinociceptive signals from descending inhibitory pathways. Spinal cord stimulation is most beneficial for neuropathic sympathetically-mediated (**2.18**) and ischemic pain in a fairly stable and localized distribution[24].

Neuroablation

Celiac plexus neurolysis may help reduce severe pain associated with intra-abdominal cancer. Neurolytic blockade may be considered in patients benefiting from diagnostic blocks with anesthetic. Neurolytic blockade using 50–100% alcohol or phenol offers temporary pain relief, lasting months (**2.19**). Neurolytic blocks can be repeated but refractory neuritis is a frequent complication months later; therefore, this procedure is not indicated for acute exacerbations of a chronic disease, such as pancreatitis.



2.18 Long-term effects of spinal cord stimulation. Patients with chronic reflex sympathetic dystrophy were randomized 2:1 to receive spinal cord stimulation plus physical therapy (N=35) or physical therapy alone (N=16). A permanent stimulation system was placed in 24 patients after successful test stimulation. The graph shows mean pain severity scores at baseline (B), the start of therapy (S), and 1, 3, 6, 12, and 24 months after treatment. Pain was rated on a visual analogue scale from 0 (no pain) to 10 (very severe pain). After 2 years, mean pain intensity was reduced by 2.1 in patients receiving stimulation plus physical therapy versus 0 among patients treated with physical therapy alone (P<0.001). Pain was reported to be much improved in 15 of the 35 patients treated with stimulation plus physical therapy (43%) versus 1 of the 16 treated with physical therapy alone (6%). At 2 years, spinal cord stimulation was successful in 20 of 35 patients (57%), with 15 reporting much improvement and 13 experiencing a 50% decrease in pain severity. (Based on Kemler MA, *et al*., 2004[24].)

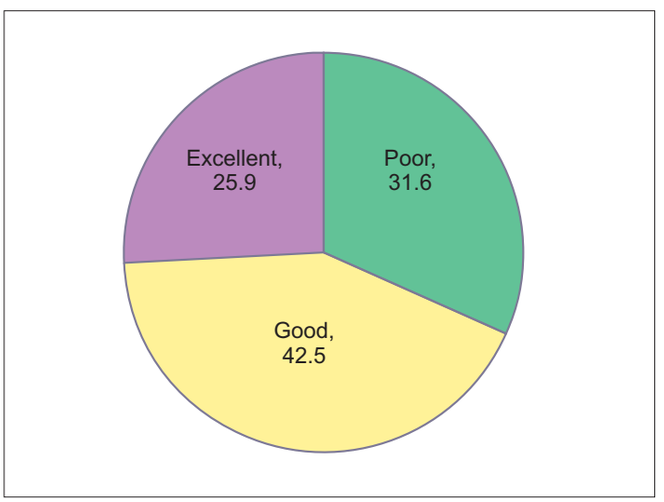


2.19 Celiac plexus block. The large, sympathetic celiac plexus surrounds the celiac artery anterior to the aorta at L1 (**A**). Blocks are performed by bilateral placement of needles at L1 (**B**). With the patient in the prone position, needles are inserted at 45° from the horizontal at the 12th rib until the L1 vertebra is reached; the needle is then withdrawn and reinserted at an increased angle to walk-off the vertebra anteriorly. Placement is confirmed fluoroscopically by injection of contrast dye.

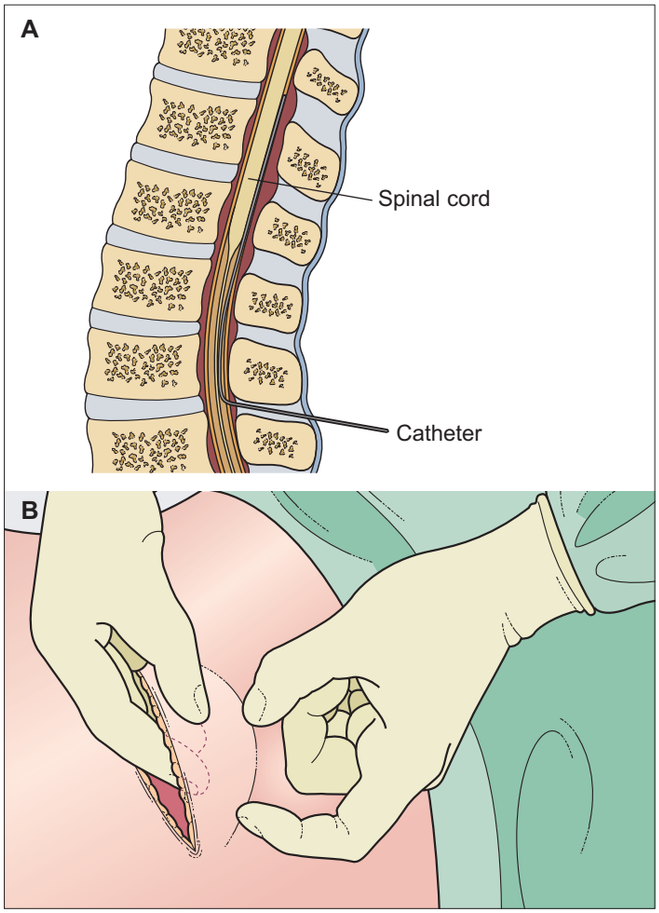
Radiofrequency neurotomy may be used to relieve facet pain. Long-term benefit has been shown in carefully selected patients who have benefited from repeated diagnostic blocks (**2.20**)[25].

Radiofrequency stimulation

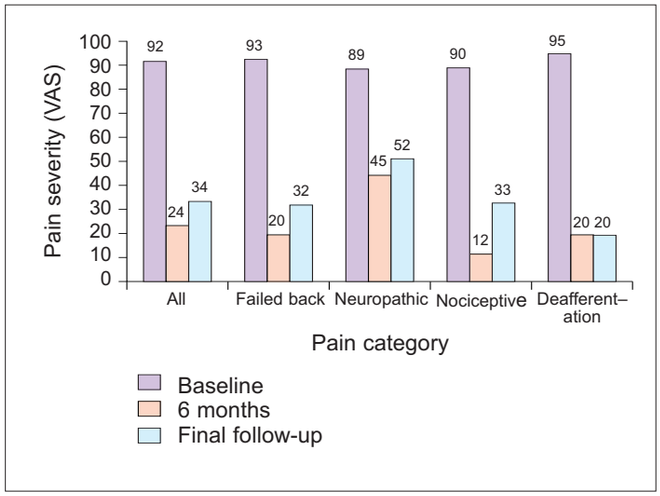
Few interventional treatments benefit nonradicular, degenerative disc disease pain of the lumbar or cervical spine. Discs are innervated by small unmyelinated fibres arising from the dorsal roots of the spinal nerve at each vertebral level. These unmyelinated fibres are highly susceptible to pulsed radiofrequency stimulation at as low a temperature as 42°C with no nerve ablation. Hypotheses of mechanism of action include: alteration of protein synthesis in pain pathways, gene transformation, and 'resetting' the homeostasis of sympathetic feedback loops. The area near the dorsal root ganglion can be safely stimulated using pulsed radiofrequency. One of the authors (DKC) has experience in >100 cervical and lumbar pulsed radiofrequency treatments at the dorsal root ganglia for degenerative disc pain, with over half of the patients experiencing long-term relief of pain, marked reduction in analgesic use, and increased function for 6 months to 1 year and only a single case of transient neuritis (unpublished data).



2.20 Percentage of patients achieving different levels of long-term relief after radiofrequency neurotomy. In this 10-year, prospective audit of patient data, patients with chronic low back pain and experiencing pain relief after two diagnostic facet blocks with local anesthetic were treated with radiofrequency denervation of the lumbar zygapophysial joints. Fluoroscopy was used to verify electrode placement at the junction of the transverse process and base of the superior articular process. Complete data were available for 174 patients, with pain relief 6 months postprocedure shown. Pain relief was considered excellent if pain was reduced by >80%, good if reduced by 50–80%, and poor if <50% reduction. The median duration of pain relief was 9 months. (Based on Gofeld M, *et al*., 2007[25].)



2.21 Intrathecal pump placement. A catheter is inserted through the middle of the back, into the subarachnoid space, and positioned near the spinal cord (**A**). Once the catheter is in place, an extension catheter is passed under the skin from the spine to the abdomen, where a pocket is created between the skin and muscle layers to hold the drug delivery pump (**B**). An external programmable device is used to adjust medication release.



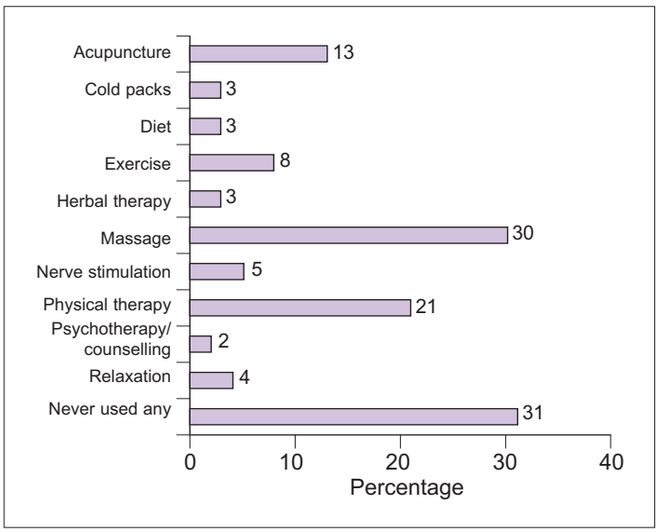
2.22 Long-term effects of intrathecal morphine. A total of 25 patients with severe, refractory, chronic nonmalignant pain were tested with intrathecal morphine infusion. Pain reduction >50% was achieved by 16 patients, who received implantable, programmable pumps for continuous morphine delivery. Patients were followed for 13–49 months. Mean time to final follow-up was 29 months. No patient was able to continue with a stable morphine dosage over follow-up. Over the first 6 months of treatment, average daily morphine dosage increased from 1.1 to 3.1 mg. Patients followed for over 2 years experienced a >10 mg/day increase in morphine dosage. Average pain reduction after 6 months was 68%, with 38% experiencing a pain reduction ≥50% and 94% experiencing a pain reduction ≥25%. At final follow-up, pain reduction was ≥50% in 44% and ≥25% in 75%. Three in four patients were considered to be treatment successes. Average changes in pain severity, as measured by a 100 mm visual analogue scale (VAS) by pain type are shown in the graph. Pain categories included failed back (N=12), neuropathic (peripheral neuropathy, arachnoiditis, and post-thoracotomy pain, N=2 for each diagnosis), nociceptive orthopedic pain (postspinal fractures, N=3 and postileosacral arthrodesis, N=2), and deafferentation in paraplegics (N=2). Pain reduction was greatest at final follow-up for deafferentation pain (75% reduction) and least for neuropathic pain (37% reduction). (Based on Kumar K, *et al*., 2001[27].)

Intrathecal pumps

The principal benefit of intraspinal medication delivery is enhanced drug efficacy with reduced unwanted side-effects. Infusable intrathecal drugs may include opioids, bupivacaine, clonidine, baclofen, ziconotide, or a drug combination (**2.21**)[26]. Modest long-term benefits have been demonstrated, although opioid dosage requirements tend to increase over time (**2.22**)[27]. Ziconotide is a synthetic peptide based on the toxin of the marine snail *Conus magnus* that acts as a potent, selective, reversible neuronal N-type voltage-sensitive calcium channel blocker. Ziconotide may provide an effective alternative for patients failing to respond adequately to opioids[28,29].

Nonpharmacological therapies

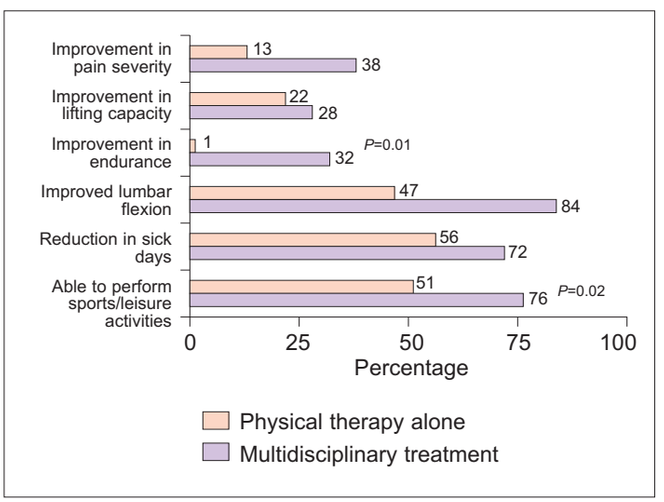
A community-based survey of people experiencing at least moderate severity chronic pain revealed that 69% used nonmedication therapies, most commonly massage, physical therapy, and acupuncture (**2.23**)[1]. A total of 38% reported that nondrug treatments were very helpful. Benefit from nonpharmacological therapies is maximized by incorporating a multidisciplinary, rehabilitative programme, focused on functional restoration. While patients often prefer to concentrate on physical therapy alone, rehabilitation programmes incorporating occupational and psychological therapies along with physical therapy maximize improvement in disability (**2.24**)[30].



2.23 The most common nondrug chronic pain therapies. A survey of adults with at least moderate severity chronic pain complaints in Europe and Israel revealed that most pain sufferers had used some type of nonmedication therapy, most frequently massage, physical therapy, and acupuncture. (Based on Breivik H, *et al*., 2006[1].)

Lifestyle management

Nicotine influences a variety of pain modulators, including endorphins[31–33]. Possibly due to changes in levels of pain-modulating neurotransmitters, smokers are more likely to experience a variety of chronic pain complaints and use opioids compared with nonsmokers (**2.25**)[34–36]. In one study, headache severity was linked to cigarette consumption, suggesting reducing nicotine use might decrease pain intensity[37].



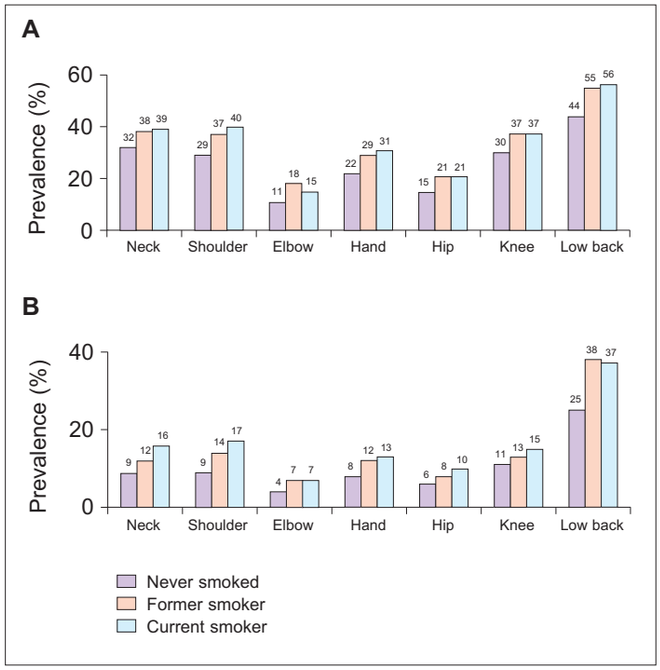
2.24 Multidisciplinary rehabilitation versus physical therapy alone. Patients with chronic low back pain were randomized to one of two 5-week training programmes: multidisciplinary rehabilitation (N=44) or active physical therapy alone (N=42). Multidisciplinary treatment included stretching, strengthening, aerobic, and endurance exercises plus occupational therapy and psychological intervention. Active physical therapy included training in stretching exercises, pain coping strategies, and functional training, with recommendations to build cardiorespiratory endurance. At the start of treatment, >90% of patients reported difficulties at work from their pain and about half were on sick leave. Patients were assessed after 6 months of treatment. Pain and disability improved for both groups, with significantly better endurance and ability to perform nonwork sports and leisure activities after multidisciplinary treatment. The mean number of sick leave days during the 6 months before treatment (101 in the multidisciplinary group and 110 in the physical therapy group) decreased significantly after both treatments (29 days after multidisciplinary treatment *vs*. 48 days after physical therapy; $P<0.001$). This numerical difference did not achieve statistical significance. (Based on Jousset N, *et al*., 2004[30].)

Poor sleep is associated with a reduced pain threshold[38]. Sleep disturbance occurs in over half of all patients with chronic pain[39,40]. One survey of 287 chronic pain patients identified sleep disturbance in 89%; the most common complaint was insufficient sleep quantity (62%)[41]. Poor sleep has been consistently linked to depressed mood. Poor sleep also increases pain-related impairment, even after controlling for the effects of mood[40,42].

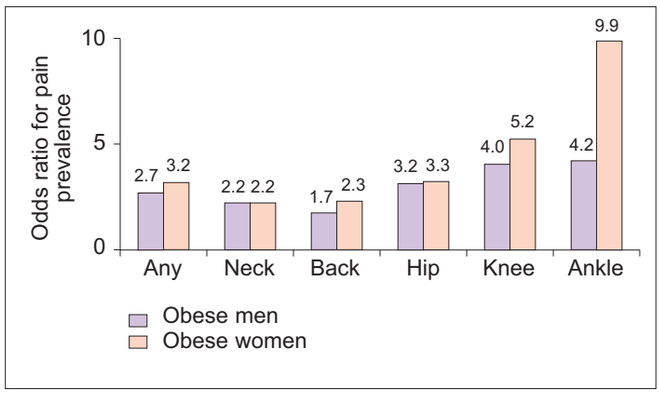
Excessive weight also affects pain complaints. The prevalence of musculoskeletal pain is significantly higher in obese versus nonobese adults (64% *vs*. 35%) (**2.26**)[43]. Obesity increases the mechanical load on joints and levels of proinflammatory cytokines that promote joint destruction[44–46]. As expected, increased body weight increases the risk for developing osteoarthritis of the hand, hip, and knee[47]. Nonarthritic pain is also more prevalent in obese individuals. Pain reduction is typically enhanced by weight loss with surgical or nonsurgical treatments[43,48–50].

Behavioural and cognitive therapies

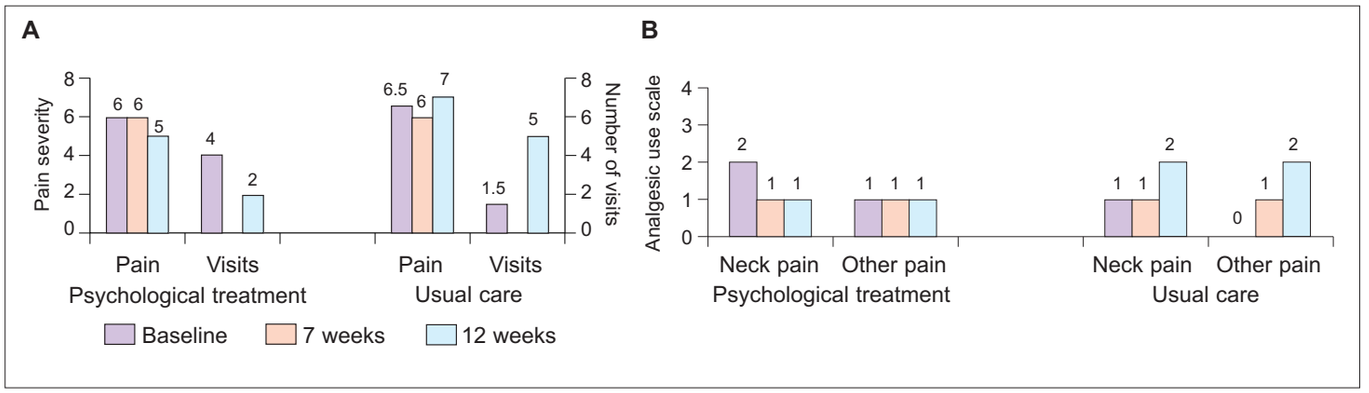
Psychology for chronic pain patients should focus on behavioural and cognitive therapies (**2.27**, *Table 2.8*)[51]. Cognitive restructuring involves replacing destructive, catastrophic thinking ('My pain will never get better; there's nothing I can do to help!') with positive, realistic thoughts ('I need to take a break and do some stretching exercises to reduce my pain.'). Emotional distress frequently accompanies chronic pain and should also be addressed through psychological therapy. The risk for depression or anxiety is four times greater in adults with chronic pain compared with pain-free controls[52]. If depression and



2.25 Effect of nicotine consumption on chronic pain. A random sample of 12,907 patients from 34 general practices in England included 6,513 former smokers and 3,184 current smokers. The prevalence of any musculoskeletal pain in the preceding year (**A**) and pain in the preceding year that prevented normal activities (**B**) by region are shown. After adjustments for age, gender, and complaints of headache, tiredness, and stress, the relative risk of pain was significantly greater for all sites for both any pain and disabling pain among former and current smokers, with the greatest risk for disabling pain among current smokers. (Based on Palmer KT, *et al*., 2003[36].)



2.26 Risk of musculoskeletal pain in obese men and women. A longitudinal study of the relationship between obesity and musculoskeletal pain was conducted in 2,460 men and 3,868 women in Sweden. The prevalence of musculoskeletal pain was significantly greater in obese individuals compared with controls for both men (58% of obese men *vs*. 32% of controls) and women (68% *vs*. 37%). Odds ratios adjusted for age, smoking, work status, and physical activity level are shown. Musculoskeletal pain occurred more frequently in every body region in obese men and women compared with controls (P<0.001). In addition, recovery from musculoskeletal pain after 2 years was significantly better in obese patients experiencing weight loss after bariatric surgery (average weight loss 27.6–29.5 kg) compared with those patients treated conventionally who did not experience significant weight loss (average weight loss 0.3–0.4 kg). (Based on Peltonen M, *et al*., 2003[43].)



2.27 Psychological pain management techniques. Thirty-seven patients with chronic neck pain were randomly assigned to treatment with psychological pain management training or an attention control. Both groups also received treatment by a physical therapist. The psychological training group received seven weekly sessions teaching relaxation training, body awareness exercises, and stress management. Pain severity was assessed before treatment and 7 and 20 weeks after treatment initiation using an 11-point scale from 0 (no pain) to 10 (excruciating pain), and the median number of healthcare visits was evaluated during the preceding 3 months at baseline and 20 weeks after treatment onset (**A**). Pain severity was unchanged in both groups, while the addition of psychological training to a standard physical therapy regimen resulted in a significant reduction in healthcare visits ($P<0.05$). Healthcare visits significantly increased for the usual care group ($P=0.05$). **B**: Median analgesic use was assessed for neck pain and pain from other parts of the body using a 5-point scale: 0=never, 1=a couple days per month, 2=1–2 days per week, 3=every other day, 4=every day. Analgesic use among psychological treatment patients significantly decreased for neck pain ($P<0.01$), while increasing in the usual care group for both neck pain ($P<0.05$) and other pain areas ($P<0.001$). (Based on Gustavsson C, von Koch L, 2006[51].)

Table 2.8 Psychological pain management skills

- Relaxation training
- Coping skills
- Stress management
- Cognitive restructuring

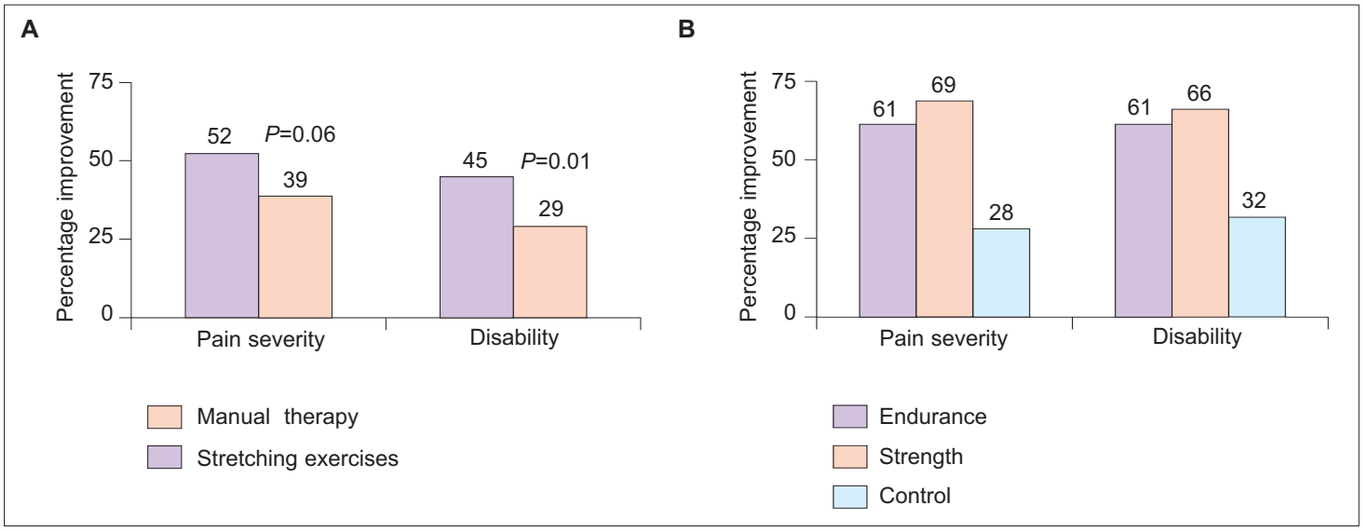
anxiety are severe, psychiatric treatment may need to precede pain management since severe distress will impair the patient's ability to fully participate in effectively learning and implementing new skills.

Exercise and physical therapy

Physical therapy and exercise training can provide both short- and long-term benefits for chronic pain (**2.28**)[53,54]. Active exercise programmes should begin with stretching exercises and advance to the combination of stretching and strengthening/endurance. Stretching and aerobic exercises alone are less effective long-term than adding strengthening/endurance exercises to a stretching and whole body reconditioning programme. Manual physical therapy also reduces chronic pain and disability and should be prescribed for patients unable to initiate treatment with active exercise effectively.

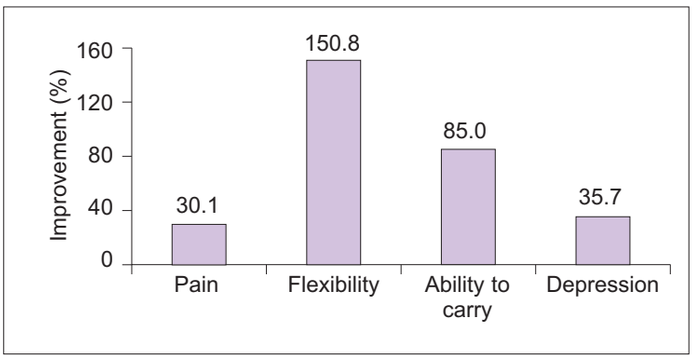
Occupational and work therapy

Occupational therapy offers an evaluation of activities of daily living and work duties that may aggravate chronic pain complaints. After an activity assessment, the therapist can suggest ways to alter activities so that disability is minimized (**2.29**)[55]. For example, patients with low back pain aggravated by sitting at work may find that placing a brick under their feet when they sit improves posture and reduces pain. Similarly, a housewife whose pain is flared by vacuuming may be instructed to walk with the vacuum rather than pushing and pulling the machine across the carpet. Simple devices, such as push carts for carrying supplies at work, may also be helpful. Occupational therapists are also effective in teaching patients proper activity scheduling and pacing techniques.



2.28 Exercise and physical therapy treatment of chronic neck pain. In two studies, groups of women with nonspecific neck pain were randomized to receive manual therapy or exercise or serve as a control group. Physical parameters and pain measures were assessed short- and long-term. Percentage improvements in pain severity and disability are shown. In the short-term study (**A**), 125 women (mean age of 43 years and mean pain duration of 3.4 years) were randomized to receive twice weekly manual therapy from a physical therapist, consisting of low-velocity mobilization of the cervical joints, massage, and passive stretching, or to perform stretching exercises 5 times weekly. Treatments were switched after 4 weeks. Significant decreases in pain and disability occurred after 4 weeks of either treatment. Between-group differences were seen for disability and a trend for pain severity, both favouring manual therapy. (Based on Ylinen J, *et al.*, 2007[53].) In the long-term study (**B**), 179 women (mean age 46 years) with chronic neck pain for an average of 8 years were randomly assigned to one of three training groups: endurance, strength, and control. The endurance group was trained to perform repetitions of neck flexions, while the strength group learned isometric neck exercises. Both groups also performed weight training of the shoulder and upper extremities, with the endurance group focusing on repetitions and the strength group on increasing maximum weight. Both groups were also instructed in stretching exercises for the neck, shoulder, and upper extremity, as well as squats and sit-ups for trunk and lower extremity strengthening and back extension exercises. Aerobic exercise three times weekly was also encouraged. Both exercise training groups were given nine training sessions, followed by written instructions suggesting 20 minute exercise sessions three times weekly. The control group received a stretching exercise training session, verbal instructions to perform aerobics three times weekly, and the same written instructions for continued stretching exercises. After 1 year, neck range of motion and muscle strength had improved in all groups, with better improvements in the training groups and the best improvement with strengthening training. Improvements in pain and disability were similar for both training groups and significantly better than the control group (P<0.001). (Based on Ylinen J, *et al.*, 2003[54].)

2.29 Benefits of work hardening. Outcome measures were reviewed in 196 adults (40% female, mean age 43 years) participating in a work rehabilitation programme designed to increase work readiness through physical and occupational therapy. The most common pretreatment chronic pain locations were the back (53%), lower extremity (31%), and upper extremity (18%). Percentage improvements in several pain-related measures are shown. Changes for each measure were significant (P<0.001). (Based on Baker P, *et al.*, 2005[55].)



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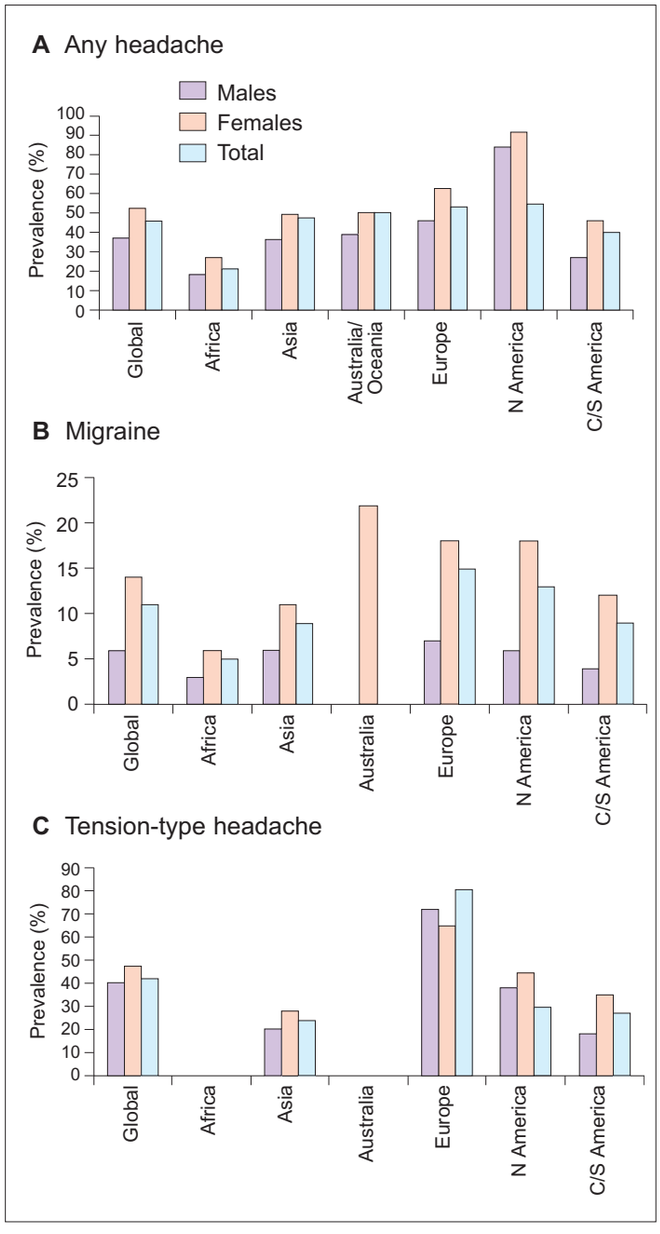
Chapter 3

Headache

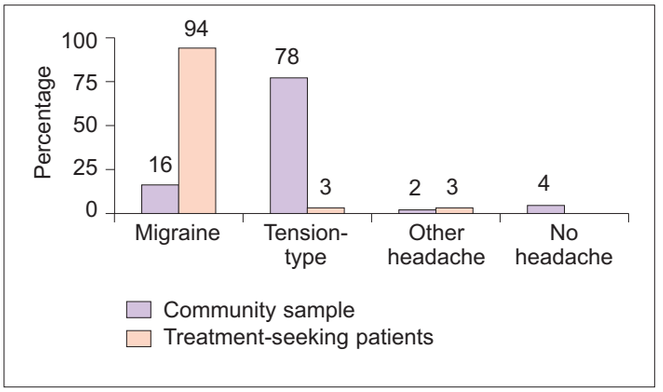
Introduction

Headache is a common complaint worldwide, affecting about half of adults in most continents (**3.1**)[1]. Regional differences occur, with both migraine and tension-type headache most prevalent in Europe. A survey of medical records from 289 primary care patients in the United States identified headache as the fourth most common somatic complaint after pain in the back, lower extremity, and upper extremity[2]. In addition, headache tended to persist.

Even though tension-type headache is the most common chronic headache identified in community surveys[3], migraine is most commonly reported among patients seeking headache treatment (**3.2**)[4]. Migraine may be over-represented in primary care practices due to the significant



3.1 Prevalence of current headache in adults. Worldwide headache prevalence was estimated using a literature review of population-based headache studies. Since some studies provided data on male and female genders, while others reported for males and females combined, headache prevalence for all patients in some cases is reported to be less than for either males and females, e.g. total headache in North America (**A**). In other cases, prevalence for the total population is nearly the same as for females alone, e.g. total headache in Australia/Oceania (**A**). Despite these flaws, general regional headache trends are provided with these data. Current headache affects about half of the population in Asia, Australia, Europe, and North America, with only about 20% affected in Africa. Migraine in the total population is most prevalent in Europe (15%) and least prevalent in Africa (5%) (**B**). Among regions reporting tension-type headache, tension-type headache is similarly most common in Europe (80%) and least common in Asia and the Americas (20–30%) (**C**). (Based on Stovner LJ, *et al*., 2007[1].)

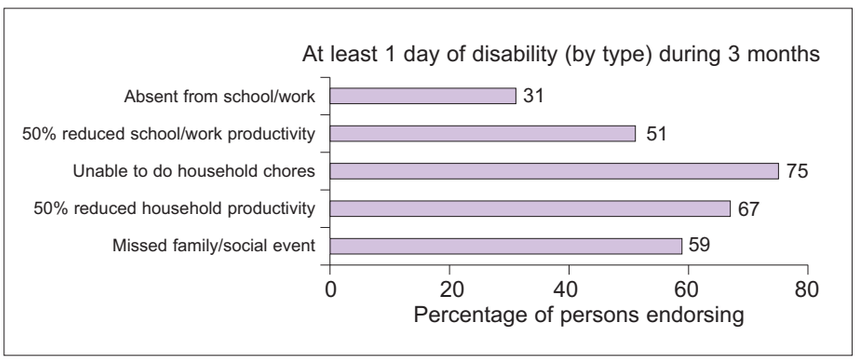


3.2 Comparison between prevalence of migraine and tension-type headache in the general population and in patients seeking treatment for headache. Community figures represent lifetime prevalence of headache. Treatment-seekers were 1,203 patients seeking care for headache as a primary or secondary complaint in 15 countries. A total of 128 clinical practices were utilized, 93% of which were primary care facilities. An international headache expert panel reviewed diagnoses using diary assessment and determined that the vast majority of patients had migraine. Although migraine occurs in only 16% of the general population, 94% of treatment-seeking patients have migraine. (Based on Rasmussen BK, *et al*., 1991[3]; Tepper SJ, *et al*., 2004[4].)

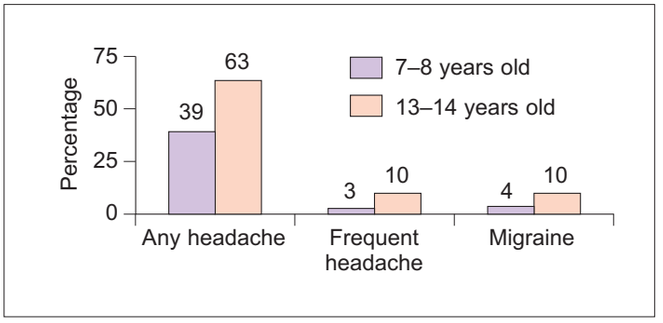
disability for work, household chores, and social activities reported by most migraineurs (**3.3**)[5]. According to the World Health Organization, migraine ranks among the top 20 causes of disability, ranking 12th for women and 19th for both genders combined[6].

Headache is also common in children and adolescents. A community survey reported headache in the preceding 6 months in over half of children surveyed (**3.4**)[7]. The mean age at headache onset was 7.5 years, with 5% of children reporting headache onset at age 3 or younger. Headache onset was earlier in boys than girls (7.3 *vs*. 7.8 years, $P<0.001$). Headache duration was shorter in children than adults, with headache episodes lasting ≤2 hours for 59% of children.

Headache may be caused by primary headache disorders (e.g. migraine, tension-type, and cluster headache) or as a secondary symptom of other medical and neurological conditions (*Table 3.1*). Primary headaches, especially migraine and tension-type headache, are thought to occur due to neurochemical imbalances with serotonin, norepinephrine, and dopamine (**3.5**, **3.6**). Iron homeostatis in the periaqueductal gray matter is affected by migraine, with increased iron deposition noted in migraineurs and level of iron deposition correlating with migraine duration (**3.7**)[8]. The pathophysiology of cluster headache is less well understood and may be influenced by changes in histamine activity.



3.3 Migraine-related disability during the preceding 3 months was evaluated in a community survey of 29,727 migraineurs ≥12 years old in the American Migraine II study. Nearly one in four households surveyed had at least one member with migraine. Ninety-one percent of migraineurs reported functional impairment with their headaches. Severe headache caused substantial impairment in activities or bed rest in 53%. Most patients had experienced impairments in work, household, and social activities due to migraine in the previous 3 months. (Based on Lipton RB, *et al*., 2001[5].)



3.4 Pediatric headache. A survey of 5,586 households in Germany produced important data about pediatric headache occurring in the preceding 6 months. A total of 53% of children (55% of girls and 52% of boys) reported any headache in the previous 6 months, with headaches more common in adolescents than younger children ($P<0.001$). Frequent recurring headache (≥1 episode/week) and migraine were also more common in adolescents ($P<0.001$). (Based on Kröner-Herwig B, *et al*., 2007[7].)

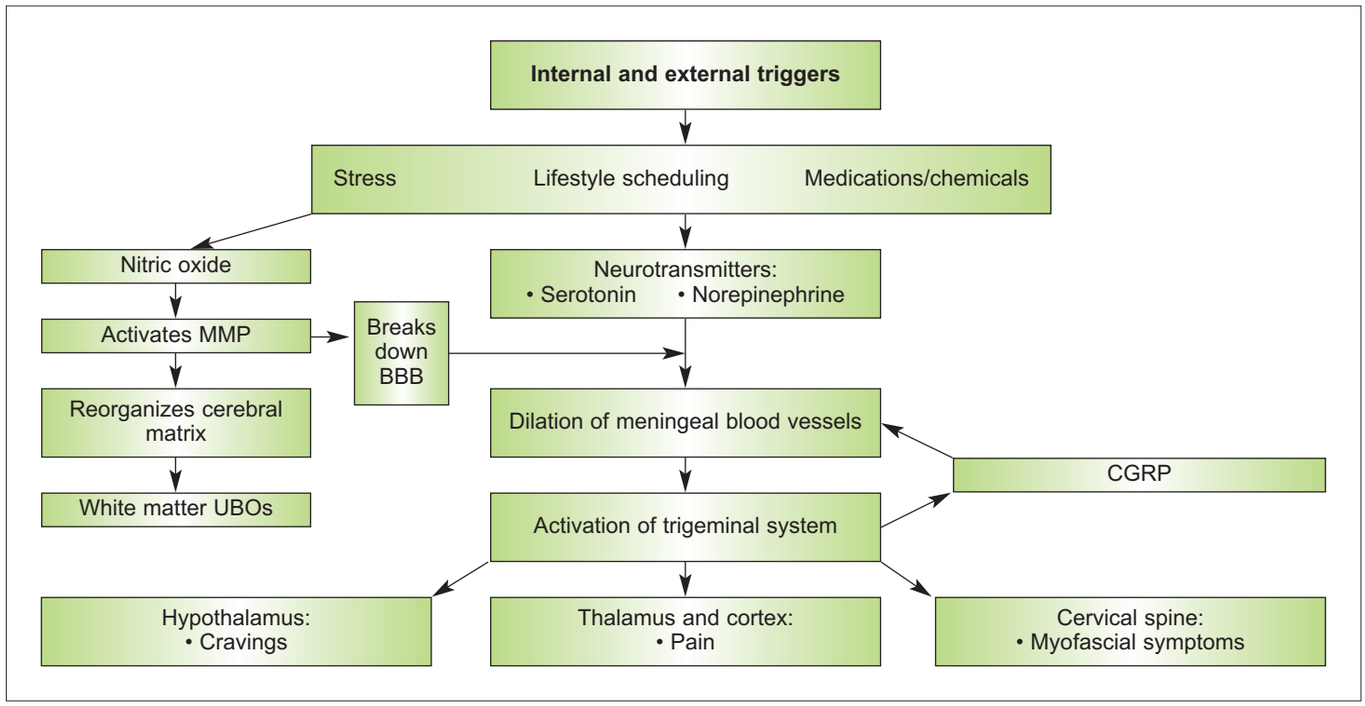


Table 3.1 Common causes of head pain

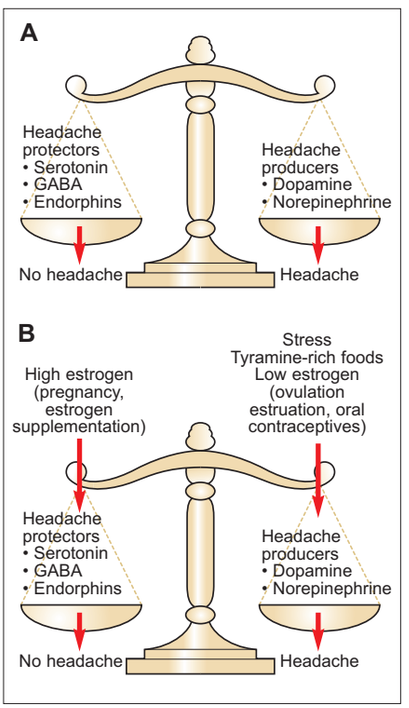
Disease category	***Specific diseases***
Primary headaches	Migraine Tension-type headache Cluster headache
Secondary headaches	
Musculoskeletal	Temporomandibular dysfunction Cervical myofascial or joint dysfunction
Inflammatory/autoimmune	Acute infection (e.g. upper respiratory infection, meningitis) Temporal/giant cell arteritis Systemic lupus erythematosus
Systemic illness	Anemia Thyroid disease
Intracranial pathology	Tumor Vascular malformation or aneurysm Subdural hematoma Cerebrovascular disease
Cranial neuralgias	Trigeminal neuralgia Postherpetic neuralgia
Medication/medication withdrawal	Analgesic overuse headache Alcohol-induced Withdrawal from caffeine, opioids, estrogen

3.5 Neurovascular model of migraine. Michael Moskowitz developed the neurovascular model of migraine to explain important relationships between vascular and neural structures in the pathogenesis of migraine. Although specific mechanisms have not been uncovered, exposure to internal and external triggers (including stress, changes in sleep and eating habits, and hormonal cycling) results in alterations in signalling from a variety of important neurotransmitters (including nitric oxide, serotonin, and norepinephrine). All of these compounds activate vascular dilation. Dilated intracranial, extracerebral blood vessels result in a perceived throbbing sensation and increased blood flow. More importantly, neurons surrounding these blood vessels become stretched, resulting in activation of neural pathways and triggering of the trigeminal system. Once the trigeminal system is activated, signals travel in several directions. Antidromic signals travel back to the meningeal vessels causing a positive feedback loop to perpetuate vascular dilation and trigeminal activation; this is mediated by calcitonin gene-related peptide (CGRP), a target of new migraine medications. The trigeminal system also activates the hypothalamus, possibly resulting in migraine-related cravings. Activation of cervical trigeminal structures may facilitate transmission to somatic neurons, resulting in muscle contraction. Signals also travel to the thalamus and cortex to relay pain messages.

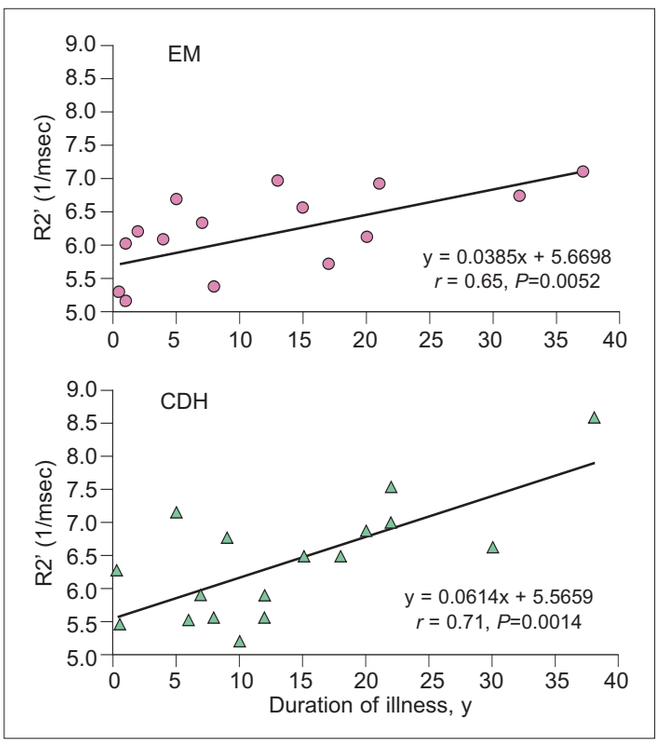
(*Continued overleaf*)

3.5 (*Continued*) Nitric oxide also activates matrix metalloproteases (MMPs), important compounds for brain development and plasticity. MMP-9 is linked to opening of the blood–brain barrier (BBB) and has an important role in the pathogenesis of brain ischemia and possibly migraine. Cortical spreading depression at the onset of migraine results in upregulation of MMP-9. This effect occurs early (within 15–30 minutes) and is prolonged (>48 hours)[9], causing breakdown of the BBB, edema, and vascular extravasation. These changes in brain fluid status may explain the occurrence of nonspecific, unidentified bright objects (UBOs) in the white matter on magnetic resonance imaging studies in about 30% of migraineurs. These effects may also help explain how medications and neurotransmitters outside the BBB can gain access to the brain during a migraine.

Headache occurs more commonly in women than men (**3.8**), with predictable changes in headache occurring in women in relation to changing patterns of estrogen (Case presentation and **3.9**)[10]. Estrogen acts as an important pain modulator, with pain effects particularly strong for patients with chronic headache. Cycling estrogen in women increases the risk for developing a chronic headache condition and affects headache patterns in women.



3.6. Neurochemical balance in chronic headache. Susceptibility to a headache episode depends on a balance between headache-protecting neurotransmitters (serotonin, GABA, and endorphins) and headache-provoking neurochemicals (dopamine and norepinephrine). When concentration and activity of headache protectors outweigh headache producers, the patient is less susceptible to headache episodes (**A**). Exposure to common headache triggers results in changes in levels and activity of a variety of neurotransmitters (**B**). Stress, the most common trigger, increases headache producers. Elevated estrogen increases headache protectors, reducing headache risk, while decreases in estrogen levels increase dopamine and norepinephrine, increasing headache susceptibility. In some patients, their scale is usually balanced toward increased headache susceptibility, so few additional triggers will activate a headache episode. Preventive therapies may help achieve and maintain a more favourable neurotransmitter balance.

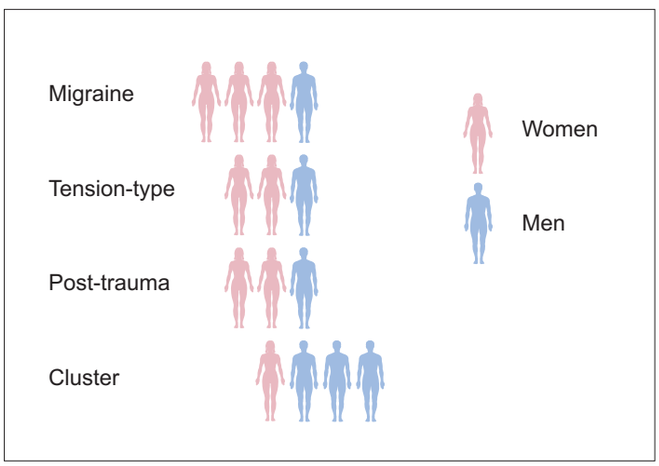


3.7 Iron deposition in migraine. Periaqueductal gray iron homeostatis was evaluated in patients with episodic migraine (EM, N=17), migraine transformed into chronic daily headache (CDH, N=17), and no headaches (N=17). Magnetic resonance imaging transverse relaxation values showed increased R2' values in migraineurs, denoting increased iron deposition (EM=6.11, CDH=6.36, controls=4.33). There were no differences between migraine with and without aura. As seen in the graphs, migraine duration correlated with iron deposition for both EM and CDH. (Based on Welch KM, *et al.*, 2001[8].)

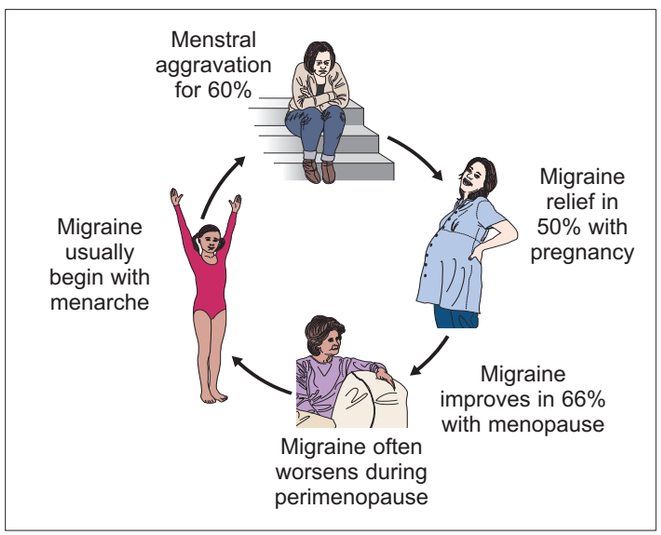
Case presentation

A 57-year-old woman presents with a complaint of headache aggravation. "I thought I'd be done with these awful migraines at this age. My headaches started 2 months after my menstrual periods began when I was 13 years old. Every month I suffered from terrible migraines that affected my vision, made me vomit, and put me in bed for half a day. My pediatrician told me they'd go away when I got pregnant and my first pregnancy was such a blessing – it was the first time in over 10 years that I didn't get a sick headache every month. When the migraines came back after the baby was born, the doctor told me they'd go away when I went through menopause. My periods have been irregular for several months now and I'm getting hot flashes, so I'm sure menopause is starting. I can't believe that these migraines are now worse than they were before. When will they ever go away?"

This patient has experienced very typical lifetime migraine changes, with headache patterns changing in relationship to changes in estrogen status. Migraines usually worsen when estrogen cycles between high and low levels, such as with monthly menses, and improve when estrogen levels become elevated, such as with pregnancy, or cycling abates, as with menopause. The perimenopausal period, however, is often a time of migraine aggravation.



3.8 Gender distribution of chronic headaches. When tested with experimental pain, women have a lower pain threshold and pain tolerance than men, resulting in increased sensitivity to painful stimuli. Women tend to perceive painful signals earlier and more acutely than their male counterparts. This increased sensitivity to pain may explain the increased prevalence of many painful conditions, including headache, in women. Most common recurring headaches occur more frequently in women. Although men are more likely to experience head injury, post-traumatic headaches occur more often in women. Historically, cluster headache has been considered a 'man's headache', with medical books often noting a 6:1 male predominance. While cluster headache is still more common in men, estimates over the last few decades show that the male predominance of cluster headache has decreased to 2–3:1. Researchers speculate that lifestyle changes, such as increased use of nicotine and alcohol, may have contributed to this increasing prevalence of cluster headache in women.

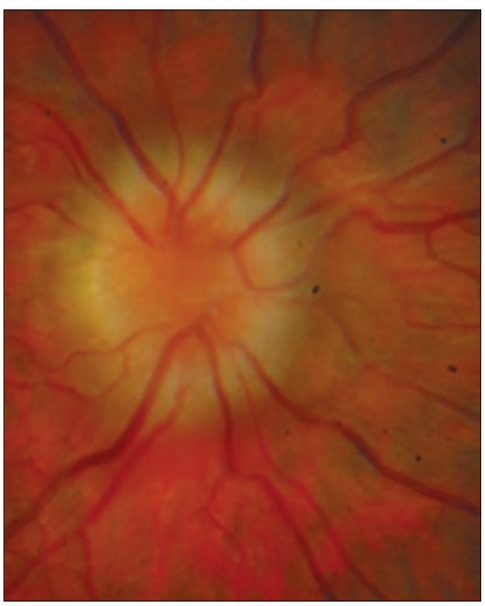


3.9 Lifetime patterns of migraine in women. In general, cycling estrogen acts as an important activating trigger to initiate migraine in women, with headaches aggravated whenever estrogen levels drop from a high to a low level, such as with menstruation or after delivery. Persistently elevated estrogen (such as with pregnancy) or lack of cycling (after menopause) tends to reduce migraine susceptibility. Women often notice an unexpected worsening of migraine in the perimenopausal period when they are also experiencing other somatic symptoms, like hot flashes. Migraine also tends to worsen after surgical menopause with hysterectomy/oophorectomy, while improving with spontaneous menopause, suggesting a possible role of ageing in migraine improvement.

Assessment strategies

Primary vs. secondary headaches

Headache may be caused by a variety of medical conditions treated by primary care. Acute headache most commonly occurs with infection and trauma. Headache is also a frequent symptom of many medical illnesses. Chronic headaches may occur as a primary condition (such as migraine, tension-type, and cluster headaches) or as a secondary headache, occurring as a reaction to, or symptom of, another condition. Patients presenting with a complaint of headache need an initial assessment to distinguish primary from secondary headaches, including a headache and medical history and detailed physical and neurological examinations (**3.10**).



3.10 A simple bedside fundoscopic examination with a hand-held ophthalmoscope is an essential part of the headache evaluation. This test can be performed within seconds and provides a window to the brain and blood vessels. Blurring of the vessels, as seen in this image, typically indicates increased intracranial pressure. Although MRI and CT scans identify many serious causes of headache, they do not identify all causes of increased intracranial pressure. For example, patients with increased intracranial pressure due to benign intracranial hypertension (pseudotumor cerebri) often have a normal imaging study even though their pressure is dangerously high. Failure to identify these patients can result in significant visual loss. (Photo courtesy of Rock Heyman, MD.)

Primary headaches are distinguished by characteristic pain patterns, nonprogressive character, and absence of additional signs and symptoms (*Table 3.2*, **3.11**)[11]. Patients with features suggesting possible secondary headaches may need additional laboratory testing (*Table 3.3*). Laboratory

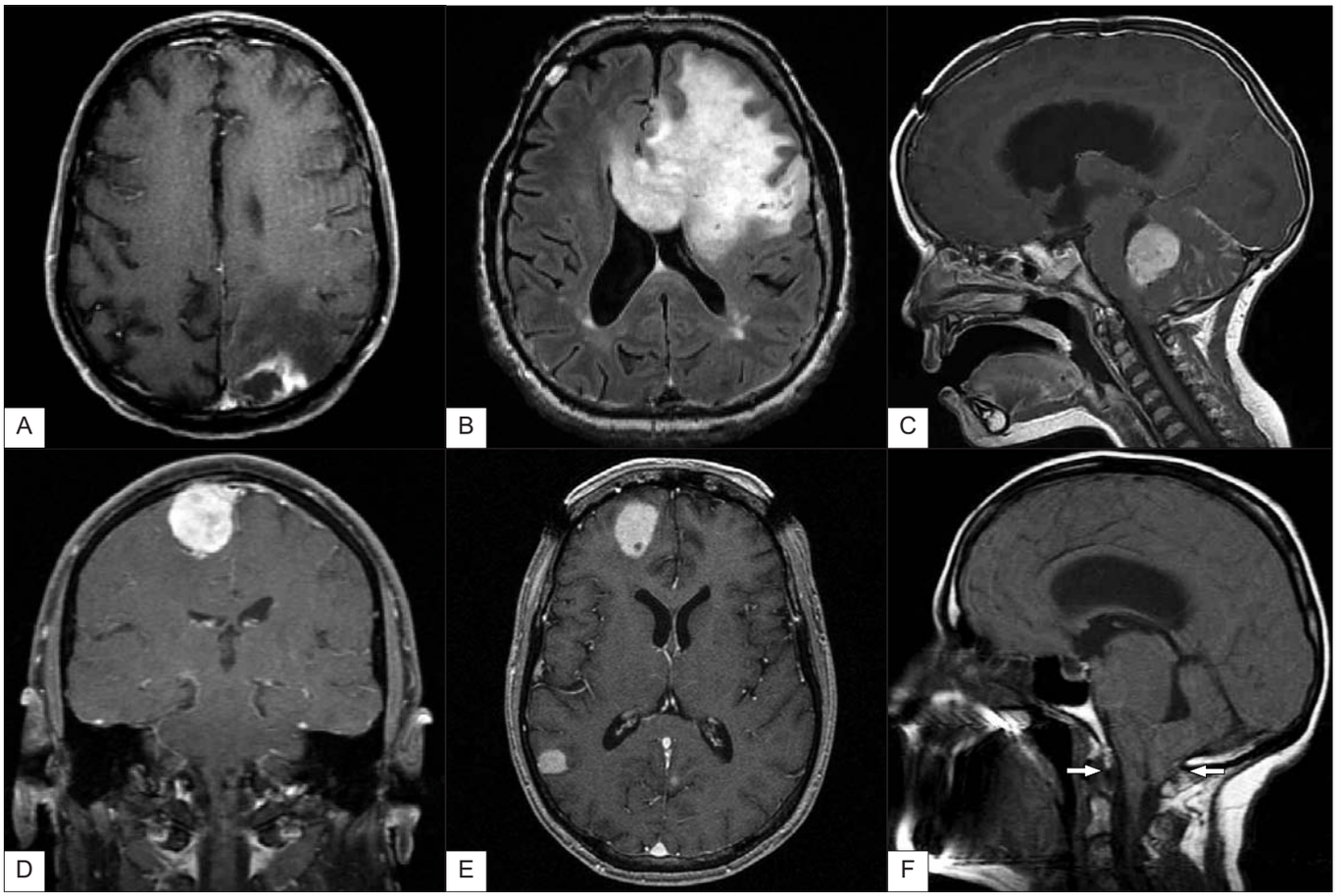
Table 3.2 Features suggesting secondary headache

- Patient ≥50 years old
- Significant change in headache quality or pattern for <2 years
- Pain in the posterior head or neck
- Additional medical symptoms
- Additional neurological symptoms
- Abnormal physical or neurological findings

Table 3.3 Laboratory testing for chronic headache

- Blood tests for medical conditions, as indicated
  - – Autoimmune tests
  - – Hematology
    - Inflammatory markers and temporal artery biopsy for new headache in patients >50 years old without obvious diagnosis
  - – Chemistries
  - – Thyroid functions
  - – Infection markers (e.g. syphilis, HIV)
- Radiographic testing
  - – X-ray of the cervical spine for mechanical signs
  - – CT or MRI brain for new onset worrisome headache or patient with neurological deficits
- Lumbar puncture if suspicious of bleed or infection

CT: computed tomography; HIV: human immunodeficiency virus; MRI: magnetic resonance imaging

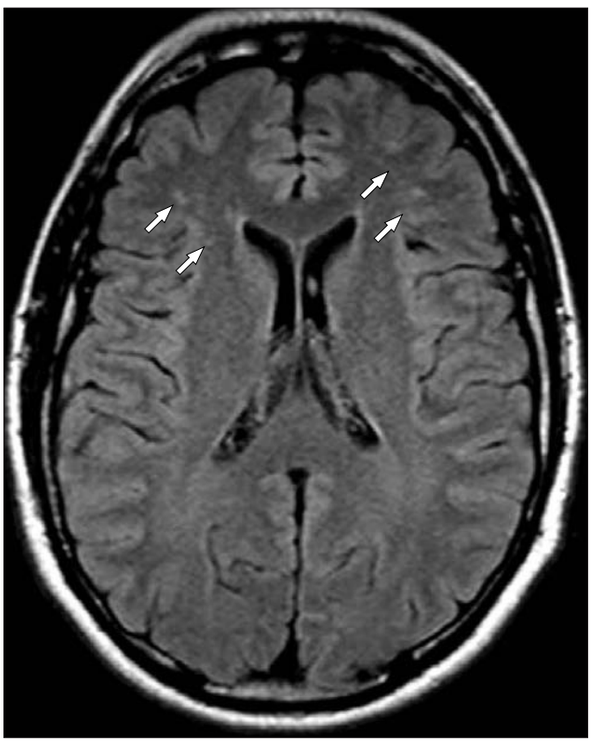


3.11 MRI scans of patients wiht secondary headache. While patients are often concerned that head pain signifies serious intracranial structural pathology, headache is typically a secondary complaint among patients with structural lesions. **A**: Occipital lobe abscess. Brain abscess may occur after infections of cranial structures (e.g. otitis media, mastoiditis, or sinus or dental infection), trauma, or via blood transfer from systemic infection. Risk increases in patients with right-to-left heart shunts or compromised immune systems. Patients typically present with headache, changes in mental status, seizure, and focal neurological symptoms or signs, such as visual deficits in this patient. **B**: Glioblastoma multiforme is the most common and aggressive primary brain tumor. Initial symptoms often involve memory, personality, and cognition, as well as headache, seizure, and focal deficits. **C**: Medulloblastoma is a glioma originating in the cerebellum or posterior fossa, most commonly affecting young children. Males are affected about twice as often as females. Symptoms include listlessness, headache, vomiting, gait imbalance, dizziness, and double vision. **D**: Meningioma is the most common benign tumor in adults, affecting women twice as often as men. Meningiomas arise from arachnoidal cells, forming an extra-axial brain mass, with the base attached to the dura. Symptoms include seizures and focal neurological deficits, in addition to headache. **E**: Cerebral metastases are the most common brain tumors, most commonly from primary sites in the lung, breast, and colon. Metastases are typically located at the gray-white matter junction. The most common symptoms are headache, focal weakness, and mental status changes. Seizures and other focal neurological deficits may also occur. The apparent symmetrical frontal skull defects are artifacts from a cranial frame used for a stereotactic procedure. **F**: Arnold–Chiari malformation is a downward displacement of the cerebellar tonsils and medulla through the foramen magnum. The arrows demonstrate the opening for the foramen magnum. Symptoms typically occur when the cerebellar tonsils are displaced at least 3 mm below the foramen magnum. Symptoms may include headache, neck pain, dizziness/vertigo, difficulty swallowing, and motor weakness. (**A–E** courtesy of Clayton A. Wiley, MD, PhD; **F** courtesy of Rock Heyman, MD.)

and radiographic studies in chronic headache patients should be targeted to specific disease states. MRI reveals nonspecific white matter abnormalities in about one in three migraineurs, with prevalence slightly higher in patients with migraine with aura (**3.12**)[12].

Differentiating common primary headaches

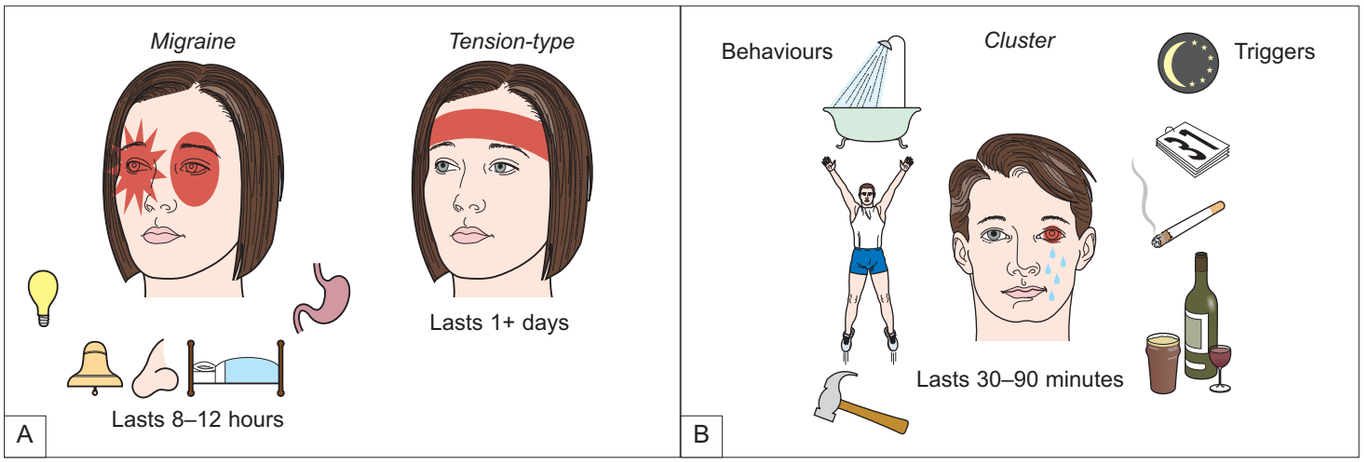
Primary headaches are distinguished by patterns of symptoms, including pain location, pain duration, and behavioural response to headache (**3.13**, *Table 3.4*). Both migraine and tension-type headache occur commonly in



3.12 Nonspecific, small white matter changes on MRI. These abnormalities will be noted in about 30% of migraine patients (arrows) and may be confused with white matter changes due to stroke, multiple sclerosis, or malignant disease[13]. In one controlled study, MRI scans were compared for 63 patients with primary headache (28 migraine; 35 tension-type; mean age 42.2 years) and 54 age-matched controls[13]. All were free of risk factors for demyelinating or cerebrovascular disease. Abnormal MRIs were noted in 43% of patients with headache and 22% of controls, with white matter abnormalities in 33.3% of headache patients and 7.4% of controls (*P*=0.001). Headache history, headache severity, and pain scores did not correlate with prevalence of white matter abnormalities in the headache patients. Interestingly, white matter abnormalities were similarly identified in 32.1% with migraine and 34.3% with tension-type headache. Lesions were predominantly frontal (85.7%), parietal (38.1%), temporal (23.8%), and occipital (14.3%). Abnormalities were bilateral in 66.7%. These data were confirmed in a meta-analysis of 7 retrospective case-controlled studies, which reported an odds ratio of 3.9 for the occurrence of white matter abnormalities in migraineurs compared with controls[14]. This increased odds ratio persisted even when patients with cardiovascular risk factors were excluded from evaluation. The significance of these changes is unclear. (Photo courtesy of Rock Heyman, MD.)

Table 3.4 Distinguishing characteristics of common recurring headaches

	Location	*Duration (hours)*	*Activity during headache*
Migraine (adults)	Unilateral (affected side should vary at least occasionally)	8–24	Reduced productivity, lays down, seeks dark and quiet retreat
Migraine (children)	Bilateral forehead	1–4	Brief curtailment of activity
Tension-type	Bilateral	8–24 or constant	No interference
Medication overuse	Bilateral	Constant with fluctuating severity	No interference
Cluster	Unilateral eye (affected side will never vary)	0.5–1.5	Avoids laying down, paces, smokes, showers, hits head

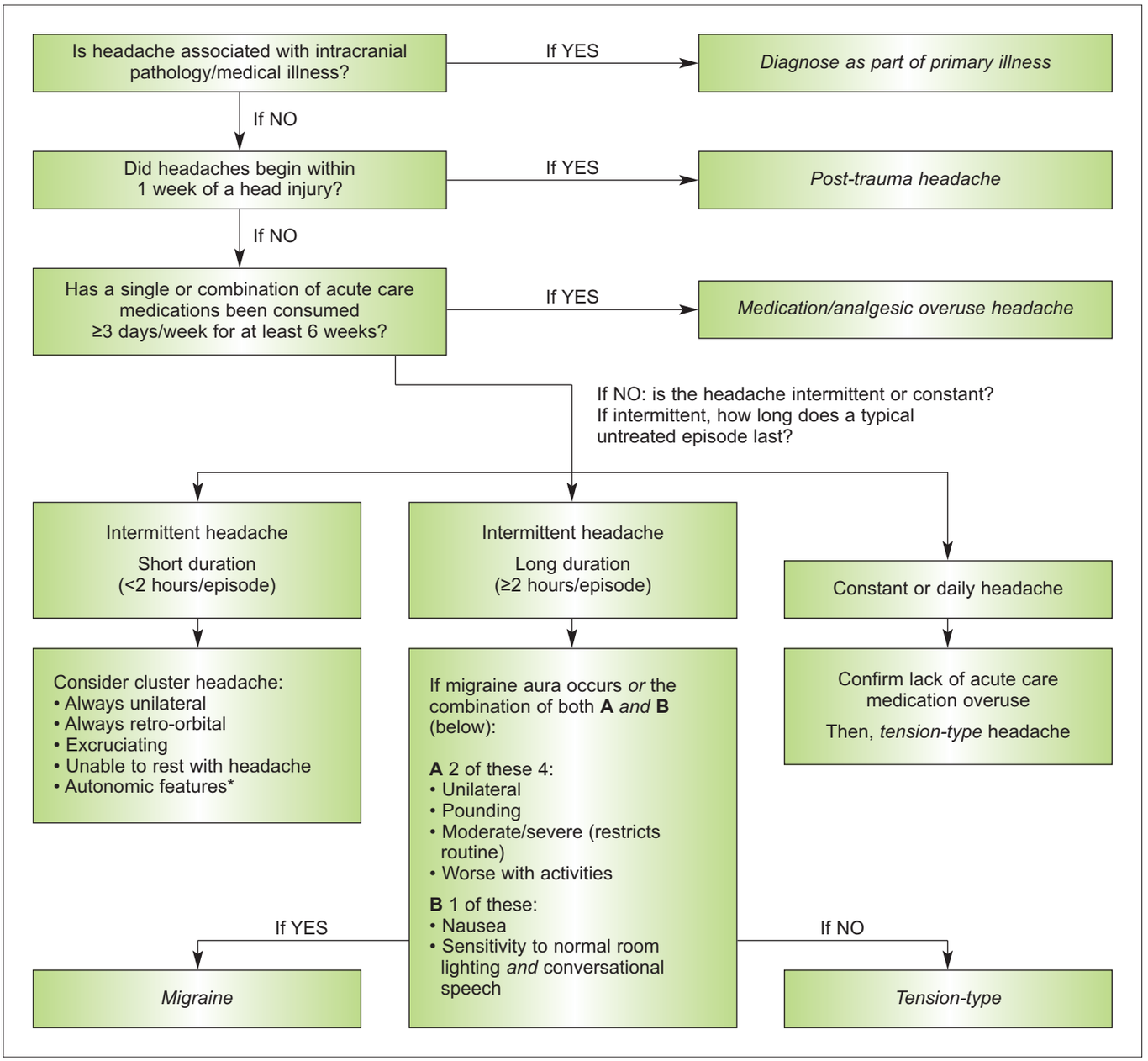


3.13 Differentiating chronic headaches. **A**: Migraine headache is typically experienced as a disabling, intermittent headache lasting about 8–12 hours. About 15–20% of migraineurs experience a migraine warning about 30–60 minutes before the painful part of the attack, called an aura. Auras are characteristically visual changes, like seeing coloured balls, zigzag lines, or blind spots (like the star burst shown in the figure), although other neurological deficits may also occur with auras. Migraine is often unilateral (often located around the forehead, eye, and cheek as shown by the red circle), although bilateral or holocranial pain is not uncommon. Migraine sufferers typically modify their activities to accommodate their migraine attacks, often finding comfort in reducing activity level and exposure to stimuli (such as lights, sounds, smells, and food). Nausea and vomiting may accompany migraine, but most attacks will occur with only mild nausea or food aversion. With severe attacks, the migraineur characteristically retreats to a dark, quiet room and puts a washcloth over the eyes and forehead. Tension-type headache is a milder, usually bilateral headache (often a band of pain across the forehead as shown here in red) that does not interfere with activities. Tension-type headaches, however, often last one or several days, with some patients reporting daily or nearly daily headache. Sensitivity to stimuli is also not characteristic of tension-type headache. **B**: Cluster headaches often occur in groups or clusters, with the patient usually headache-free except for 1–2 annual clusters of attacks each lasting about 6 weeks, typically occurring in the spring and autumn. During a cluster period, episodes tend to occur about 90 minutes after falling asleep, when entering dream sleep. Patients wake with a severe orbital pain that drives them out of bed. Autonomic features, like eye tearing, are common. During the episode, the cluster patient often paces, showers, and smokes. Many patients severely press their eye or hit their head against the wall or books. Fortunately, each episode is relatively brief, resolving after about 30–90 minutes. During a cluster period, daytime attacks may be precipitated by using nicotine or alcohol. Generally, patients experience about 1–3 severe pain episodes nightly during a cluster period, with frequency least during the beginning and end of the cluster.

Case presentation

A 48-year-old well-dressed businessman in no acute distress presents with a complaint of severe headache episodes lasting 20–30 minutes, and then resolving spontaneously. "I saw a doctor for these a few years ago, and he said not to worry about them if they went away in less than an hour. My wife thinks I'm going crazy and she insisted I see a doctor again." His wife gets migraines and always goes to bed with her headaches. She can't understand why he paces around the room yelling or goes into the shower when he gets a headache. Recently, the pain has been so unbearable, he has started banging his head against the floor when the headache starts.

Cluster headache patients and their families are often fearful of describing the characteristic bizarre behaviours seen in many cluster headache patients. Cluster headache behaviour contrasts sharply with the quiet solitude sought by migraineurs. The brief nature of each individual attack often leads to treatment dismissal, as occurred in this patient. Although each individual attack is relatively short-lived, the severity and predictable recurrence of attacks warrant aggressive preventive therapy.



3.14 Diagnostic algorithm for chronic headaches. *Autonomic symptoms include conjunctival injection, lacrimation, rhinorrhea, ptosis, and miosis. Patients with cluster headache tend to under-estimate the severity of their autonomic features, while those with migraine tend to exaggerate them. Possibly the extreme pain severity during a cluster attack distracts patients from awareness of autonomic changes.

children and adolescents, although characteristic features of adult migraine, such as unilateral pain, long duration of headache episode, sensitivity to noises and sounds, and nausea, are often lacking in pediatric migraine. Patients with chronic headache who regularly use prescription or over-the-counter pain medication ≥3 days per week typically develop medication overuse headache. A diagnostic algorithm can be used to help distinguish common chronic secondary and primary headaches typically seen in primary care (**3.14**).

Migraine mimics

Migraineurs often attribute their headaches to sinus disease, due to the presence of pain over the sinuses, autonomic symptoms, and occurrence with changes in the weather, seasons, or allergen exposure (*Table 3.5*)[15]. In addition, migraineurs frequently over-emphasize the occurrence and severity of autonomic symptoms with their headaches, sometimes leading to a false diagnosis of cluster headache (*Table 3.5*)[16].

Migraine is frequently confused with 'sinus' headache, due to pain over the sinus area and symptoms of suggesting sinus congestion or involvement. Evaluation of 100 consecutive patients with self-diagnosed 'sinus' headache determined that 85% had migraine, while only 3% had headache associated with rhinosinusitis. Among patients with definite migraine (*Table 3.5*), several headache features were reported that resulted in the false attribution of

Table 3.5 Migraine mimics: symptoms suggesting sinus or cluster headache in patients diagnosed with migraine

'Sinus' symptoms (%)	*Unilateral autonomic 'cluster' symptoms (%)*
Pain over sinus(es) 97	Any unilateral symptom 26.9
Nasal congestion 56	Nasal congestion/rhinorrhea 4.9
Eyelid edema 37	Eyelid edema 4.3
Rhinorrhea 25	Conjunctival injection 6.8
Conjunctival injection 22	Lacrimation 10.8
Lacrimation 19	Ptosis/miosis 5.2
Ptosis 3	
'Sinus' triggers:	
Weather changes 83	
Seasonal variation 73	
Exposure to allergens 62	
Change in altitude 38	

(Based on Eross E, *et al*., 2007[16]; Obermann M, *et al*., 2007[17])

Case presentation

A 49-year-old woman presents with a complaint of sinus headache, requesting an antibiotic and antihistamine. "My headaches are always over the sinuses in my forehead and cheek on one side of my face. Whenever changing weather patterns are predicted, I know I'm in for one of my sinus headaches. The pain just throbs and I feel a terrible sinus pressure. Sometimes my nose also gets congested. The only thing I can do is go to bed and make the room dark and quiet. If I take an over-the-counter sinus remedy, I feel better after a day and can get out of bed."

Migraines are often confused with sinus headaches. Although this patient describes characteristic migraine features of an incapacitating headache, unilateral location, throbbing pain, and sensitivity to noises and lights, she tends to focus on those features that incorrectly suggest a diagnosis of sinus headache: relationship to weather, location over sinuses, mild nasal congestion, and relief with antihistamines.

headache to the sinuses. Allergens included grass, trees, dust, foods, animal dander, and mould.

Migraine may also be confused for cluster headache. While cluster headache patients tend to under-report the occurrence of autonomic symptoms, migraine patients often do endorse cluster-type symptoms. A community survey of 841 migraineurs revealed one or more unilateral autonomic symptoms regularly occurring with migraine attacks in one in four migraineurs.

Autonomic symptoms were reported more frequently in the 'sinus' study compared with the 'cluster' study. In the 'sinus' study, only 57% of migraineurs endorsing autonomic symptoms reported that those symptoms occurred in temporal relationship to their migraine. One-third of these patients reported chronic and persistent autonomic symptoms. Positive reports in the cluster study required a regular occurrence of autonomic symptoms with headache attacks.

Secondary headaches

Medication overuse headache

Medication overuse headaches occur as a reaction to excessive analgesic or headache medication use and affect 0.5–1% of adults worldwide[1]. Regular daily, or near daily, use of medications designed to treat individual headache episodes can result in a change and worsening of underlying headache. Generally, medication overuse needs to occur for at least 6 weeks before headache aggravation begins. The overuse of headache medications causes down-regulation of serotonin, with resultant increase in headache severity and decreased responsiveness to headache remedies. Medication overuse headache does not occur in nonheadache patients using analgesics for other pain complaints, like chronic arthritis or back pain, or in patients using low-dose, cardioprotective dosing of aspirin.

Medication overuse headache typically occurs in patients with a primary complaint of frequent migraine, tension-type, or post-trauma headache, who begin overusing headache remedies to treat frequent headache episodes or act as a preventive therapy. All acute care medications (triptans, ergotamine, analgesic or analgesic combinations, opioids, and butalbital combinations) may contribute to medication overuse headache. Medication overuse headache is typically a mild, bilateral, pressure headache with fluctuating severity. Patients with medication overuse headache often experience daily mild, bilateral headaches plus intermittent, severe migraines. Probable medication overuse headache should be considered in patients with benign headache taking any acute care medication or combination of acute care medications on a regular basis 3 or more days per week. Switching among different acute care agents on different days does not minimize the risk of medication overuse headache.

Post-trauma headache

Mild head injury with concussion produces alterations in serotonin and other brain chemicals, similar to changes seen in spontaneously-occurring migraine[17]. Post-trauma headaches occur within 7 days of a head injury with concussion. A concussion should be diagnosed when patients have any of the following symptoms following head trauma: 'feel dazed', 'see stars', have amnesia for events before or after the accident, or experience a brief loss of consciousness. Postconcussive syndrome features often accompany post-traumatic headaches and may include: depressed or irritable mood, memory loss, dizziness or vertigo, and tinnitus. Post-traumatic headache should improve from constant and severe to milder and less frequent over the first 2 weeks. Headaches failing to improve, worsening, or associated with progressive postconcussive symptoms should be re-evaluated with imaging studies to rule out subacute pathology, such as subdural hematoma or undiagnosed fracture. Headache features are often consistent with migraine in the early phases of post-trauma headache, and become milder like tension-type headache when post-trauma headache persists.

Trigeminal neuralgia

Trigeminal neuralgia is experienced as a unilateral, intermittent, electric-like jolt of pain into one or more divisions of the trigeminal nerve, usually over the cheek or jaw. Interestingly, pain most commonly affects the right side of the face[18, 19]. Pain is typically triggered by activating a discrete facial trigger point, such as with touching, shaving, talking, or chewing. Curiously, patients with trigeminal neuralgia will often sit holding the painful side of the face, possibly to prevent stimuli from activating their trigger point. Between painful spasms, mild residual pain may persist over the face or jaw. Idiopathic trigeminal neuralgia generally affects adults >40 years old as a unilateral pain. Younger patients and patients with bilateral symptoms should be evaluated for multiple sclerosis. Although sensory loss occurs in a minority of patients with idiopathic trigeminal neuralgia, all patients with sensory loss require neuroimaging. (This condition is also described in Chapter 6, Neuropathic Pain.)

Case presentation

A 67-year-old woman is brought to the clinic by her son. She looks miserable, holds her face, and occasionally winces and cries out with pain. Her history is provided by her son, who says talking causes his mother to have severe jolts of facial pain. The pain is also brought on by touching of brushing her lower molars and jaw and she initially was evaluated by her dentist. After repairing two small dental caries, her pain was not improved.

Trigeminal neuralgia pain is very characteristic and severe. Patients often mistake neuralgia pain for dental disease, initially seeking treatment from a dentist. While pain is characteristically provoked by touching discrete trigger areas on the face or inside the mouth, patients often limit the physical examination due to severe pain caused by facial movement or touching. Diagnosis, therefore, is generally based primarily on historical pain descriptions often provided, as in this case, by family members.

Temporal or giant cell arteritis

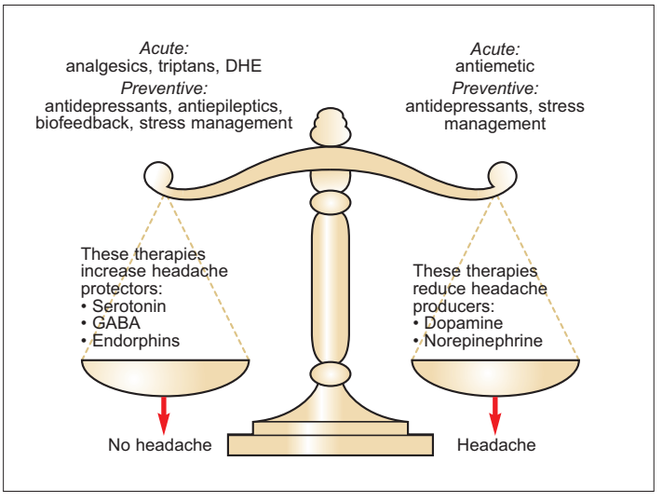
Temporal arteritis or giant cell arteritis is experienced as head pain or scalp tenderness, often associated with fatigue with chewing, visual disturbance, and low-grade fever. Temporal arteritis may also occur in patients with polymyalgia rheumatica, with head pain associated with proximal limb stiffness and weakness, fatigue, and weight loss. Temporal arteritis is a medical emergency that should be considered in the differential diagnosis of new headache in elderly patients because of the significant risk for vision loss and stroke. Visual ischemic complications occur in 26% and irreversible blindness in 15% of patients with biopsy-proven temporal arteritis[20]. Stroke, usually in the vertebrobasilar distribution, occurs in about 3% of temporal arteritis patients[21].

Evaluation begins with measuring serum inflammatory markers, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) with hematocrit. CRP is a more sensitive marker for diagnosing temporal arteritis than ESR[22]. Patients with a strong clinical diagnosis of temporal arteritis or anterior ischemic neuropathy should be treated with steroids presumptively before laboratory confirmation, immediately after blood work is obtained. A temporal artery biopsy should be performed within 2–3 days of initiating steroid therapy. Inflammatory changes in temporal arteritis often skip areas of the blood vessels, so a minimum of 1 cm of artery should be removed to improve diagnostic yield[23].

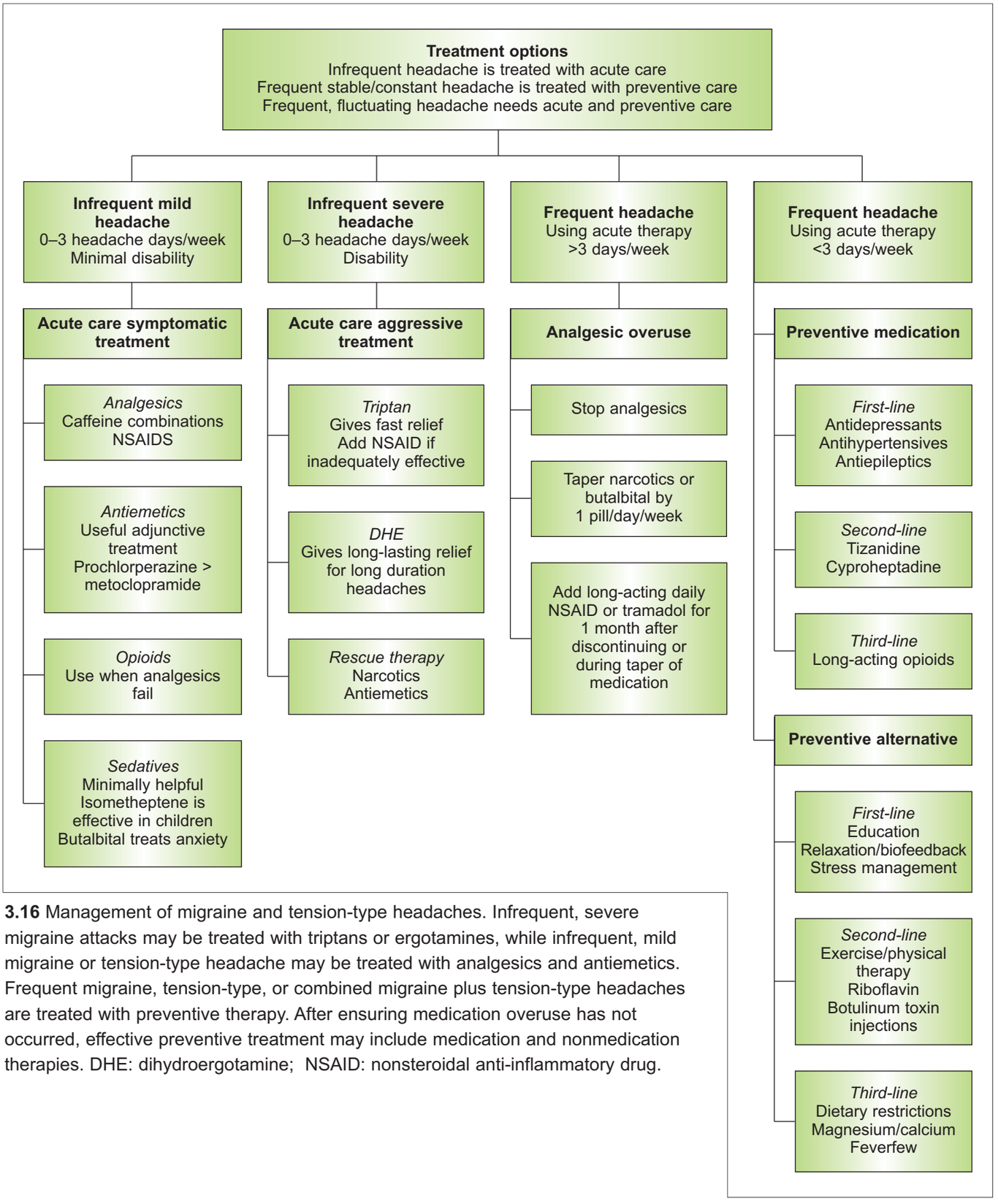
Treatment

Primary headaches

Primary headaches are treated with acute therapy to treat individual headache episodes and preventive therapy to reduce headache occurrence. Both acute and preventive therapies help improve headache susceptibility by increasing headache protective neurotransmitters and/or reducing headache producers (**3.15**).



3.15 Balancing headache. Acute and preventive treatments work by modifying neurochemical balance. Training in relaxation techniques, like biofeedback, and stress management also results in improved neurotransmitter balance to reduce headache susceptibility. DHE: dihydroergotamine; GABA: gamma aminobutyric acid.



3.16 Management of migraine and tension-type headaches. Infrequent, severe migraine attacks may be treated with triptans or ergotamines, while infrequent, mild migraine or tension-type headache may be treated with analgesics and antiemetics. Frequent migraine, tension-type, or combined migraine plus tension-type headaches are treated with preventive therapy. After ensuring medication overuse has not occurred, effective preventive treatment may include medication and nonmedication therapies. DHE: dihydroergotamine; NSAID: nonsteroidal anti-inflammatory drug.

Migraine and tension-type headache

Similar neurochemical pathology occurs with migraine and tension-type headache. Consequently, treatment strategies are similar, using acute therapy for infrequent headaches and prevention for frequent headaches (**3.16**–**3.18**). Post-trauma headaches typically respond to these same therapies. Combining medication and nonmedication treatments maximizes headache control. Headache education is an important part of preventive therapy and should focus on understanding headache diagnosis, pathophysiology, and treatment strategies. Instruction provided in group settings and administered by trained lay people minimizes staff time requirements and effectively reduces headache activity, disability, and inappropriate/excessive medication use[24, 25]. Nutritional supplements may also be beneficial, although their benefit is generally less than with either traditional medication or nonmedication therapies (*Table 3.6*)[26].

Estrogen-related migraines in women may be treated by using standard migraine acute and preventive therapies, as well as hormonal supplementation (*Table 3.7*). Prior to diagnosing a hormonal relationship to migraines, 2–3 months of diaries should be obtained to establish a clear pattern. Pregnancy-related headaches can also be safely and effectively treated with

Table 3.6 Nutritional supplements for headache prevention

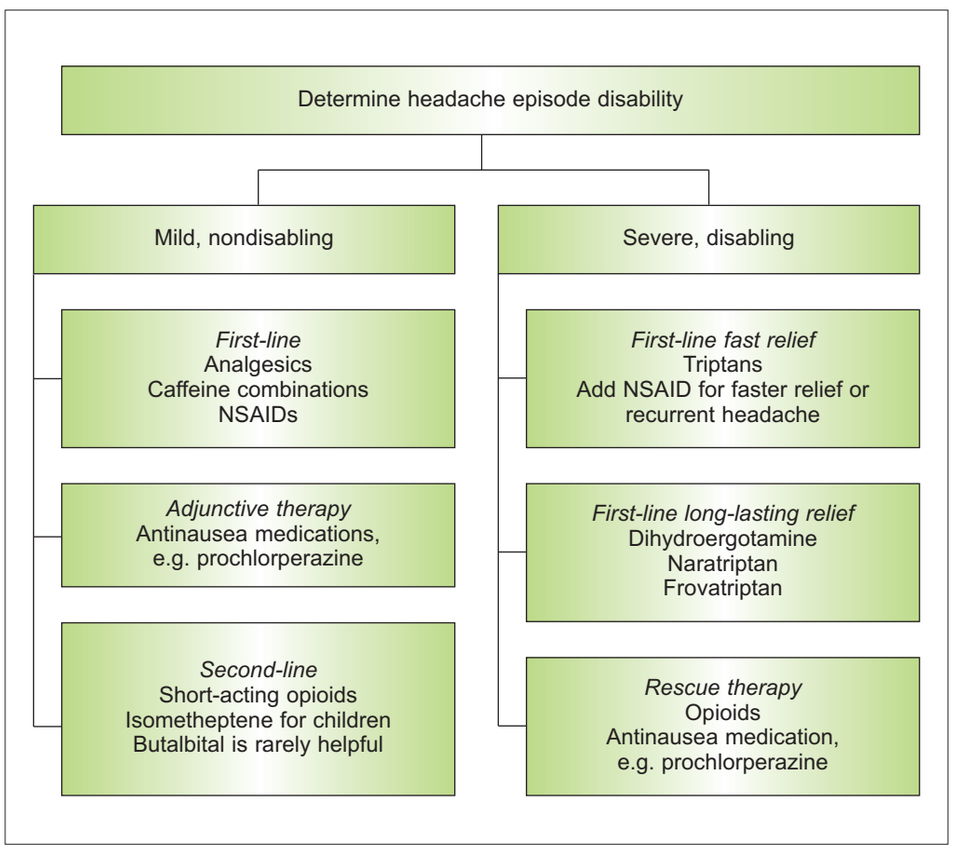
Vitamins and minerals:

- Riboflavin 400 mg daily
- Coenzyme Q10 150 mg daily
- Magnesium 600 mg daily

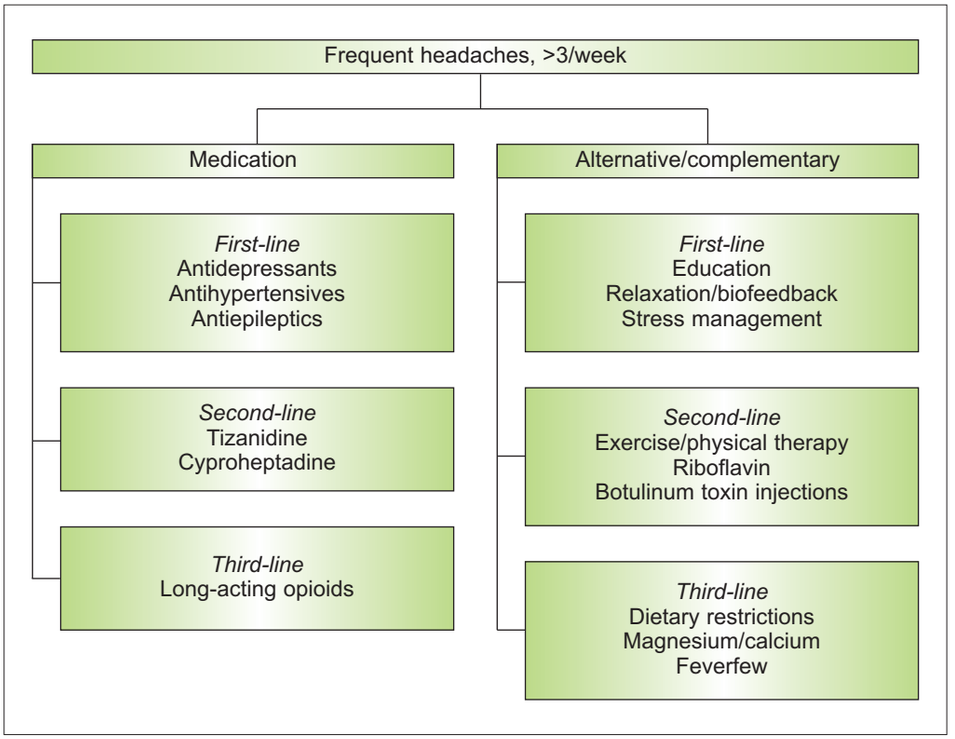
Herbs:

- Feverfew 100 mg 0.2% parthenolide daily
- Butterbur 50–100 mg twice daily
- Peppermint oil 10 g in alcohol applied topically as needed

Melatonin 3 mg at bedtime



3.17 Choosing acute care medication. Mild, nondisabling headaches can usually be effectively managed with analgesics. Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) are more effective than acetaminophen and opioids for reducing headache. Adding 100 mg caffeine to acute analgesics improves the number of people getting headache relief by 1.5 times[27]. Fast-acting triptans, like sumatriptan, rizatriptan, eletriptan, and zolmitriptan, are used for typical severe migraines lasting ≤1 day. Patients who typically experience severe migraines lasting >1 day may achieve more long-lasting relief with dihydroergotamine, frovatriptan, naratriptan, or a fast-acting triptan plus naproxen. Opioids and antiemetics may be helpful as rescue therapy.



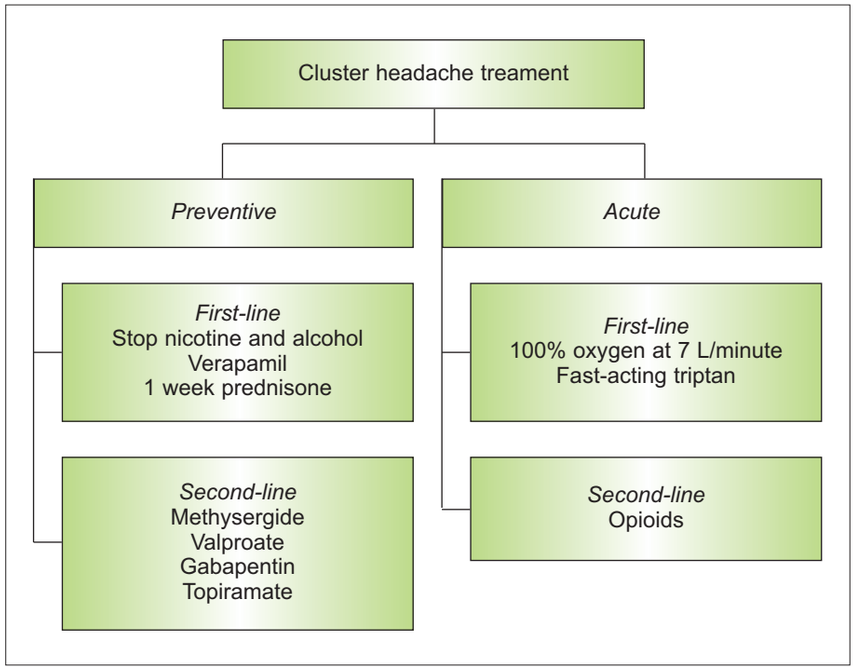
3.18 Choosing preventive therapy. The most effective headache preventive medications are the tricyclic antidepressants, antihypertensives (such as beta-blockers and calcium channel blockers), and neural stabilizing antiepileptics (including valproate, gabapentin, and topiramate). In general, relaxation and biofeedback treatment are as effective as first-line medications. Combining medication and alternative therapies maximizes treatment outcome.

Table 3.7 Treating women's headaches

Menstrual headache
- Acute care medications
  - Nonsteroidal anti-inflammatory (excluding aspirin or ibuprofen)
  - Dihydroergotamine nasal spray BID
  - Low-dose, twice-daily triptan (sumatriptan, naratriptan, frovatriptan)
- Preventive medications
  - Beta-blocker
  - Antidepressant (all effective,excluding fluoxetine)
  - Calcium channel blocker
  - Antiepilepsy (valproic acid or gabapentin)
- Hormonal therapy
  - 7-day low-dose estrogen patch
- All medications should be used at regular dose for 4 days before the expected menstrual period and the first 3 days of menses.

Pregnancy headache
- Acute care treatment (maximum use 2–3 days per week)
  - Ensure patients are not using excessive or daily analgesics
  - Acetaminophen
  - Short-acting opioids
  - Antiemetics
- Preventive treatment for frequent headache
  - Medications
    - Beta-blocker
    - SSRI antidepressant (except paroxetine)
    - Bupropion
    - Gabapentin (in early pregnancy; stop in 3rd trimester)
  - Nonmedication therapy
    - Relaxation and biofeedback
    - Stress management
    - Discontinuation of nicotine and caffeine
    - Regular meals and sleep

Menopause headache
- Consider work-up for secondary headache if there has been a significant headache change
- Adjust estrogen replacement if estrogen replacement aggravates headache
  - Noncycling estrogen
  - Transdermal route
  - Reduce estrogen dosage
  - Switch estrogen replacement product
  - Add androgen
  - Add standard headache preventive therapy in conjunction with estrogen replacement



3.19 Treating cluster headache. First-line preventive therapy for cluster headache is verapamil. A short course of steroids may be used infrequently for particularly severe or recalcitrant cluster cycles. Patients failing to achieve a response may alternatively try the synthetic ergot alkaloid methysergide, or an antiepileptic, such as valproate, gabapentin, or topiramate. 100% oxygen delivered at 7 L/minute for 10 minutes by face mask may provide effective rescue therapy. Analgesics and triptans used for migraine are generally ineffective rescue therapies for cluster headache, since pain relief is not expected to begin until after the usual cluster attack has already ended. Anecdotally, some recalcitrant cluster patients achieve headache prevention from a bedtime dose of a long-acting triptan, such as frovatriptan[39].

a variety of medication and nonmedication therapies. Pregnancy registries have not identified congenital malformations in babies exposed to triptans *in utero*, although the number of exposed babies is too small to establish safe use in routine practice. In general, medications that are safe to use during pregnancy can also be safely used while breastfeeding. The American Academy of Pediatrics has determined that analgesics, as well as sumatriptan, can be safely used while breastfeeding[28]. Drug exposure to the nursing baby can be minimized by administering medications immediately after completing breastfeeding, allowing the ingested drug to be metabolized and excreted before the next breastfeeding session.

Pediatric primary headache

The primary goal of treating pediatric migraine is to minimize functional disability by limiting interference from headache and to maximize school and social participation. School absence should be discouraged since most pediatric headaches are brief. Children may need a short visit to the nurse, particularly if nauseated, but they should generally be able to return to classes within an hour after receiving treatment. School is important for social and emotional development, in addition to intellectual growth. Frequent school absence creates a sense of isolation and fear of both academic and social deficiencies, additional stressors that may further aggravate pain complaints. Family therapy will be necessary when parents are hesitant to insist on school attendance, to help parents develop strategies to ensure school participation and identify manipulative behaviours that erode parents' resolve to encourage activity normalization.

Both nonmedication and medication therapies can effectively manage chronic headaches in children and adolescents. Stress management, relaxation, and biofeedback are effective nonmedication headache therapies in pediatric patients[29, 30]. Ibuprofen and triptans are valuable and safe acute therapies, although dose adjustments are needed[31–34]. Generally, triptans are administered at about half of the starting adult dose in adolescents. Nasal spray and orally disintegrating triptans may be particularly useful in children. Preventive therapy with antidepressants and antiepileptics can be helpful in children with frequent and recalcitrant migraine not responding to nonmedication therapy, although side-effects must be closely monitored (especially effects on cognition, energy level, weight, and menstruation)[35–38]. Magnesium and butterbur have also been effectively used to treat pediatric headache.

Cluster headache

The intensity of each individual cluster headache episode is so severe that therapy should focus on prevention rather than acute care (**3.19**). Most people experience mild and less frequent attacks when the cluster period first begins, with attacks becoming more severe and frequent during the middle of the cluster period. Preventive treatment is most effective when initiated at the first sign of a new cluster period. Successful cluster treatment typically results in reduced frequency and duration of headache episodes, without diminution of pain severity.

Secondary headaches

Medication overuse headache

Medication overuse headache improves only after discontinuation of the offending medication(s). Analgesics may be abruptly discontinued, while butalbital products and opioids should be tapered to minimize withdrawal symptoms. Improvement typically begins about 6–8 weeks after medication discontinuation has been completed (**3.20**)[40]. During the first month after medication discontinuation or while tapering off butalbital or opioids, patients may be treated with low-dose, twice daily nonibuprofen NSAIDs or tramadol. Both of these analgesics have a low likelihood for producing medication overuse headache. After 1 month, standard migraine preventive therapies may be initiated. Since preventive therapies will not be effective if used concomitantly with daily acute care therapies, therapies that previously failed while also overusing acute therapy may be retried at this time. To avoid aggravation of headache by medication overuse, patients should have at least 5 days per week during which they use no acute care medication.

Post-trauma headache

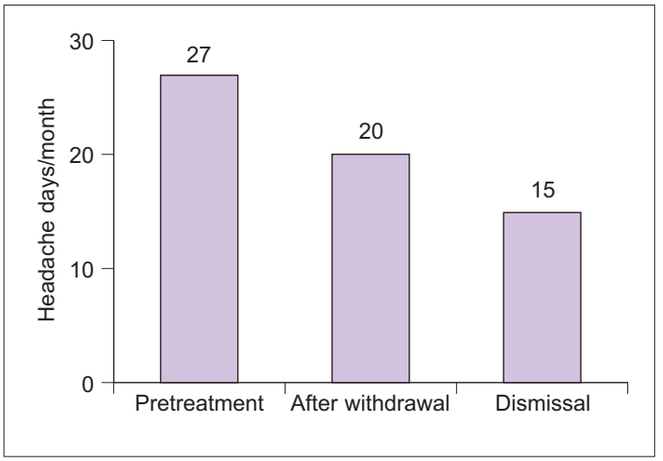
Headaches occurring after concussion typically have features similar to migraine or tension-type headache and respond well to standard therapies for those headache types. Because post-traumatic headaches may be frequent or constant, treatment should focus on preventive therapies rather than acute treatments to avoid the development of medication overuse headaches.

Trigeminal neuralgia

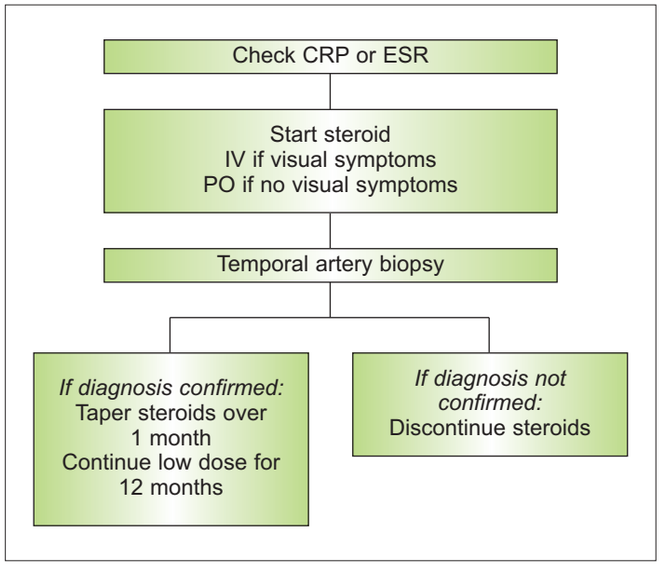
Trigeminal neuralgia is usually first treated with antiepilepsy or antispasmodic medication. First-line treatment includes carbamazepine or phenytoin. Complete treatment recommendations are provided in Chapter 6, Neuropathic Pain.

Temporal or giant cell arteritis

Temporal arteritis should be considered to be a medical emergency, necessitating rapid assessment and intervention (**3.21**). In presumptive cases, treatment should be initiated based on clinical suspicion. Continuation of treatment will depend on confirmation by serological inflammatory markers, temporal artery biopsy, and response to initial steroid therapy. Although a positive response to steroids does not specify termporal arteritis as a definitive diagnosis, failure to achieve rapid reduction in pain with steroids is highly unusual in temporal arteritis and should provoke consideration of alternative diagnoses.



3.20 Medication overuse headache. A total of 216 chronic headache patients with medication overuse were initially treated with analgesic medication withdrawal. Headache frequency was assessed while patients were still overusing analgesics (pretreatment), 2 months after completing medication withdrawal (after withdrawal), and after dismissal from treatment. Average time to dismissal was 228 days. During the first 2 months of treatment, the only therapy was medication withdrawal. Patients continuing to experience frequent headaches were then offered preventive therapy after the 2-month after withdrawal assessment. During the initial 2 months after medication withdrawal, only 7% of patients experienced headache aggravation. The remainder were evenly divided between reduction in headache frequency and no change. Interestingly, patients who failed to improve after 2 months of analgesic abstinence experienced a 26% reduction in headache frequency by dismissal (29 days/month to 22 days/month, $P<0.0001$), supporting the need to continue avoidance of analgesic overuse long-term. At dismissal, headaches decreased by an average of 46% ($P<0.0001$). In addition, patients who had failed to benefit from preventive medications while overusing analgesics experienced an average reduction in headache frequency of 49% after retrying preventive therapy, demonstrating that analgesic overuse both increases headache frequency and prevents usual treatments from being effective. (Based on Zeeberg P, *et al.*, 2006[41].)



3.21 Treating giant cell (temporal) arteritis. Inflammatory markers (C-reactive protein [CRP] or erythrocyte sedimentation rate [ESR]) should be evaluated in patients with suspected temporal arteritis. Patients with visual complaints should be urgently treated with intravenous (IV) steroids (e.g. 1,000 mg methylprednisolone daily pulsed in 2–4 divided doses for several days). Patients without visual complaints are typically treated with oral (PO) prednisone 60–100 mg daily. Headache should resolve within several days after initiating steroids. Prednisone dosage should be gradually tapered during the first month of treatment, so that most patients will be taking about 40 mg daily after 4 weeks. Prednisone is maintained for about 6–18 months, with the dosage decreased by 10% per week or 2.5–5 mg every 1–2 weeks to a maintenance dosage of 10–20 mg daily. The tapering schedule is dependent on maintenance of symptomatic control and reduction in inflammatory markers. Remember that small increases in inflammatory markers often occur during steroid tapering and should not result in increasing steroid dose if the patient remains asymptomatic. Because treatment is started before a diagnosis is complete, the treating physician must not feel obligated to maintain a full 6–18 months treatment in patients for whom the diagnosis has been ruled out (e.g. normal inflammatory markers and negative biopsy). This is particularly true because of the serious adverse events associated with chronic steroid use (including cataracts, glucose intolerance, osteoporosis and aseptic necrosis of the femoral head, myopathy, and infection risk).

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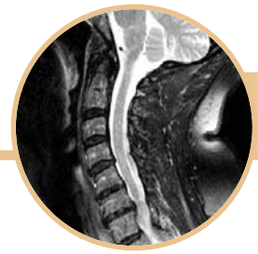
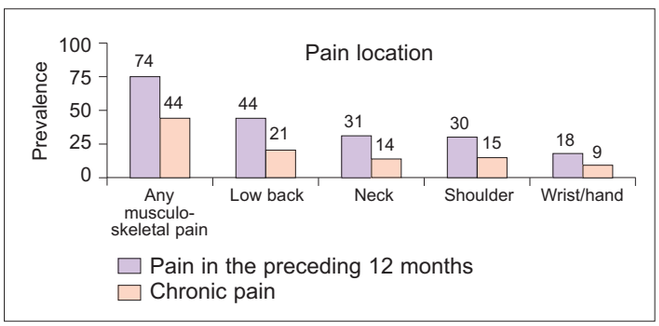


Chapter 4

Neck and upper extremity pain

Introduction

Neck pain is one of the most common pain complaints heard by primary care practitioners. After low back pain, the neck and upper extremity are the next most common sites of musculoskeletal pain (**4.1**)[1]. Neck and upper extremity pain are often disabling. A community survey of musculoskeletal pain in the Netherlands reported limitations to daily life from pain in about one in three people and work absences for one in four people with neck, shoulder, or upper extremity pain[1]. Interestingly, disability due to neck and upper extremity pain was similar to that for people with low back or lower extremity pain.



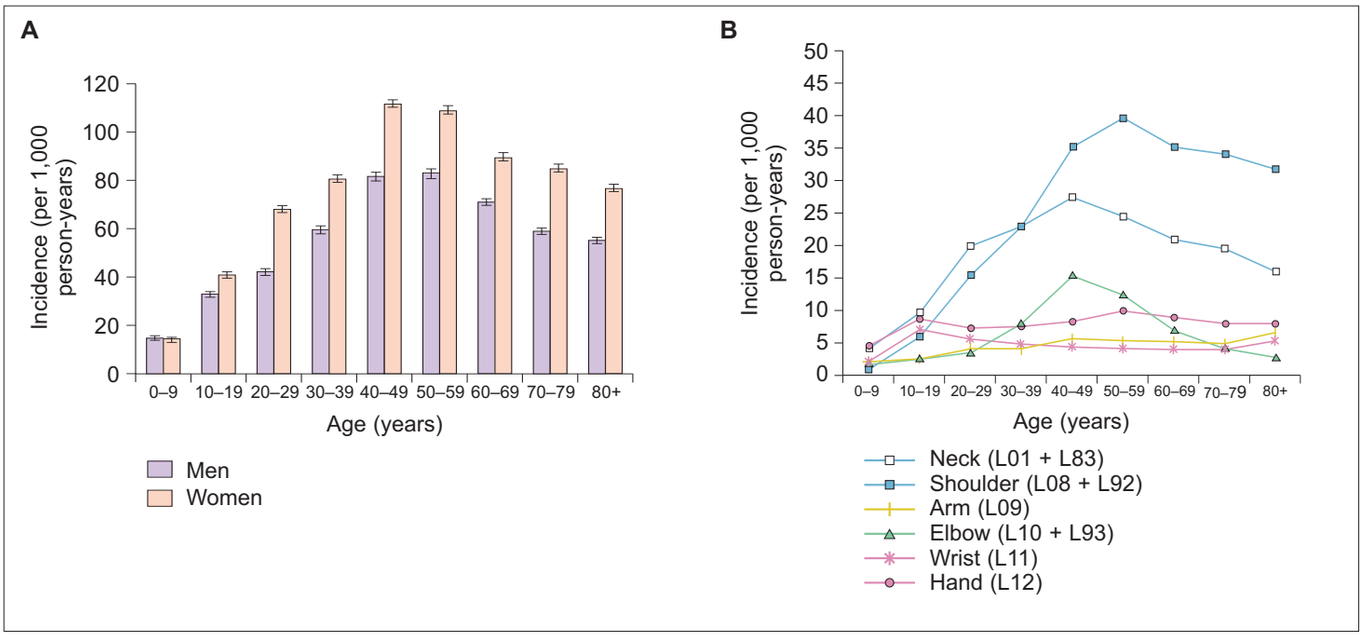
4.1 Community survey of musculoskeletal pain. A population-based survey of 3,664 adults ≥25 years old in the Netherlands was used to determine the prevalence of musculoskeletal pain. The most frequently reported anatomical sites for musculoskeletal pain were ranked as follows: low back, neck, shoulder, knee, and wrist/hand. People were about twice as likely to report musculoskeletal pain in the preceding year than chronic pain in each location. (Based on Picavet HJ, Schouten JG, 2003[1].)

A 12-month survey of general practice patients revealed that neck and upper extremity complaints resulted in 147 general practice consultations for every 1,000 registered patients[2]. Complaints were most commonly attributed to the neck (23.1 per 1,000 person-years) and shoulder (19.0 per 1,000 person-years). The incidence of neck and upper extremity pain was higher in women and increased until ages 40–49 (**4.2**).

A recent survey of 5,752 patients registered with a primary care practitioner identified hand pain in 7% of men and women between ages 16 and 44 and 13% of men and 20% of women ≥45 years old[3]. A similar survey of 6,038 adult primary care patients (ages 25–64 years) reported a specific hand and/or wrist pain syndrome (De Quervain's or wrist tenosynovitis or carpal tunnel syndrome) in about 3% of patients, with nonspecific hand and/or wrist pain in about 10%[4]. Hand pain can significantly impair both work and leisure activities.

Assessing neck and upper extremity pain

Chronic neck and upper extremity pain is often caused by musculoskeletal or neurological conditions (*Table 4.1*). Myofascial pain is characterized by muscle spasm and tender muscles. Areas of discrete tenderness within the muscles, called trigger points, can be locally painful (latent trigger point) and refer pain (active trigger point). Myofascial trigger points in the neck typically refer pain to the head. Myofascial pain from the scalene and serratus anterior muscles refer pain into the upper extremity, while myofascial triggers in the levator scapulae and rhomboids refer to the shoulder (**4.3**). Pain may also be referred from the heart and lungs.



4.2 Lifetime epidemiology of neck and upper extremity pain. In this Dutch survey, all patient contacts for 96 general practices were evaluated for 12 consecutive months. Incidence density was calculated by determining the number of patients with a first, new episode of a neck or upper extremity complaint during the study year, divided by the sum of person-years at risk. Incidence peaked in the fifth decade, with a higher incidence in women in all age brackets (**A**). Among the different anatomical locations evaluated, neck and shoulder pain were the most common (**B**). International Classification of Primary Care (ICPC) codes are shown next to each anatomical location. (Based on Bot AM, *et al*., 2005[2].)

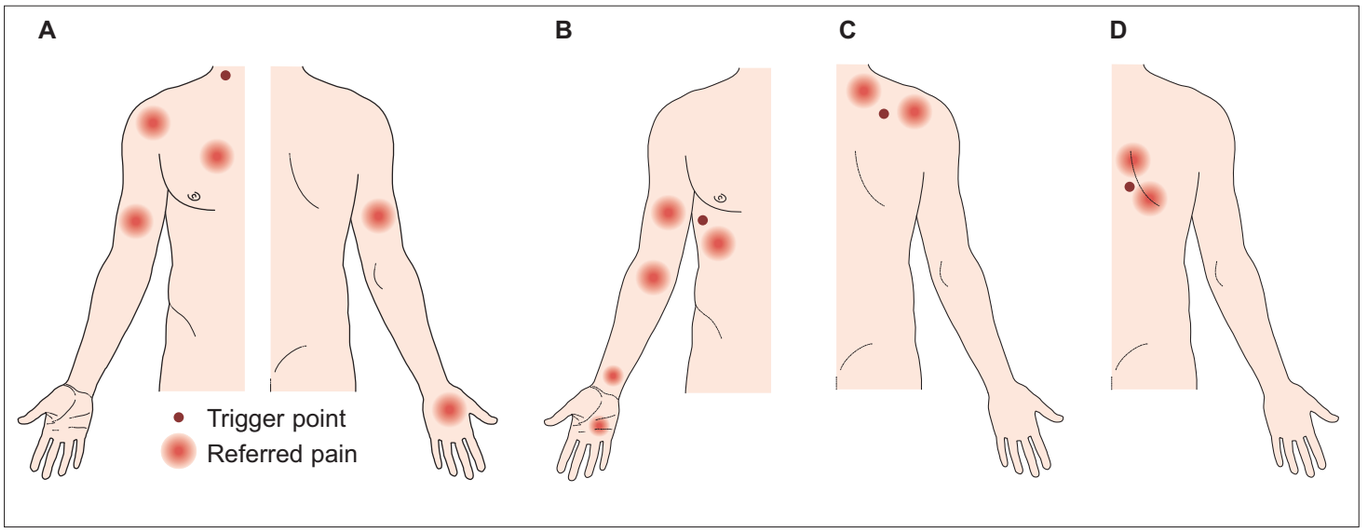
Table 4.1 Common causes of neck and upper extremity pain

Pain location	*Diagnosis*
Neck	Arthritis
	Cervical radiculopathy
	Myofascial pain
Shoulder	Arthritis
	Bursitis
	Myofascial pain
	Rotator cuff tendonitis/tear
Upper extremity	Carpal tunnel syndrome
	Cervical radiculopathy
	De Quervain's tenosynovitis
	Myofascial pain

Table 4.2 Evaluation for common cervical radiculopathies

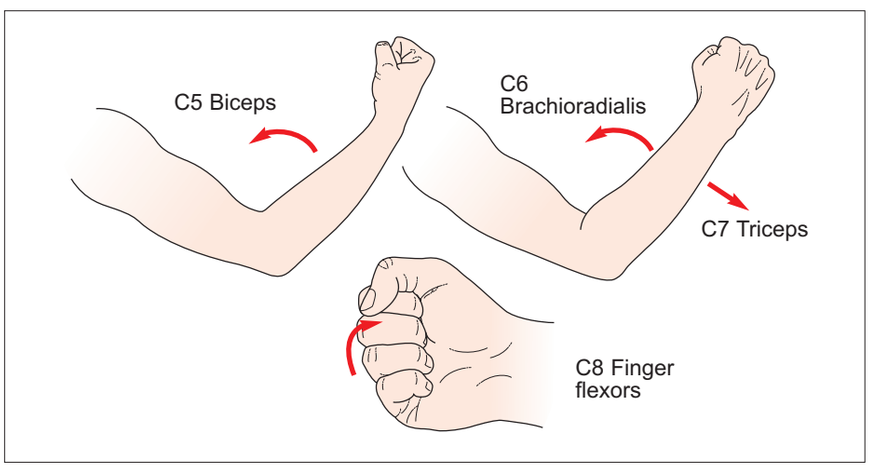
Nerve involved	*Motor loss*	*Reflex loss*	*Sensory loss*
C5	Biceps	Biceps	Lateral upper arm
C6	Brachioradialis	Biceps	Lateral lower arm
C7	Triceps	Triceps	Middle finger
C8	Finger flexors	None	Medial lower arm

A herniated cervical disc usually affects the nerve for the vertebra below, e.g. C5 radiculopathy occurs when the C4–C5 disc is herniated. A C8 radiculopathy occurs with a C7–T1 herniated disc.

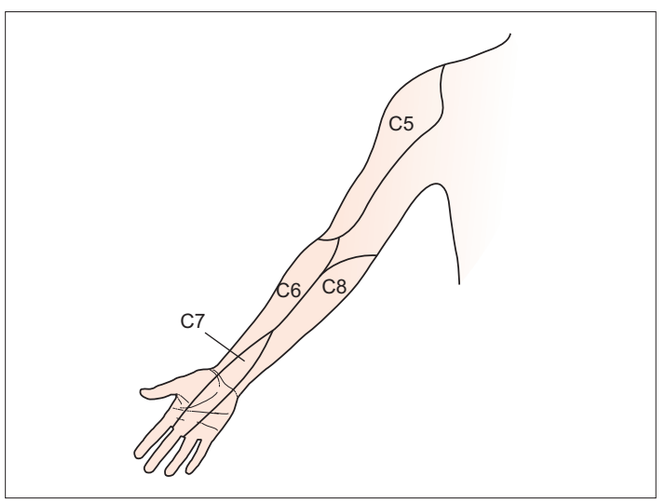


4.3 Myofascial pain patterns in the shoulder and upper extremity. **A**: Scalene; **B**: serratus anterior; **C**: levator scapulae; **D**: rhomboids.

4.4 Motor testing for cervical radiculopathy. Arrows denote direction of movement required to test specific muscles. Test biceps strength with the palm facing up. Test brachioradialis strength with thumb pointed up.



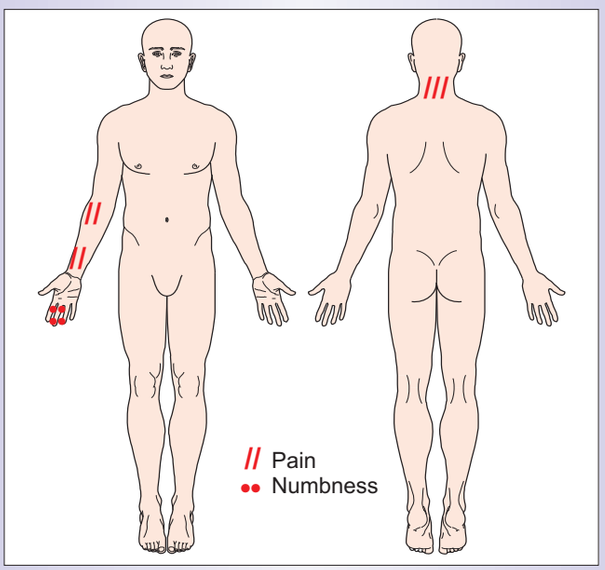
Neurological causes of chronic neck and upper extremity pain can be diagnosed by establishing patterns of motor and sensory loss that suggest peripheral nerve or radicular dysfunction. Neurological loss in cervical radiculopathies can be localized to specific nerves by evaluating motor and sensory tests (**4.4**, **4.5**, *Table 4.2*).



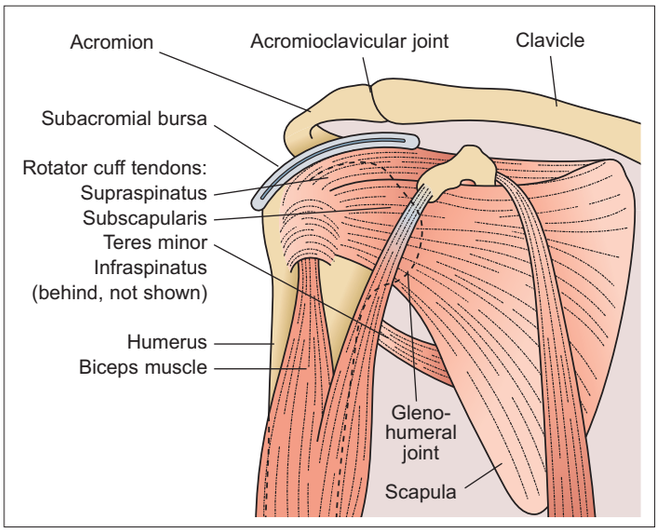
4.5 Sensory testing for cervical radiculopathy. Arm viewed from the anterior aspect, with palm facing toward the viewer. Skin areas served by specific cervical nerve roots are marked.

Case presentation

A 43-year-old pharmaceutical representative presents with neck and right upper extremity pain that began after a work injury. While lifting boxes of drug samples and other supplies from her car, she experienced a popping in her neck and searing pain into her right forearm and hand. She also notes tingling and hyperesthesia in her right middle finger. Her pain drawing is below. She is in good general health, except for two previous episodes of work absence for low back pain and foot drop after lifting at work. Current examination reveals decreased triceps strength and reflex on the right, suggesting a C7 radiculopathy.



The clinical diagnosis of right C7 radiculopathy was confirmed with MRI testing. Similar to this patient, about 40% of patients with cervical radiculopathy have a prior history of lumbar radiculopathy[5].



4.6 Anatomy of the shoulder. The shoulder contains four articulations: the glenohumeral, sternoclavicular, acromioclavicular, and scapulothoracic joints. The rotator cuff is composed of four muscles and their tendons, providing full shoulder motion and joint stability. The subacromial bursa sits on top of the supraspinatus tendon, helping to reduce friction with tendon movement.

Table 4.3 Common causes of shoulder pain

- Adhesive capsulitis
- Osteoarthritis glenohumeral or acromioclavicular joint
- Rotator cuff tear
- Rotator cuff tendonitis/impingement syndrome
- Subacromial bursitis
- Tendonitis of biceps or supraspinatus tendons

Shoulder pain

The shoulder is a complex structure (**4.6**). Shoulder pain can be caused by overuse in older adults or trauma in young patients (*Table 4.3*). Pain in the anterior shoulder often results from osteoarthritis of the true shoulder joint (glenohumeral joint) or more commonly acromioclavicular joint or biceps tendonitis. Anterior and lateral pain occur with subacromial bursitis and rotator cuff tendonitis.

History of trauma or overuse, pain features, and physical examination can help distinguish among common causes of shoulder pain (*Table 4.4*). Although these features can assist in determining a diagnosis, the clinical evaluation of shoulder pain can be difficult. Several studies have compared results among clinicians when evaluating patients with shoulder pain complaints. In general, diagnostic agreement is poor to moderate. In one study, 44 patients

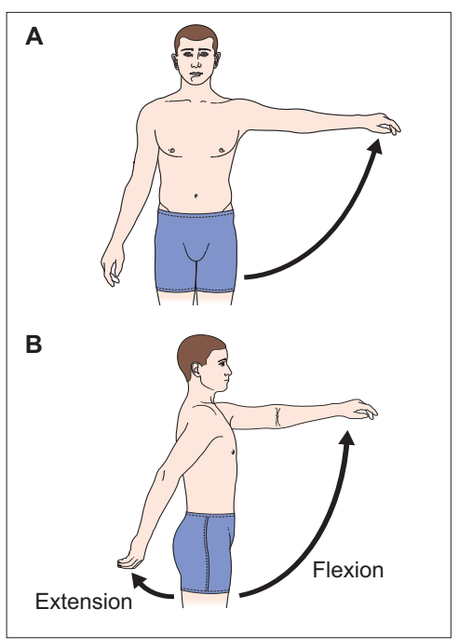
Table 4.4 Distinguishing features among shoulder pain diagnoses

Diagnosis	*Pain at night*	*Range of motion*		*Crepitus*
		Active	*Passive*	
Osteoarthritis	No	Reduced	Reduced	Present
Rotator cuff tendonitis/impingement	Yes	Reduced	Normal	Absent
Rotator cuff tear	Yes	Reduced	Normal	Absent
Subacromial bursitis	Yes	Reduced	Reduced	Absent

Table 4.5 Radiographic studies for shoulder pain

Test priority	*Imaging study*	*Conditions diagnosed*
First-line	Plain X-ray	Osteoarthritis, complete rotator cuff tear
	Arthrogram	Adhesive capsulitis, bursitis, complete rotator cuff tear
Second-line	Magnetic resonance imaging	Partial rotator cuff tear
	Ultrasound	Partial rotator cuff tear

with shoulder pain were evaluated by three rheumatologists[6]. Agreement among clinicians was only 46%. When the three rheumatologists evaluated the patients together and discussed diagnostic signs and symptoms, agreement improved to 78%. In another study, diagnostic agreement between two experienced physical therapists for 201 patients with shoulder pain was only moderate (60%)[7]. Agreement was worse among patients with bilateral, chronic, or severe pain. Clinical tests assessing shoulder function and range of motion are also notoriously unreliable in shoulder pain patients[8–10]. For this reason, most patients with chronic shoulder pain will require radiographic studies in addition to history and physical examination (*Table 4.5*). Partial rotator cuff tears are best assessed with MRI or ultrasound. A comparison of both techniques against arthroscopic findings in 71 patients with rotator cuff tears showed similar good identification and size measurement for both full and partial tears[11].



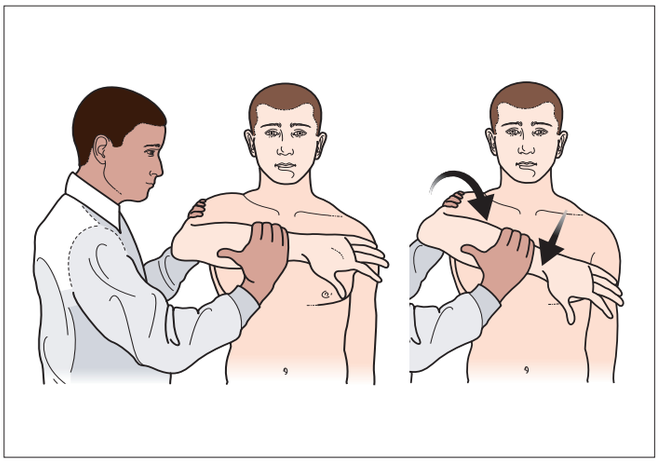
4.7 Shoulder motion. Patients with subacromial bursitis report pain and weakness with shoulder abduction (**A**). Flexion and extension are generally not impaired (**B**).

Subacromial bursitis

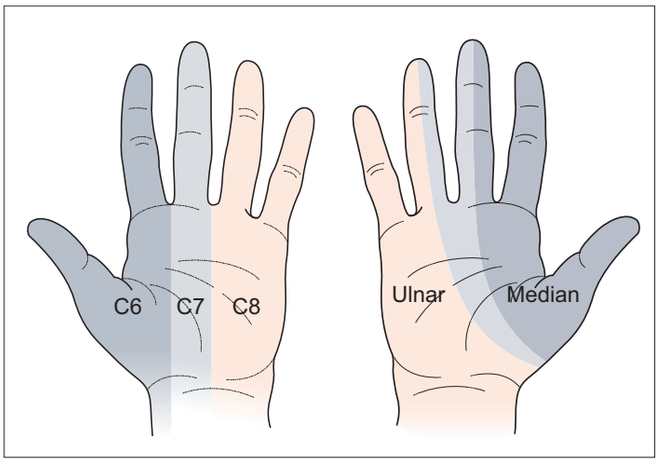
Inflammation of the subacromial bursa results in pain in the lateral shoulder and upper arm, aggravated with overhead activities. Pain is generally relieved by rest. There is no pain when elevating the upper extremity in front of the body or behind. Shoulder rotation and abduction, however, are painful (**4.7**).

Rotator cuff tendonitis

Rotator cuff tendonitis is a common cause of shoulder pain. A prospective, 1-year survey of 131 patients presenting to their primary care physicians for shoulder pain identified rotator cuff tendonopathy in 85%[12]. Inflammation within the rotator cuff is often combined with subacromial bursitis and termed impingement syndrome. Pain is generally



4.8 Hawkins test. With the elbow flexed and arm elevated in front of the body, the examiner passively internally rotates the upper extremity.



4.9 Comparison of sensory loss from radiculopathy versus peripheral mononeuropathy. The left hand shows sensory distribution from cervical roots. The right hand shows sensory areas served by the median and ulnar nerves. Part of the middle and ring fingers may receive sensory supply from either the median or ulnar nerve.

located over the anterior and lateral shoulder. Impingement syndrome can be confirmed with the Hawkins test (**4.8**). Rotator cuff tendonitis pain is aggravated with overhead activities and is worse at night. Clicking or popping may occur in the affected shoulder.

Hand pain

Hand pain is commonly caused by musculoskeletal, neurological, and vascular pathology (*Table 4.6*). Hand pain may occur in isolation, e.g. De Quervain's tenosynovitis and carpal tunnel syndrome, or as part of a more diffuse pain condition, e.g. cervical radiculopathy and rheumatoid arthritis. Sensory dysfunction in the hand can help distinguish pain caused by cervical radiculopathy or compressive mononeuropathy (**4.9**).

De Quervain's tenosynovitis

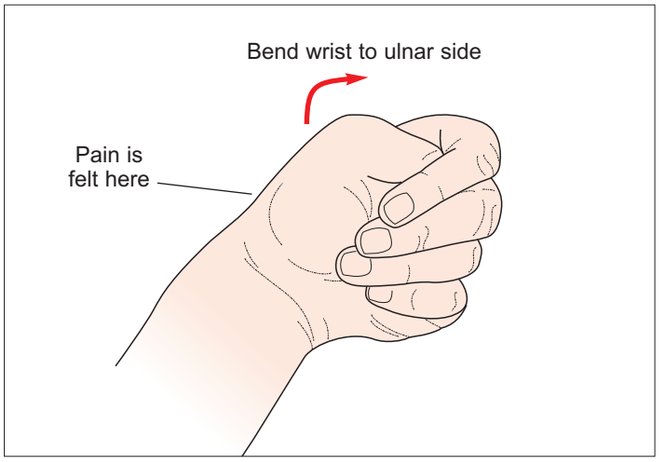
De Quervain's tenosynovitis is a common painful inflammatory condition of the thumb. The tendons for the abductor pollicis longus and extensor pollicis brevis travel into the thumb through a small compartment in the wrist. With thumb extension, these tendons can be seen at the base of the thumb, where they form the radial border of the anatomic 'snuff box'. Inflammation of the synovial lining of this tunnel may occur due to trauma or repetitive overuse injury (**4.10**). This pain is typically aggravated by grasping, twisting, or pinching manoeuvres. Patients with diabetes, thyroid disease, and rheumatoid arthritis have increased risk for developing De Quervain's tenosynovitis.

Table 4.6 Common causes of hand pain

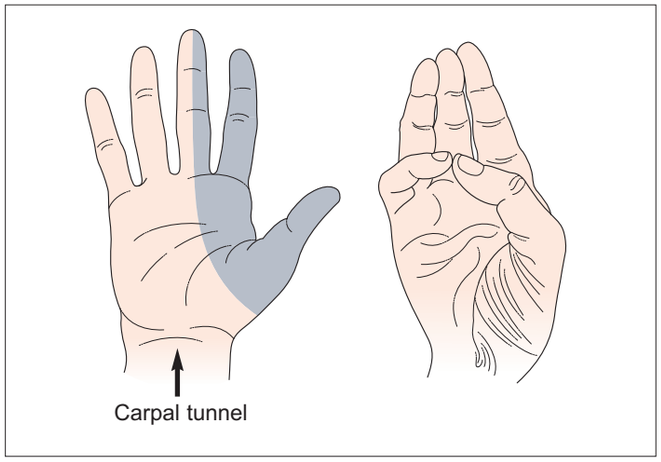
Disease category	*Specific diseases*
Musculoskeletal	Traumatic (e.g. sprain or fracture)
	Arthritic (e.g. rheumatoid arthritis)
	Compressive tenosynovitis (e.g. De Quervain's)
	Ganglion cyst
Neuropathic	Cervical radiculopathy
	Compressive neuropathy (e.g. carpal tunnel syndrome)
	Complex regional pain syndrome
Vascular	Raynaud's syndrome

Carpal tunnel syndrome

The median nerve supplies sensation to the lateral hand, thumb, and first two fingers and motor function for thumb opposition (**4.11**). Pain and dysesthesia are typically aggravated by compressing or stretching the wrist and sleeping, possibly due to the combination of wrist hyperextension or flexion with sleep and increased hand swelling with expected fluid redistribution while lying down. Carpal tunnel symptoms may be aggravated or reproduced



4.10 Finkelstein's test for De Quervain's tenosynovitis. Finkelstein's test is performed by asking the patient to make a fist with the thumb covered by the fingers. The examiner then bends the wrist toward the ulnar side. Pain occurring at the base of the thumb denotes a positive test.



4.11 Carpal tunnel syndrome. Area of sensation (grey in the left picture) and motor function (opposition of the thumb in the right picture) supplied by the median nerve. (Based on Marcus DA, 2005[13].)

with the Phalen's test (in which patients are asked to flex the wrist for 1 minute) and percussion of the carpal tunnel. Production of tingling in the thumb, index, and middle fingers with percussion is a positive Tinel's sign. Phalen and wrist percussion testing were evaluated in 112 patients with clinical carpal tunnel syndrome confirmed by nerve conduction studies and 50 pain-free controls[14]. The sensitivity and specificity, respectively, were 85% and 89% for Phalen's test and 67% and 68% for Tinel's sign. Interestingly, both of these tests were negative in 17 patients with confirmed carpal tunnel syndrome (15%). A positive Phalen's test is also associated with increased carpal tunnel syndrome severity, suggesting that follow-up Phalen's testing may help to identify treatment effectiveness[15].

Case presentation

A 37-year-old primigravida complains of bilateral hand pain starting at the end of her second trimester. The pain has severely limited her ability to use a keyboard at work and frequently causes her to wake at night. She also reported hand weakness. Sensory loss was present over her palm and thumb in her dominant hand and she was diagnosed with carpal tunnel syndrome. Although carpal tunnel syndrome can usually be diagnosed without additional testing, nerve conduction studies showing slowing across the carpal tunnel can be helpful in cases where the diagnosis is questionable. In general, median nerve conduction across the wrist is delayed in pregnant women, although comparing delays in median and ulnar nerve conduction in pregnant women can effectively discriminate symptomatic from asymptomatic delays[16].

A survey of obstetric patients in their 8th and 9th months of pregnancy identified pre-existing carpal tunnel symptoms in 12% and pregnancy-related carpal tunnel in 50%[17]. Paresthesias were reported in both hands in 41% in this survey. Carpal tunnel symptoms during pregnancy are different from nonpregnancy carpal tunnel symptoms since pregnant women often complain of bilateral sensory symptoms and motor loss[18]. Carpal tunnel symptoms during pregnancy are typically treated conservatively as symptoms usually resolve after delivery. A survey of 46 women developing carpal tunnel syndrome with pregnancy reported persistent symptoms in only 18 (39%) 1 month postpartum, and 2 (4%) 1 year postpartum[18]. Surgical release is rarely necessary for carpal tunnel syndrome occurring with pregnancy.

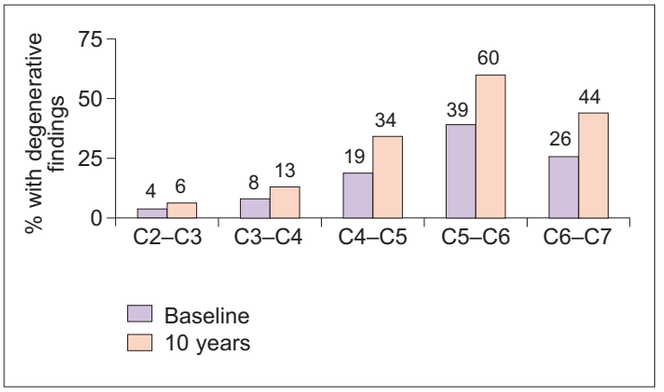
Imaging studies

Imaging studies often help refine the diagnosis in patients with chronic neck and upper extremity pain. As with other chronic pain problems, imaging studies should be used to confirm rather than develop diagnoses. Inconsequential radiographic abnormalities often occur, especially with ageing, in asymptomatic individuals. Therefore, diagnoses should be initially established based on clinical examination and history.

Cervical spine X-rays and MRI scans often reveal radiographically apparent changes suggesting significant degenerative disease, even in asymptomatic controls[19] (**4.12**, *Table 4.7*). Degenerative changes are most prevalent with increased age, with cervical spine X-rays abnormal in 70% of women and 95% of men aged 60–65[21]. Degenerative disc disease can be diagnosed on MRI scans in 25% of asymptomatic subjects <40 years old and nearly 60% of asymptomatic subjects ≥40 years old[22,23]. In an MRI study of symptom-free young adults (ages 24–26), cervical disc degeneration was identified in 29% and disc bulges in 32%[20].

Radiographic studies can help confirm or refute clinical diagnoses, especially in patients with suspected mechanical and radicular pain (**4.13**). For example, cervical MRIs were compared in young adults (ages 24–27) with recurrent or persistent neck and shoulder pain and asymptomatic controls. While there was no difference in the prevalence of most MRI abnormalities, disc protrusion was more common in controls (19% of disc spaces in symptomatic adults *vs*. 32% of disc spaces in controls; $P<0.05$) and disc herniation (4% of discs in symptomatic adults *vs*. 0 in controls; $P=0.05$) occurred more commonly in symptomatic patients[20].

Imaging studies of shoulders have similarly identified abnormalities in asymptomatic adults. Rotator cuff tears should not be diagnosed based on imaging studies alone. Asymptomatic full and partial tears occur commonly. A literature survey identified tears in 39% of asymptomatic adults evaluated with ultrasound and 26% evaluated with MRI[24]. A prospective study following young athletes similarly identified frequent MRI abnormalities in asymptomatic individuals[25]. In this study, 20 competitive athletes participating in college baseball or professional tennis (mean age 26 years) with no shoulder complaints were evaluated with MRI scans of the shoulder. Full or partial rotator cuff tears were identified in 8 of the athletes (40%). After 5 years, none of these athletes had developed shoulder problems, including those with rotator cuff tears previously diagnosed by MRI. These data further support the need to use imaging studies to verify clinical diagnoses rather than as a primary tool to first establish a diagnosis.



4.12 Radiographic abnormalities in asymptomatic adults. The prevalence of radiographically-diagnosed degenerative disease in the cervical spine was evaluated in 159 asymptomatic adults (ages 20–65 years) at baseline and after 10 years. Lateral cervical spine X-rays showed abnormalities in the lower spine in about one in three patients at baseline and up to over half of patients when X-rays were repeated after 10 years. Although only 15% of subjects experienced neck pain during the ensuing 10 years, progressive degenerative changes were noted in 45% of subjects. When degenerative changes were noted at C5–C6, they were also typically present at C6–C7, resulting in reports of multilevel degenerative disease. (Based on Gore DR, 2001[19].)

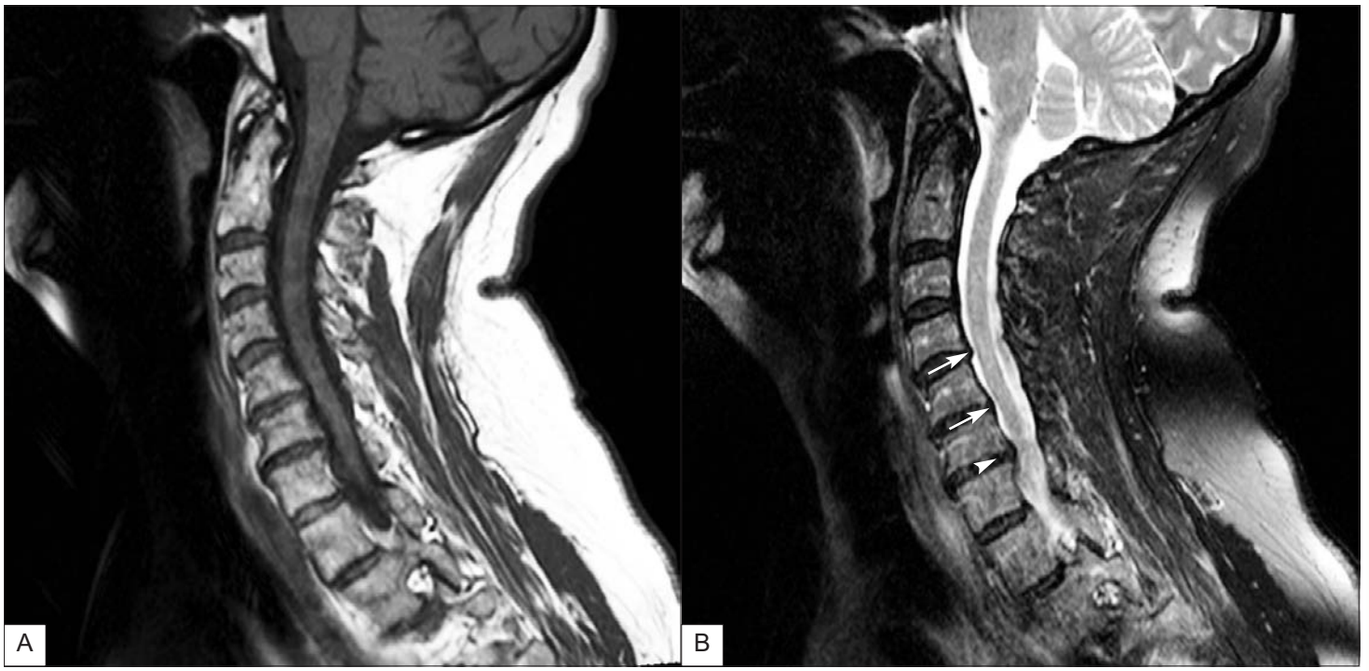
Table 4.7 MRI cervical spine abnormalities in asymptomatic adults

Abnormality	*Prevalence in normal adults (%)*
Disc degeneration	73
Annular tear	67
Disc bulge	87

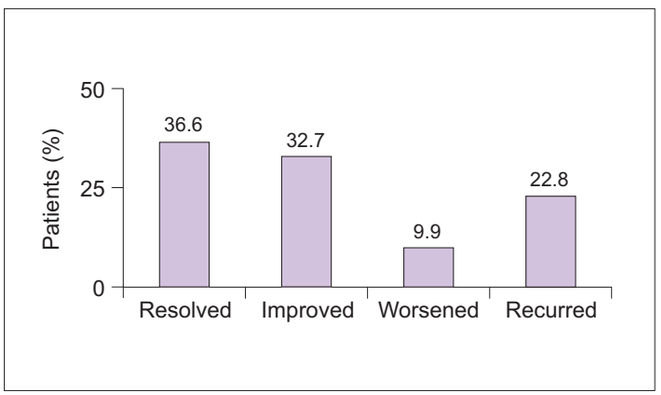
(Based on Siivola SM, *et al.*, 2002[20])

Treatment

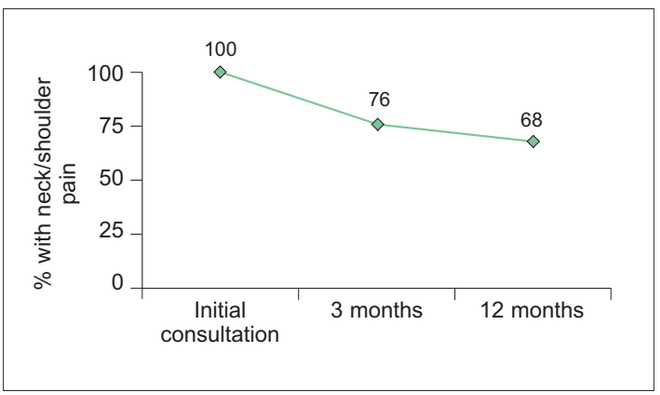
Neck and upper extremity pain tend to become chronic in many patients. In two studies conducted in Canada and the Netherlands, pain resolved in only about one in three patients followed for 12 months (**4.14**, **4.15**)[26,27]. For this reason, treatment is generally necessary to minimize long-term disability.



4.13 Sagittal MRI cervical spine. This cervical MRI shows degenerative spondylosis at multiple levels seen on the T1-weighted image (**A**). The T2 image (**B**) highlights multiple levels of disc bulges (arrows) and herniation at C6–7, resulting in canal stenosis and effacement of the spinal cord (arrowhead).



4.14 Population-based survey of 12-month outcome of baseline neck pain. 1,100 randomly selected Canadian adults were evaluated for neck pain at baseline and after 1 year. Mean age of the sample was 43.4 years. Neck pain was reported at initial evaluation by 587 participants (53%). Pain resolved for about one in three patients and improved in another one in three. The remainder experienced pain worsening or recurrence. (Based on Côté P, *et al*., 2004[26].)



4.15 Long-term prognosis of new neck and shoulder girdle pain. A total of 443 adults consulting 97 general practitioners with a new complaint of neck or shoulder pain was evaluated in the Netherlands. Questionnaires were completed about symptom persistence or resolution after 3 and 12 months. Symptoms were typically persistent, with recovery occurring in only 24% of patients at 3 months and 32% at 12 months. (Based on Bot SM, *et al*., 2005[27].)

Neck pain

A number of nonmedication therapies are used to reduce chronic neck pain. Adequate data are available to support benefit from only acupuncture for short-term pain relief and exercise for long-term benefit (*Table 4.8*)[28–30]. For example, although chronic pain treatment experts routinely endorse behavioural and multidisciplinary treatment for patients with persistent and disabling pain, the literature includes insufficient data to demonstrate conclusive efficacy from these therapies in chronic neck pain patients. Treatment algorithms provide guidelines for empiric management of patients with acute and chronic neck pain (**4.16**).

Cervical radiculopathy

Conservative therapy is the initial approach with cervical radiculopathy, unless motor or spinal dysfunction is present. Most symptoms besides pain improve with conservative treatment in patients with cervical radiculopathy (**4.17**)[31]. Cervical epidural steroid injections may resolve radiculopathy and improve range of motion in the cervical spine in elderly patients with persistent pain or patients wishing to avoid surgery. While short-term pain relief is superior with surgery, long-term pain reduction has been shown to be similar among patients with cervical radiculopathy without myelopathy randomized to conservative treatment or surgery (**4.18**)[32]. A long-term outcome study for surgical treatment of patients with cervical radiculopathy showed no effect of presurgical duration of symptoms on surgical outcome until symptoms had been present for >48 months[33]. This study suggests that using conservative measures as first-line therapy in patients without myelopathy will not generally reduce the success from surgery if surgical intervention is later deemed necessary.

4.16 Algorithms for management of neck pain.
IV: intravenous; NSAIDs: nonsteroidal anti-inflammatory drugs.

Chronic shoulder pain

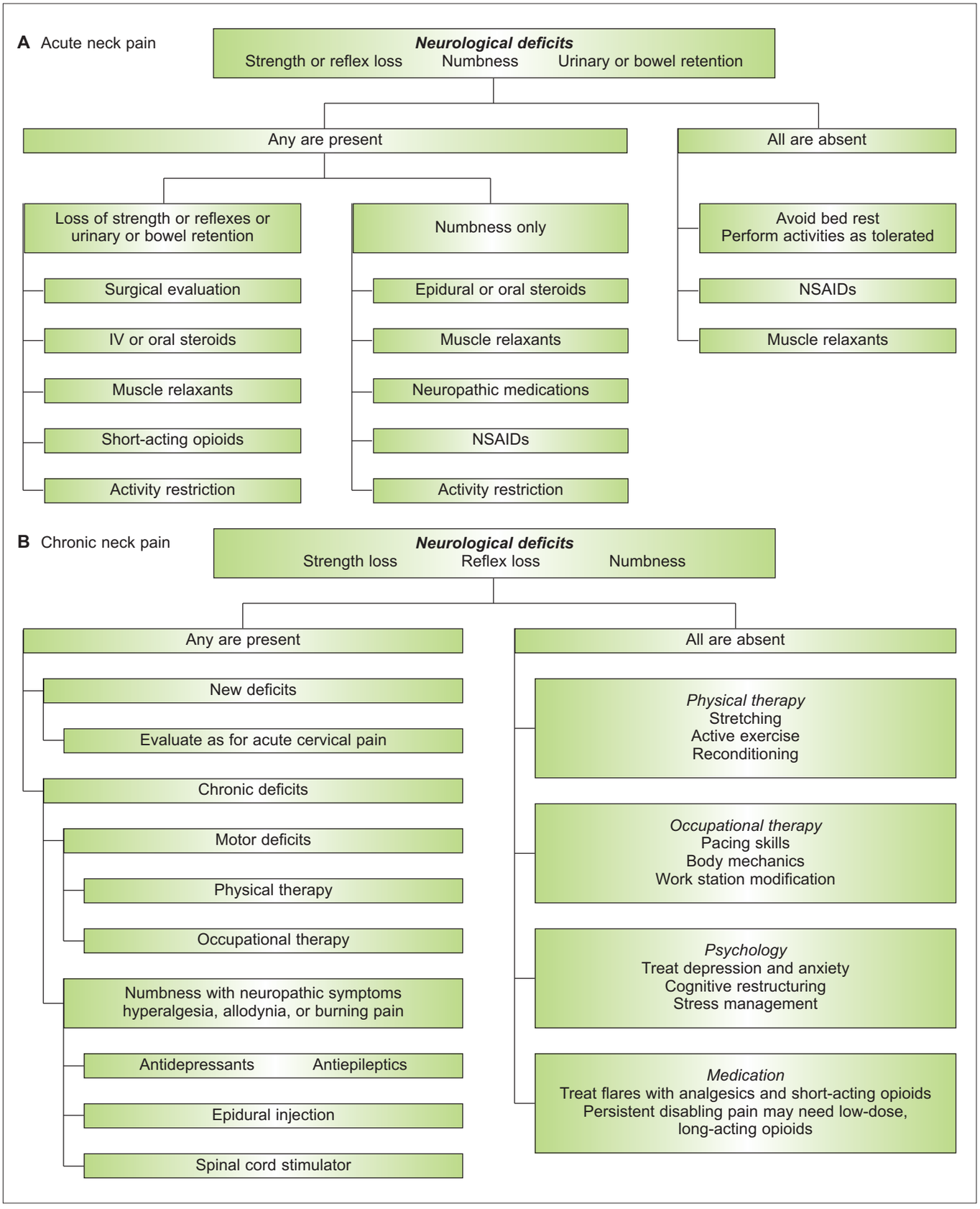
The initial treatment of chronic shoulder pain is generally conservative therapy, including NSAIDs and physical therapy. Physical therapy should include stretching and strengthening exercises of rotator cuff, scapula, and deltoid. A literature review confirmed both short- and long-term benefits from exercises for shoulder pain[34]. Adding mobilization to physical therapy exercises improves outcome. Occupational therapy may also be helpful. In a study following the outcome of 124 rotator cuff tears treated conservatively for an average of 3.4 years, good or excellent improvement occurred in 82%[35]. Conservative therapy was most effective in patients who initially presented with a good range of motion and strength.

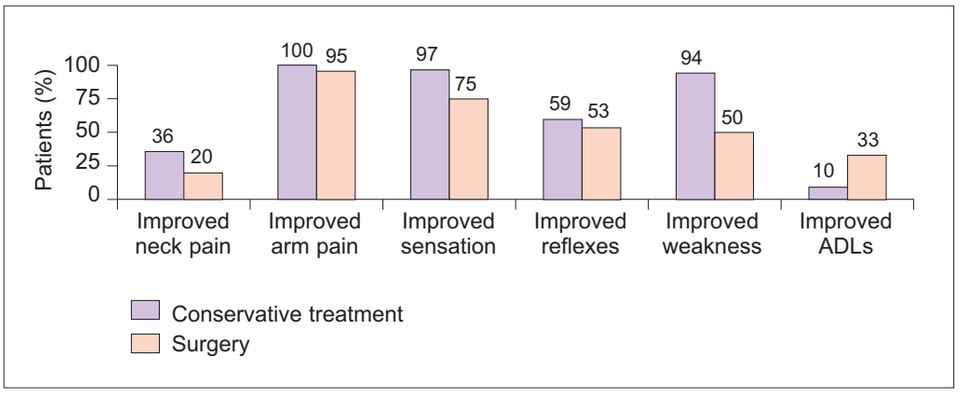
Corticosteroid injections may be used to supplement conservative therapy. Sonographic guidance with local corticosteroid injections for shoulder pain resulted in significantly better pain reduction and functional improvement in 41 consecutive patients randomized to receive steroid injections with or without ultrasound guidance[36]. Patients failing to achieve benefit from steroid

Table 4.8 Effective therapies for chronic neck pain

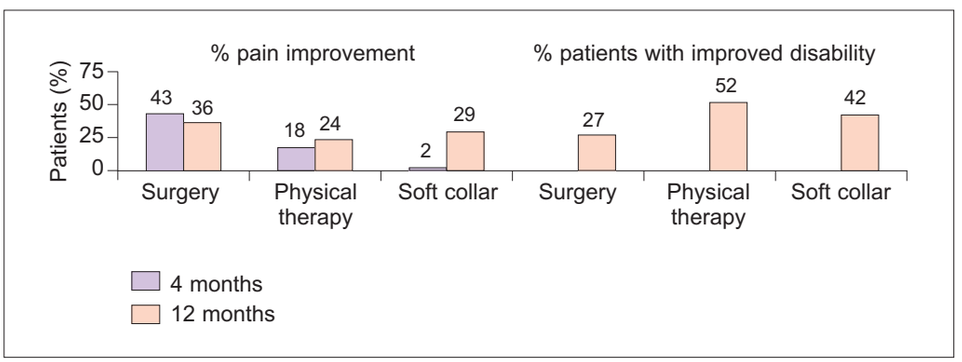
Treatment	*Effective*	*Ineffective*	*Insufficient data*
Exercise	X (long-term)		
Acupuncture	X (short-term)		
Traction		X	
Ultrasound		X	
Massage			X
Electrical stimulation			X
Multidisciplinary rehabilitation			X
Biofeedback			X
Behavioural interventions			X

(Based on Harris GR, Susman JL, 2002[28]; Nabeta T, Kawakita K, 2002[29]; and Swenson RS, 2003[30])


A Acute neck pain
Neurological deficits
Strength or reflex loss
Numbness
Urinary or bowel retention
Any are present
All are absent
Loss of strength or reflexes or urinary or bowel retention
Numbness only
Avoid bed rest
Perform activities as tolerated
Surgical evaluation
IV or oral steroids
Muscle relaxants
Short-acting opioids
Activity restriction
Epidural or oral steroids
Muscle relaxants
Neuropathic medications
NSAIDs
Activity restriction
NSAIDs
Muscle relaxants
B Chronic neck pain
Neurological deficits
Strength loss
Reflex loss
Numbness
Any are present
All are absent
New deficits
Evaluate as for acute cervical pain
Chronic deficits
Motor deficits
Physical therapy
Occupational therapy
Numbness with neuropathic symptoms hyperalgesia, allodynia, or burning pain
Antidepressants
Antiepileptics
Epidural injection
Spinal cord stimulator
Physical therapy
Stretching
Active exercise
Reconditioning
Occupational therapy
Pacing skills
Body mechanics
Work station modification
Psychology
Treat depression and anxiety
Cognitive restructuring
Stress management
Medication
Treat flares with analgesics and short-acting opioids
Persistent disabling pain may need low-dose, long-acting opioids



4.17 Post-treatment outcome for cervical radiculopathy. In a survey of 119 consecutive cervical radiculopathy patients, treatment was assigned as deemed clinically appropriate. Improved was defined as complete symptom resolution or marked improvement. Although arm pain and neurological symptoms improved for patients treated either conservatively or with surgery, neck pain improvement was only modest in both groups. Efficacy benefits cannot be directly compared between conservative and surgical treatment since patients were not randomly assigned to treatment. These data, however, do support good improvement in appropriate patients treated with conservative therapy. ADL: activities of daily living. (Based on Heckmann JG, *et al.*, 1999[31].)



4.18 Long-term outcome in patients with cervical radiculopathy randomized to surgical or conservative therapies. Eighty-one patients with cervical radiculopathy without myelopathy were prospectively randomized to receive decompressive surgery, physical therapy (including passive modalities, traction, and stretching and strengthening exercises) for 3 months, or use of a soft cervical collar worn at least during the daytime for 3 months. Pain was assessed at baseline and 4 and 12 months after treatment initiation. Disability was also assessed after 12 months. Although pain reduction was superior with surgery at the first post-treatment assessment, outcome was similar after 1 year. (Based on Persson LG, *et al.*, 1997[32].)

injections may need to have injections repeated using sonographic guidance. Surgical intervention is typically reserved for disabling impingement or rotator cuff tears that have failed to respond to conservative therapy.

De Quervain's tenosynovitis

De Quervain's syndrome typically responds to conservative therapy with NSAIDs, splints, and/or local steroid injections. A large, retrospective study evaluated treatment outcome from conservative therapy for De Quervain's syndrome, based on initial symptom severity (N=300)[37]. NSAIDs plus splints provided complete relief for 88% with initially mild symptoms, 35% with moderate symptoms, and 25% with severe symptoms. Injections relieved symptoms in 100% with mild symptoms, 80% with moderate symptoms, and 76% with severe symptoms. Surgical decompression is rarely needed and is typically reserved for patients failing to achieve adequate relief from more conservative measures.

Carpal tunnel syndrome

Postural correction and night time splints typically improve carpal tunnel symptoms. Local steroid injections may also be considered, especially when motor loss is present. Patients who are not candidates for injections may benefit from iontophoresis with corticosteroids. Physical therapists administering iontophoresis use electric current to deliver topically applied medications to soft tissues. A prospective study in 30 patients randomized to either corticosteroid

iontophoresis every other day for 1 week or a single steroid injection showed benefit from both treatments, although injection led to superior improvement[38]. Pain reductions 2 and 8 weeks after treatment, respectively, were 29% and 51% with iontophoresis and 27% and 71% with injection. The number of patients experiencing paresthesia decreased between pretreatment and 8 weeks after therapy from 96% to 35% with iontophoresis and 95% to 15% with steroid injection.

Two recent studies compared outcome in patients experiencing carpal tunnel syndrome for <1 year who were prospectively randomized to treatment with 1–2 steroid injections or surgical decompression. In one study (N=50), improvement in symptoms and nerve conduction occurred in patients with either treatment, although benefits were greater with surgery than after a single steroid injection[39]. In this same study, grip strength improved in patients receiving injections and worsened slightly after surgery. In a similar study (N=101), injections produced better short-term symptomatic relief and comparable long-term results to surgical decompression[40]. In this second study, patients could receive a second injection after 2 weeks, with 84% receiving two injections. These studies suggest that both injections and surgical decompression effectively relieve carpal tunnel symptoms; however, injections may produce better results when patients are offered a second injection after 2 weeks rather than using only a single injection.

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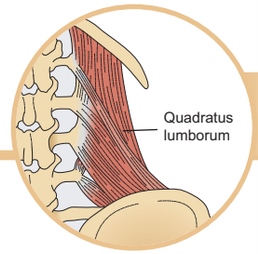
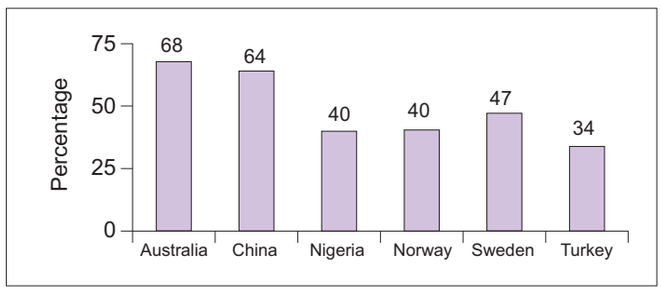


Back and lower extremity pain

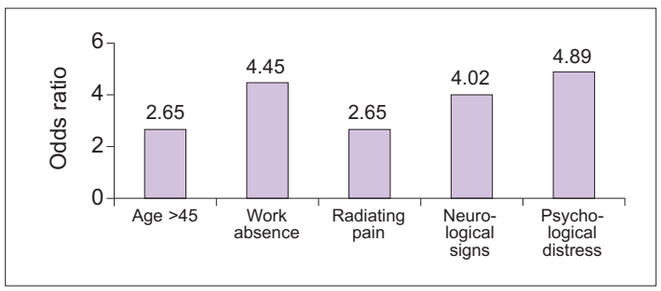
Introduction

The back and lower extremities are areas commonly affected by chronic pain. Lower extremity pain may occur in conjunction with back pain (as radicular, referred, or radiating pain) or as isolated musculoskeletal or neuropathic pain. Back pain with or without associated lower extremity pain occurs frequently and is often disabling. Using data from two large, national surveys in the United States, low back pain during the preceding 3 months was endorsed by one in four adults ≥18 years old and one in three adults after age 45[1]. The prevalence of back pain varies by region, with typically higher prevalence among developed countries (**5.1**)[2–6].

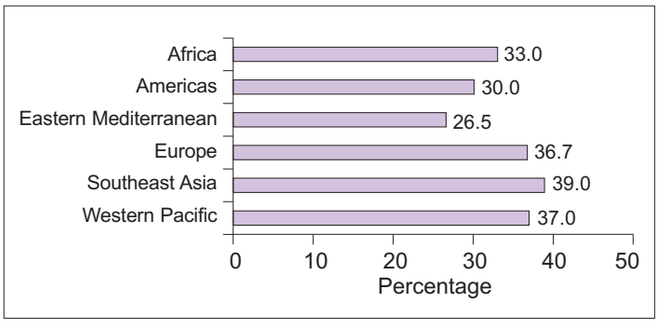
Most episodes of acute back pain resolve, with the greatest reduction in pain expected during the first 3 weeks[7]. Pain becomes chronic for about one in four patients. Persistent back pain can be predicted by patient demographics, physical examination, and psychological distress (**5.2**).



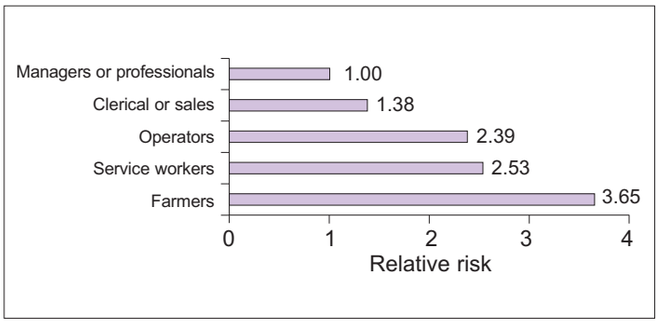
5.1 World-wide 1-year prevalence of low back pain. (Based on Ihlebæk C, *et al.*, 2006[2]; Oksuz E, 2006[3]; Walker BF, *et al.*, 2004[4]; Barrero LH, *et al.*, 2006[5]; Omokhodion FO, 2002[6].)



5.2 Predictors of nonrecovery from acute back pain after 3 months. Adult patients with acute low back pain for <3 weeks who contacted a primary care health provider for the first time for a back pain complaint were followed weekly for the first month and then at 3 months. Significant predictors of persistent low back pain after 3 months are shown. Work absence was significant when people lost 4 or more days during the preceding month. Neurological signs were associated with the development of chronic pain when two or more of the following were abnormal: straight leg raise, knee or ankle reflex, sensation, and strength in the thigh or foot. (Based on Grotle M, *et al.*, 2005[7].)



5.3 Percentage of chronic low back pain attributable to occupation by region. (Based on Punnett L, *et al*., 2005[8].)



5.4 Relative risk of low back pain based on occupation. Compared with managers and professionals, all other occupations evaluated had a higher relative risk of low back pain based on occupation. Operators include drivers, construction and manual labour workers, plumbers, carpenters, and automobile mechanics. Service workers include nurses and other hospital workers, warehouse and stock workers, baggage handlers, waitresses, and custodians/caretakers. (Based on Punnett L, *et al*., 2005[8].)

Occupation is another important risk factor for chronic back pain, with 37% of low back pain attributable worldwide to occupational factors[8]. Occupational contribution is highest in Europe, Southeast Asia, and the Western Pacific (**5.3**). Risk varies among occupation types, with lowest risk in managerial and professional jobs and highest risk among farmers (**5.4**).

Assessing back and lower extremity pain

Chronic back pain is commonly caused by musculoskeletal or neurological abnormalities. Other medical conditions, including vascular, gastrointestinal, and gynecological pathology may also result in back pain (*Tables 5.1*, *5.2*). Therefore, the physical examination must include a general medical screening, as well as abdominal and gynecologic evaluations.

Signs and symptoms help differentiate among common causes of back pain. Neurological symptoms or deficits suggest additional evaluations for spinal, root, or peripheral nerve abnormalities. Attention to factors that aggravate or relieve pain, localization of pain to the back or radiation to the lower extremity, and response to postural changes can help distinguish common myofascial, mechanical, inflammatory, radicular, and stenotic pain syndromes in the lumbar spine (*Table 5.3*).

Table 5.1 Nonmusculoskeletal and non-neurological causes of back pain

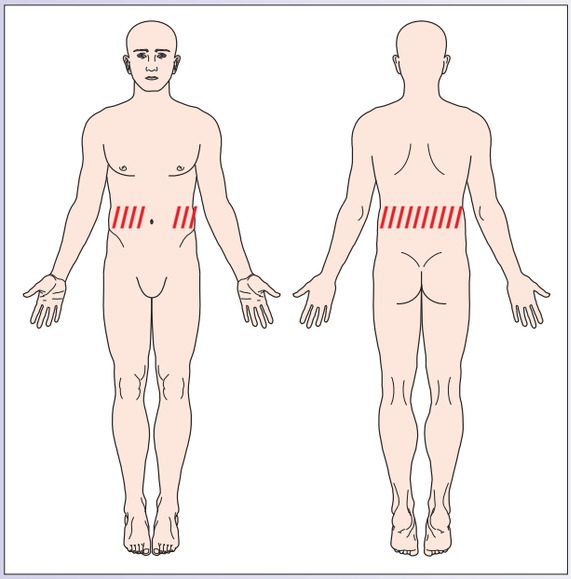
- Abdominal aortic aneurysm or aorto-iliac disease
- Abscess
- Endometriosis or other gynecological pathology
- Gastric or duodenal ulcer
- Kidney disease
- Neoplasm
- Pancreatitis or pancreatic tumor
- Sickle cell crisis

Table 5.2 Common causes of thoracic pain

- Myofascial pain
- Osteoporosis with vertebral fracture
- Metastatic neoplasm
- Postherpetic neuralgia

Case presentation

A 65-year-old woman complains of a girdle-like squeezing around her waist for the last 1 month, which has been getting progressively worse. Her pain drawing (below) shows a band of pain circling her abdomen. Reflex testing was limited due to patient guarding and sensation was slightly decreased bilaterally below the waist.



Thoracic pain forming a band on one side or around the entire thorax is suspicious for neurological pain, such as postherpetic neuralgia (PHN) or, as in this case, metastatic cancer. A survey of patients with malignant spinal cord compression found complaints of localized back pain and/or spinal nerve root pain in 94%, typically experienced as a band around the chest or abdomen[9]. Pain was generally described as severe and progressive, and in 66% of cases bilateral. Coughing, bending, and/or sneezing aggravated pain for about 40% of patients. Unfortunately, patients typically waited about 3 weeks before reporting pain to their doctors, who typically did not diagnose metastatic disease until about 3 months after symptom onset. At the time of diagnosis, only 18% of patients were still ambulating independently. Once patients lost ambulation, it was rarely regained. MRI is the most effective tool for diagnosing spinal cord compression.

Table 5.3 Differentiating common causes of chronic lumbar pain

Myofascial	*Mechanical*	*Inflammatory*	*Radiculopathy*	*Stenosis*
Pain with rest and activities	Pain worsens with activity	Pain improves with activity	Pain with rest and activities	Pain typically with walking, relieved by sitting
Nondermatomal pain*	Nonradiating pain	Nonradiating pain**	Radiates to sensory dermatome; dermatome may be numb or tingly	Pain, numbness, and cramping in both legs with walking
Muscle spasm may restrict active lumbar flexion, extension, and side bending	Restricted lumbar flexion with passive and active testing	Restricted lumbar flexion with passive and active testing	Aggravation by lumbar flexion (e.g. pain with straight leg raise); relief with lumbar extension	Aggravation with lumbar extension (e.g. walking downhill); relief with lumbar flexion (e.g. stooped gait)

*Stimulating myofascial trigger points may lead to pain radiating in nondermatomal patterns
**Alternating buttock pain may occur with sacroiliitis

Myofascial lumbar pain

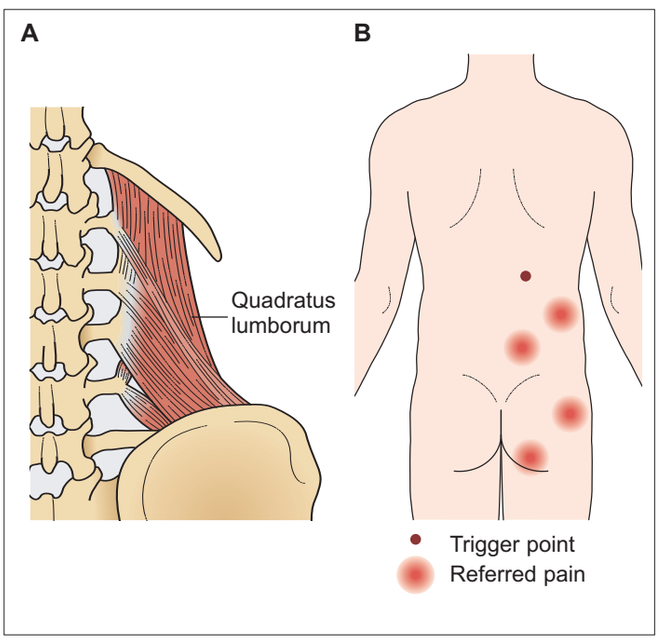
Pain of the muscles and surrounding soft tissues is termed myofascial pain. Myofascial pain is characterized by localized areas of muscle spasm and discrete points of tenderness within tight muscles, called trigger points. Trigger points are locally tender (latent trigger points) and may refer pain in predictable patterns (active trigger points) that assist in diagnosis. Myofascial pain affecting the quadratus lumborum muscle, quadratus lumborum syndrome, is one of the most common causes of low back pain. The quadratus lumborum muscles on either side of the

spine contract to cause lateral bending (**5.5**). Pain typically occurs in the small of the back and may be referred into the buttocks.

Piriformis syndrome is another common myofascial pain condition. The piriformis muscle connects the hip to the greater trochanter, resulting in hip stability and allowing external rotation (**5.6**). Pain usually occurs in the lateral buttocks with referral to the lower back and hip.

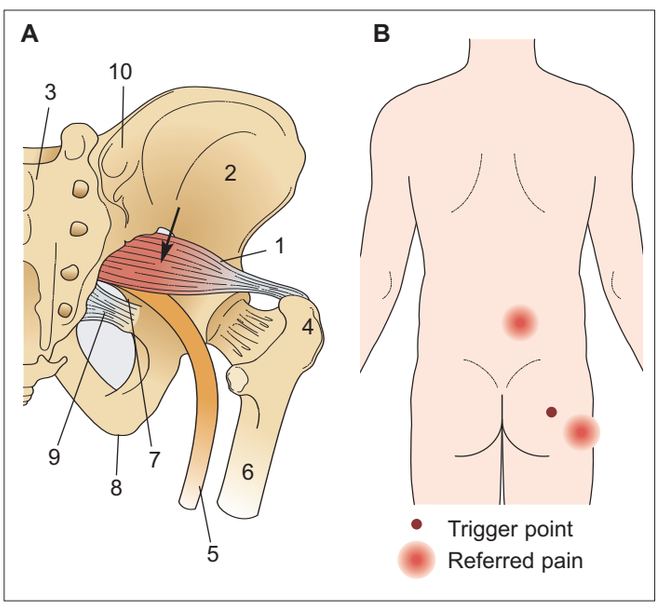
Mechanical and inflammatory lumbar pain

Restrictions of both active and passive motion in the joints in the back suggest mechanical or inflammatory pain. Pain and restrictions in joint movement in the lower back are usually caused by mechanical pain, such as degenerative arthritis. Less commonly, chronic low back pain and restricted movement may be caused by an inflammatory spondyloarthropathy. Pain and stiffness are characteristically worse later in the day with mechanical pain, aggravated by activity or exercise. Inflammatory pain and stiffness, conversely, are worse in the early morning or after resting in bed, improving with activity.

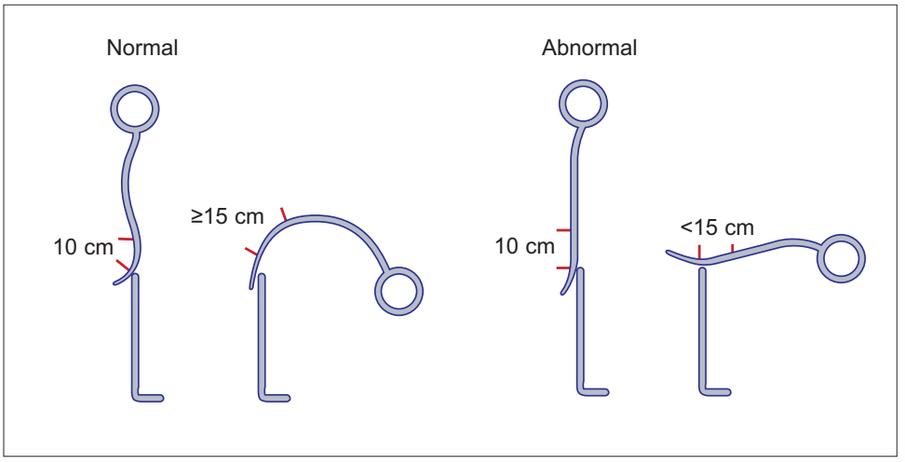


5.5 Quadratus lumborum syndrome. The quadratus lumborum muscle connects at the 12th rib, iliac crest, and lumbar vertebrae, with muscle contraction causing lateral bending of the lumbar spine (**A**). Quadratus lumborum trigger points occur at the waistline and may refer pain into the upper or lower buttocks (**B**).

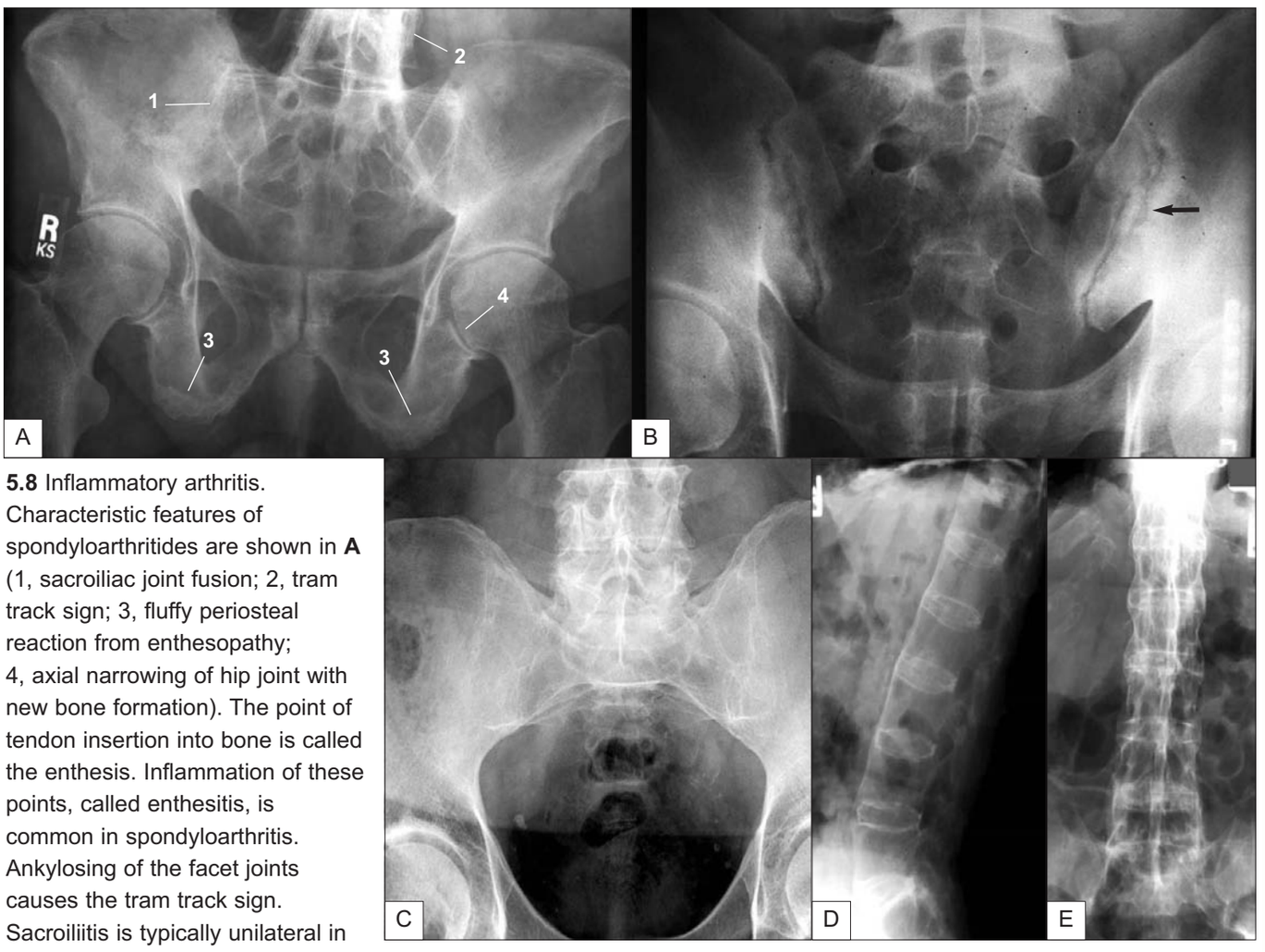
Inflammatory spondyloarthritides include ankylosing spondylitis, psoriatic arthritis, reactive arthritis (Reiter's syndrome), and inflammatory bowel-related arthritis. While there are no specific tests for spondyloarthritides, patients often have blood tests showing elevation of inflammatory markers, like CRP, anemia of chronic disease, and the absence of rheumatoid factor. A modified Schober's test is a nonspecific measure of reduced spine mobility (**5.7**). The most common spondyloarthritis is ankylosing spondylitis, which typically becomes symptomatic in young adulthood. Patients experience inflammatory changes in the spine and sacroiliac joints, with eventual fusion of the spine. While X-ray changes may be dramatic, patients typically display clinical symptoms for 5–10 years before radiographic changes are seen (**5.8**).



5.6 Piriformis syndrome. The piriformis muscle (1) attaches from the inner ileum (2) and sacrum (3) to the greater trochanter (4), providing hip stability and external rotation (**A**). Trigger points occur on the buttocks and may refer into the lower back or hip (**B**). The sciatic nerve (5) may become compressed beneath the piriformis muscle, resulting in leg pain. A piriformis trigger point is often performed by drawing a line from the posterior superior iliac spine to the greater trochanter and injecting immediately lateral to the midpoint of this line. The needle goes through the muscle at the site indicated by the arrow and under the muscle belly, with the injection spreading out under the muscle. 6: femoral shaft; 7: sciatic notch; 8: ischial tuberosity; 9: sacrospinous ligament; 10: posterior superior iliac spine.



5.7 Modified Schober's test. The centre of the patient's spine around L5, located between the posterior superior iliac spines, is marked. A mark is placed 10 cm above this point. The patient is asked to bend forward as far as possible and the distance between the two points is remeasured. This distance should now measure ≥15 cm. A new measure <15 cm suggests restricted lumbar spine flexion.

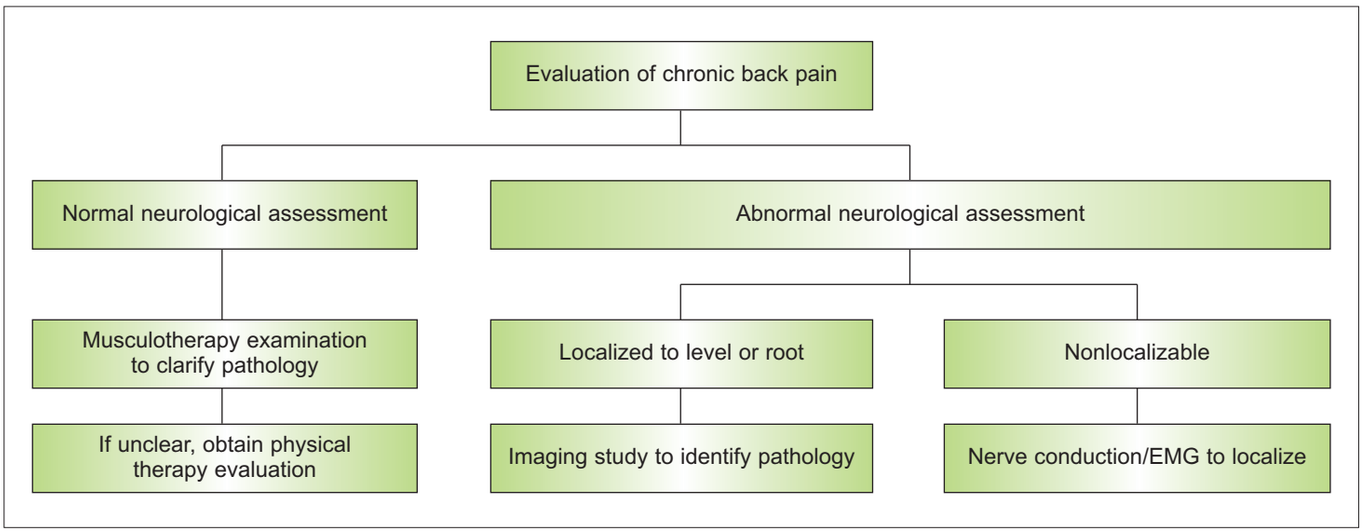


5.8 Inflammatory arthritis. Characteristic features of spondyloarthritides are shown in **A** (1, sacroiliac joint fusion; 2, tram track sign; 3, fluffy periosteal reaction from enthesopathy; 4, axial narrowing of hip joint with new bone formation). The point of tendon insertion into bone is called the enthesis. Inflammation of these points, called enthesitis, is common in spondyloarthritis. Ankylosing of the facet joints causes the tram track sign. Sacroiliitis is typically unilateral in psoriatic and reactive arthritis, as seen on the left in **B** (arrow), and bilateral in ankylosing spondylitis and inflammatory bowel-related spondyloarthritis (**C**). The lateral view of the spine (**D**) shows the square appearance of the vertebral bodies and 'bamboo spine' pattern characteristic of ankylosing spondylitis. The AP view (**E**) shows a dense central line resulting from ossification of supraspinous and interspinous ligaments, called the dagger sign.

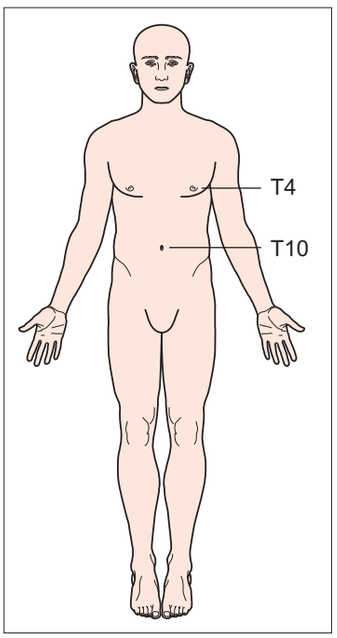
Neurological lumbar and lower extremity pain

A neurological assessment of back pain patients is necessary to help differentiate musculoskeletal from neurological causes of chronic back pain (**5.9**). Neurological symptoms or signs suggesting radiculopathy or myelopathy, such as pain with straight leg raise testing, loss of motor strength or reflexes, and sensory loss or allodynia, warrant additional testing. Patients with motor or sensory findings suggesting a localizable spinal level or nerve root should be evaluated with a targeted imaging study, such as CT or MRI. When a particular level or root cannot be localized, nerve conduction studies with EMG should be considered.

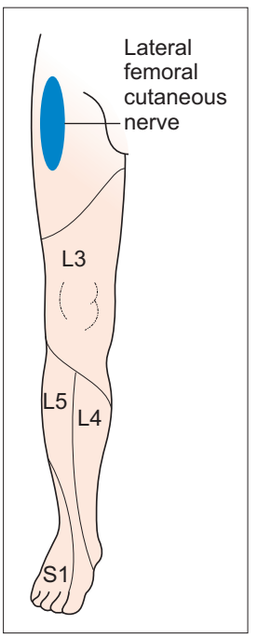
Sensory dermatomes commonly affected by spinal pathology are shown for the thoracic spine (**5.10**) and lumbar roots (**5.11**). Patterns of expected strength, reflex, and sensory loss for commonly compressed roots in the low back are shown in *Table 5.4*.



5.9 Algorithm for evaluating chronic back pain. EMG: Electromyography.



5.10 Thoracic sensory dermatomes. Landmarks to identify thoracic dermatomes are the nipples for T4 and the umbilicus for T10.



5.11 Neural patterns of lower extremity sensory loss. Skin areas served by nerves commonly affected with compression injury are highlighted. The lateral femoral cutaneous nerve passes through the groin and provides sensation to the upper and outer thigh. Compression by the inguinal ligament commonly occurs with postural changes occurring with pregnancy and obesity. Lateral femoral nerve compression results in pain and numbness in the area shown in blue, a condition termed meralgia paresthetica. Skin areas around the knee, lower leg, and foot area are supplied by lumbar nerve roots. Compression from individual herniated discs, for example, results in tingling and numbness in the highlighted areas.

Table 5.4 Neurological assessment for common lumbar radiculopathies

Nerve involved	*Motor loss*	*Reflex loss*	*Sensory loss*
L3	Knee extension	Knee reflex	Anterior medial thigh
L4	Knee extension	Knee reflex	Medial lower leg
L5	Foot dorsiflexion: walking on heels	None	Lateral lower leg and great toe
S1	Foot plantar flexion: walking on toes	Ankle jerk	Lateral foot and sole

Lumbar herniated discs usually affect the nerve for the vertebra below the herniation. For example, an L4 radiculopathy usually occurs when the L3–L4 disc is herniated

Understanding imaging studies

Imaging studies of the spine are notorious for revealing clinically meaningless abnormalities. Spine MRI scans of asymptomatic controls show radiographic abnormalities in most adults (*Table 5.5*)[10–12]. As expected, the prevalence of radiographic abnormalities increases with age. Significantly, a 7-year prospective study failed to link radiographic changes to the subsequent development of clinical low back pain[13].

Case presentation

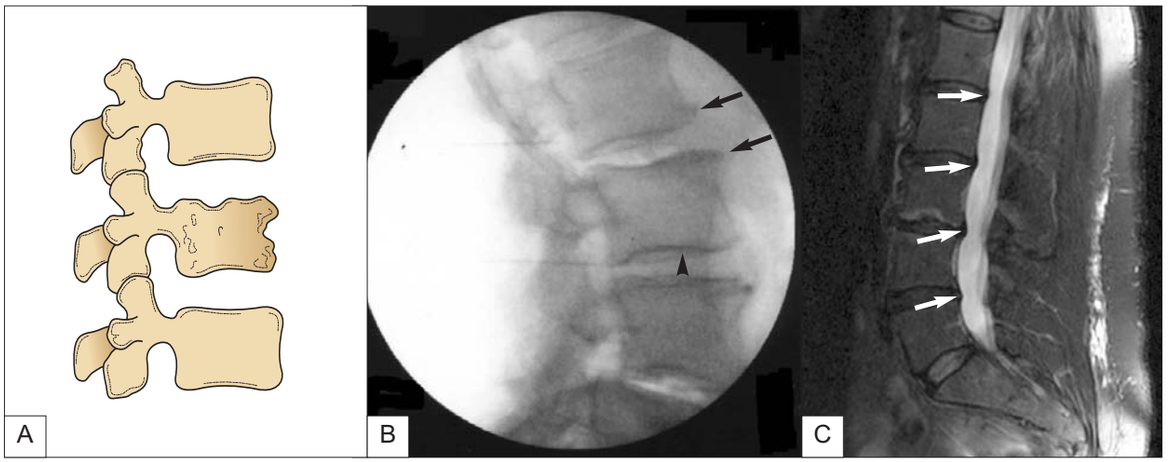
A 54-year-old construction worker presented with a 5-year history of disabling, focal low back pain that began after a lifting injury at work. There were no neurological deficits. His initial imaging studies showed bulging and herniated discs between L4/5 and L5/S1. Pain continued unchanged after discectomy at both levels. Two years later, a herniated disc was seen at L3/4. Pain worsened after a second discectomy with fusion. He presents for a second opinion after his most recent imaging study diagnosed spinal stenosis and a third operation was suggested.

Persistent low back pain after surgery or 'failed back syndrome' is frustrating for patients expecting good surgical recovery and is associated with substantial disability. Good surgical outcome is maximized by selecting patients with clinical evidence of neural compression rather than a radiographic diagnosis. Understanding the range of clinically unimportant abnormalities on imaging studies can help avoid unnecessary and unhelpful surgical procedures.

Table 5.5 Spine MRI abnormalities in asymptomatic adults

Abnormality	***Prevalence in normal adults (%)***
Thoracic spine	
Degenerative changes	56
Disc bulge	53
Disc herniation	37
Annular tear	58
Spinal cord deformation	29
Scheuermann endplate irregularities or kyphosis	38
Lumbar spine	
Disc bulge	52
Disc herniation	24
Stenosis	4

(Based on Jensen MC, *et al.*, 1994[10]; Boden SD, *et al.*, 1990[11]; Wood KB, *et al.*, 1995[12])

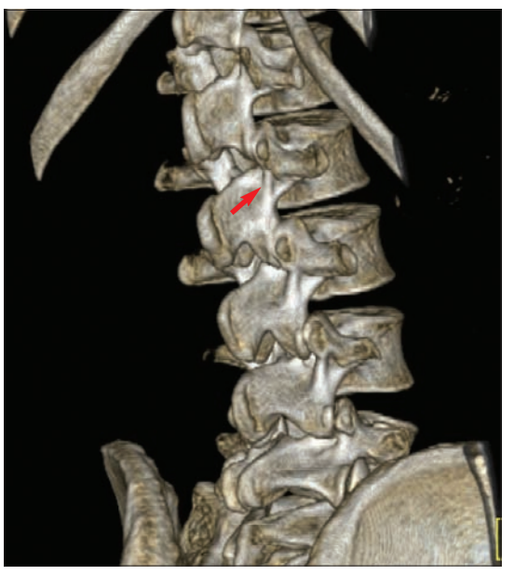


5.12 Spondylosis. **A**: Degenerative changes of the vertebral body; **B**: X-ray showing spondylosis in the lumbar spine, with scalloping of the vertebral body (arrowhead) and anterior bony growth or osteophytes (arrows); **C**: T2-weighted lumbar MRI showing spondylosis with multilevel scalloping of the spinal canal (arrows).

Spine abnormalities unrelated to clinical symptomatology are similarly identified with CT scanning. In a group of 52 controls, 35% had abnormal lumbar studies, with the percentage of abnormalities increasing to 50% after the age of 40[14]. In those controls younger than 40, 20% had CT scans that revealed herniated discs.

Selecting candidates for imaging studies

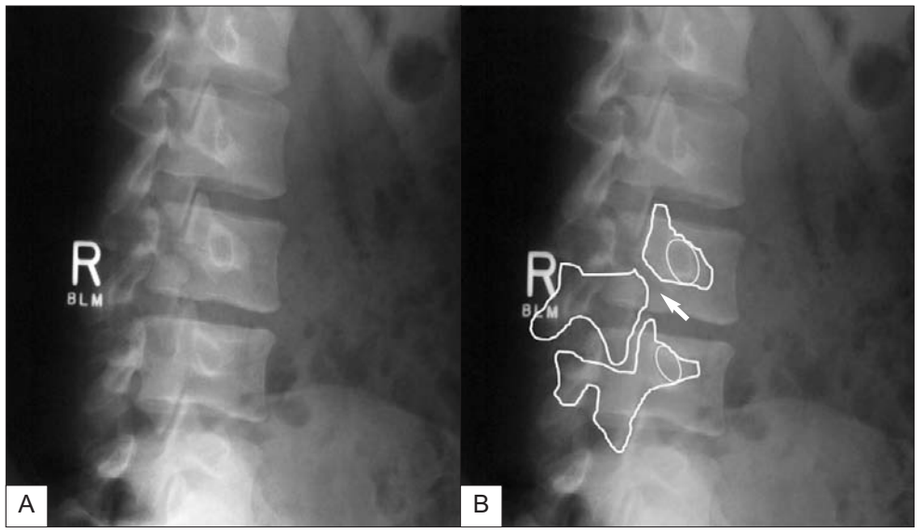
According to recent recommendations from the American College of Physicians and American Pain Society, diagnostic testing beyond a history and physical examination should not be routinely performed in patients with nonspecific, chronic low back pain[15]. Patients with acute low back pain may need imaging studies if they have a history of trauma, infection, or cancer or their examination reveals a neurological deficit. Most patients with chronic low back pain require plain X-rays, including assessment with flexion and extension, to evaluate possible mechanical factors. CT or MRI testing is best reserved for patients with a strong clinical suspicion of myelopathy or radiculopathy (**5.9**).



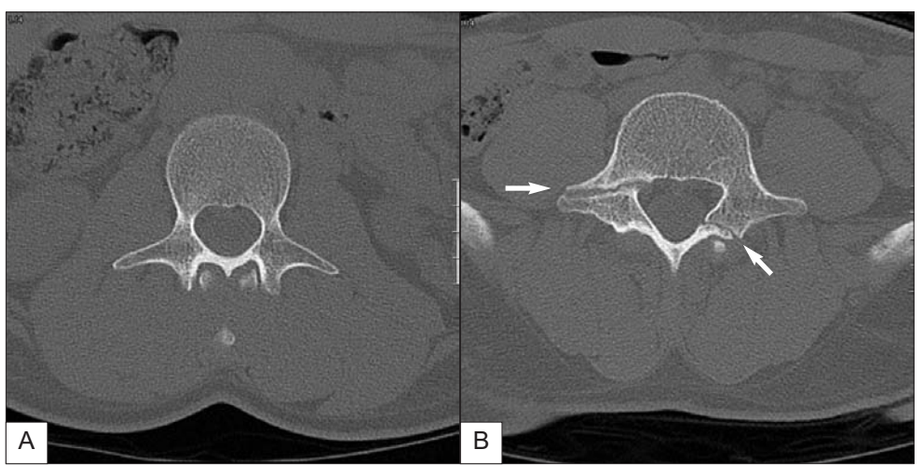
5.13 Oblique lumbar spine anatomy. This computer-enhanced image of the lumbar spine shows bony anatomy from the lateral oblique angle. Notice the appearance of the pars interarticularis, which forms the neck of the 'Scottie dog' image seen on X-ray (arrow).

Interpreting imaging studies

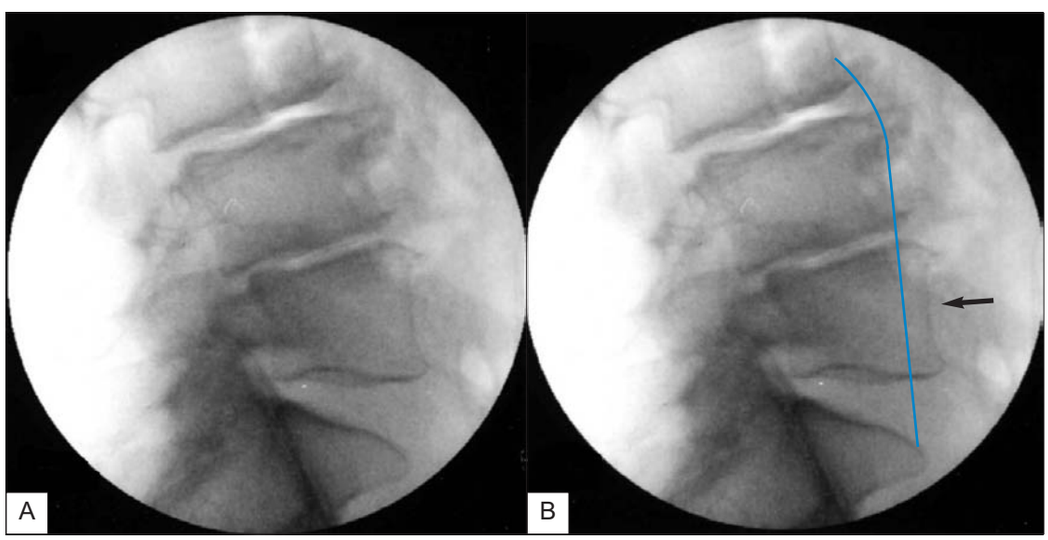
Plain X-rays can effectively identify mechanical abnormalities causing chronic back pain, including spondylosis, spondylolysis, and spondylolisthesis. Spondylosis is a degeneration of vertebral disc spaces, typically occurring in patients with osteoarthritis (**5.12**). Spondylolysis is separation of the pars interarticularis, recognized as the neck of the 'Scottie dog' on an oblique X-ray of the lumbar spine (**5.13**–**5.15**). Spondylolysis may result in abnormal vertebral movement or spondylolisthesis. Spondylolisthesis is a forward movement of one of the vertebrae, typically L5 in children and L4 in adults. Spondylolisthesis is graded from 1 to 4, depending on the amount of slippage (**5.16**, **5.17**, *Table 5.6*). Grades 1 and 2



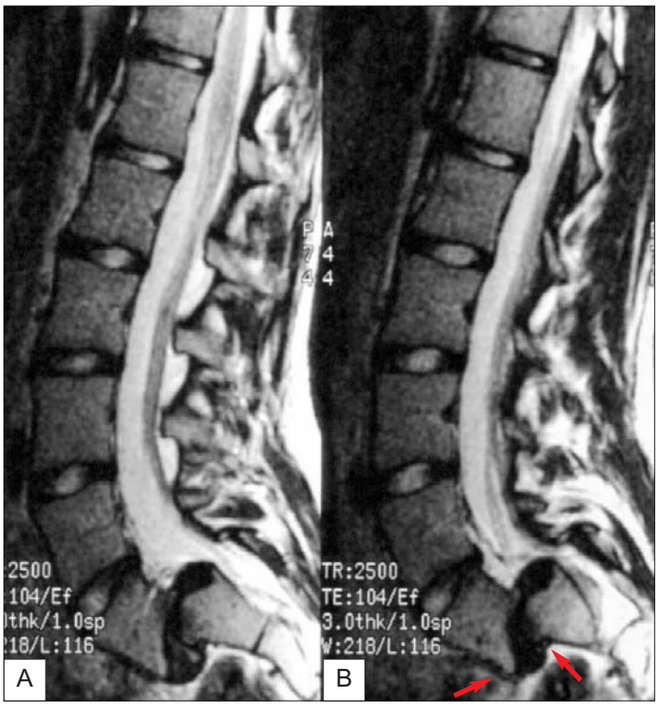
5.14 Oblique lumbar spine X-ray (**A**) showing 'Scottie dog' appearance of defective and intact pars interarticularis; **B**: marked X-ray of the same oblique lumbar spine highlighting spondylolysis defect. The lower dog is intact, while the upper dog shows a characteristic defect in the pars interarticularis, missing bone at the collar area (arrow).



5.15 CT showing spondylolysis of lumbar spine. **A**: Normal lumbar vertebral body; **B**: L5 spondylolysis with defects in the pars interarticularis on the left and pedicle and transverse process on the right (arrows) in the same patient.



5.16 Grade 1 spondylolisthesis of L5. **A**: Lateral X-ray; **B**: marked X-ray with blue line showing the expected location of the anterior aspect of L5 vertebral body. The arrow shows the actual location, clearly in front of a line connecting the anterior aspects of the vertebra above and the sacrum below.



5.17 MRI of grade 3 spondylolisthesis of L5 with T1- (**A**) and T2-weighted (**B**) images. Arrows highlight marked anterior displacement of L5 on S1.

Table 5.6 Grading system for spondylolisthesis

- Grade 1: ≤25% displacement
- Grade 2: >25–50% displacement
- Grade 3: >50–75% displacement
- Grade 4: >75–100% displacement

Case presentation

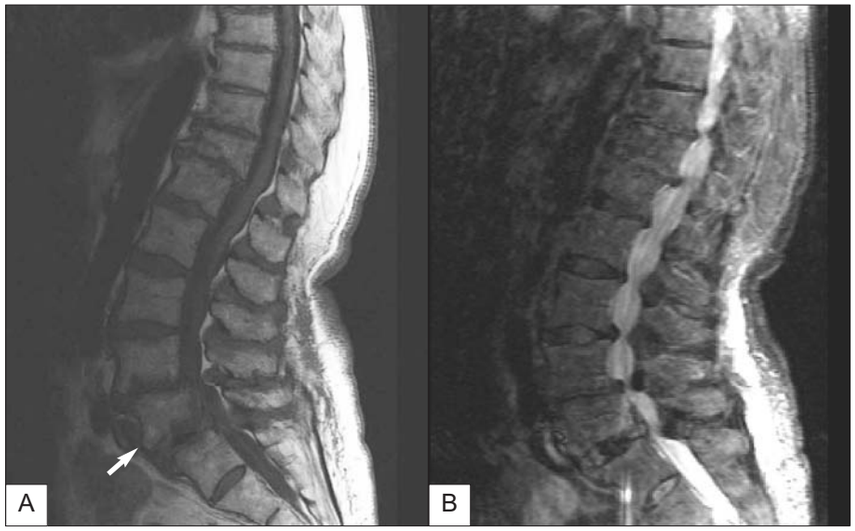
A 72-year-old man with mild heart disease and high cholesterol is brought to the clinic by his wife, who reports that he has become depressed. She complains that he never wants to go out of the house anymore, complaining of back pain after walking a few blocks or going shopping for more than 15 minutes. He does better in the grocery store, but still complains of back pain before she finishes their shopping. He says he feels better when he can sit down, and spends excessive time watching television instead of the usual bird watching and golfing that he used to enjoy. His physical examination is normal, with no pain while walking up and down the hallway, touching his toes, or with straight leg raise testing. There is no loss of sensation, strength, or reflexes. The feet are well perfused.

This patient's story is characteristic of spinal stenosis. Standing straight and back extension (such as with walking downhill or bending backward) reduce the diameter of the spinal canal, causing severe pain. Back flexion widens the canal, relieving pain. For this reason, lumbar stenosis pain is typically relieved with sitting, bending forward, or a stooped posture, such as when pushing a shopping cart.

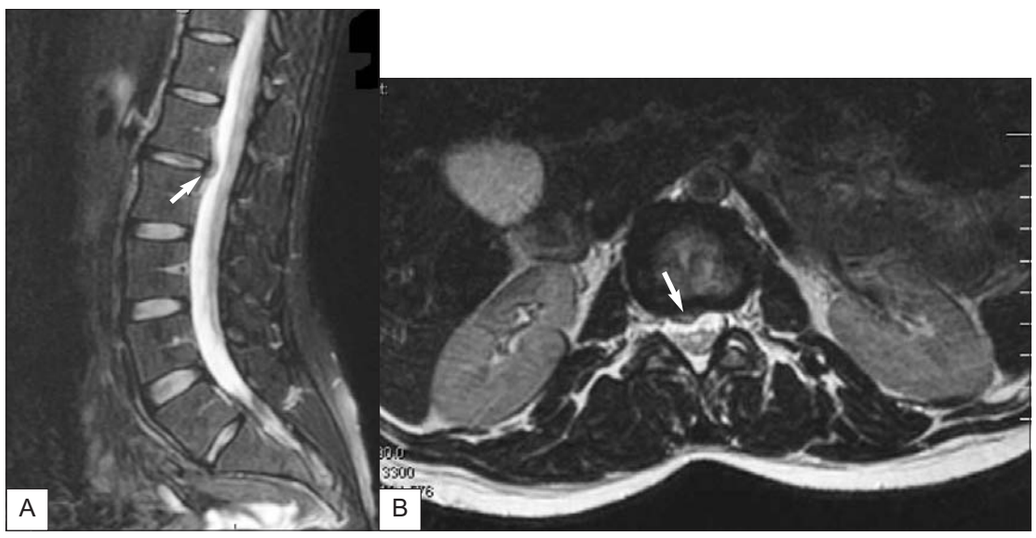
are typically managed with physical therapy. Grades 3 and 4 may result in neural impingement and may require surgical correction. Pediatric spondylolisthesis is typically related to a congenital malformation, while adult changes often occur as part of degenerative processes, such as osteoarthritis. Spondylolisthesis may also occur due to a stress fracture (e.g. from gymnastics), trauma, or bone disease.

MRI studies define neural tissue in patients with suspected radiculopathy or myelopathy more clearly than CT. Bony structures are less well defined with MRI compared with plain X-rays. Due to the high prevalence of MRI abnormalities seen in asymptomatic patients, requests for MRI studies should include clinical information, such as 'patient with right L5 radiculopathy' or 'patient with depressed left knee jerk reflex', to maximize the clinical relevance of radiological interpretation. Sagittal images often reveal multiple levels of clinically asymptomatic bulging discs (**5.18**), while axial or cross-sectional images can reveal important lateral impingement on nerve roots or central compression of the spinal cord or roots (**5.19**).

MRI images can also effectively confirm the presence of spinal stenosis in patients with posturally-related claudication. A detailed clinical history distinguishes neurological from vascular claudication, which can be confirmed by examining the relationship of back pain to postural changes and the absence of vascular abnormalities (see Case presentation).



5.18 Marked degenerative changes on lumbar MRI. **A**: T1-weighted image; **B**: T2-weighted image showing severe spondylosis at multiple levels, with osteophytes, disc bulges, and scalloping of the spinal canal. Spondylolisthesis is also noted at L4–5 (**A**, arrow).

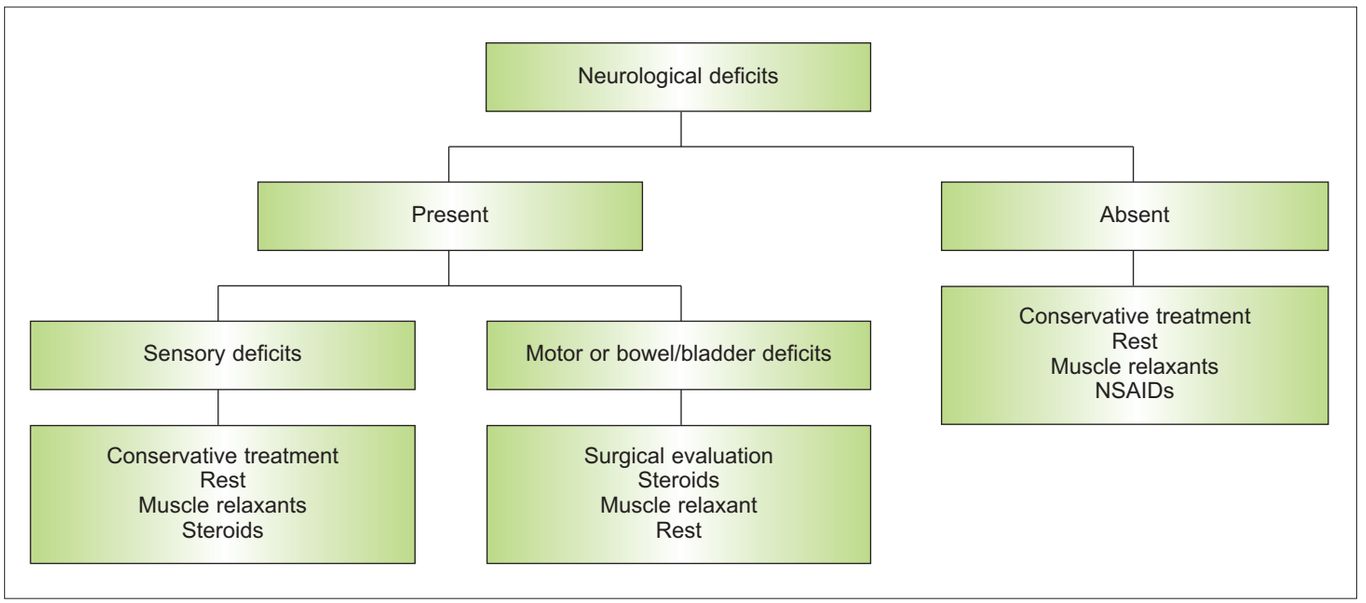


5.19 MRI of herniated disc. Sagittal (**A**) and axial (**B**) lumbar MRI showing right paracentral herniation at L1 (arrows). The compression of neural structures suggested on the sagittal view is confirmed on the cross-sectional image.

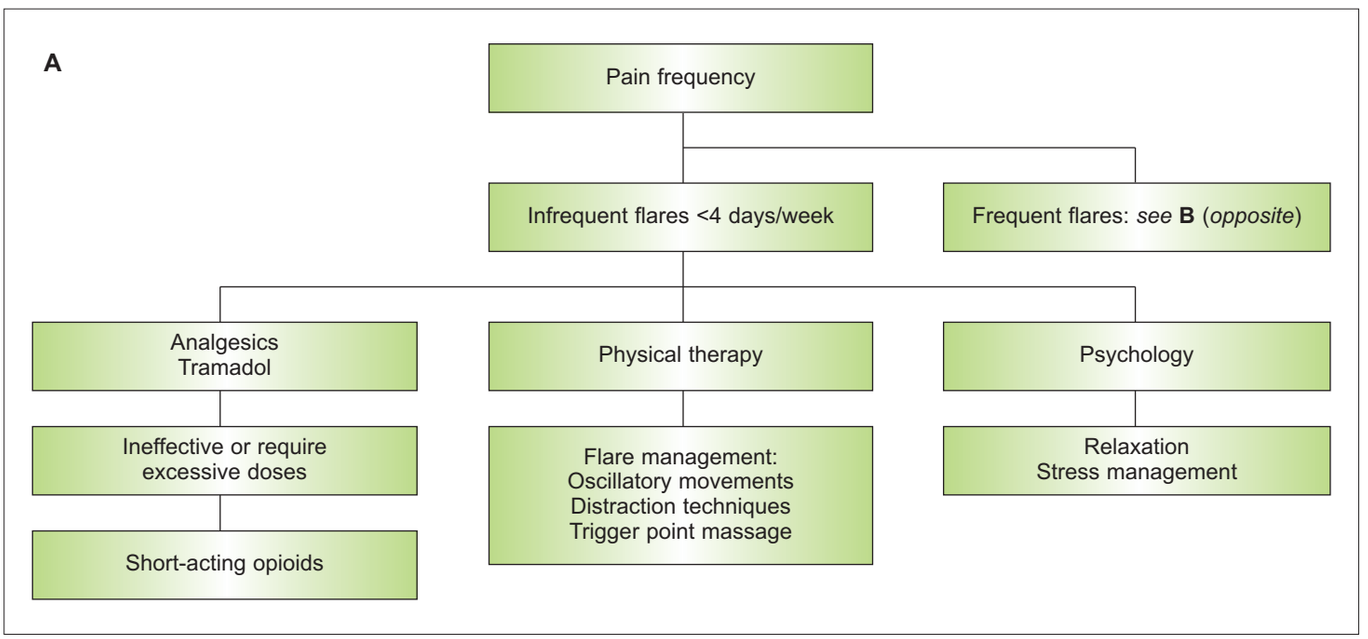
Treating chronic low back pain

Acute low back pain should be evaluated for the presence of neurological deficits, suggesting radiculopathy or myelopathy (**5.20**). In the absence of neurological abnormalities, conservative treatment with symptomatic therapy and activities permitted as tolerated is more effective than bed rest or physical therapy exercises[16].

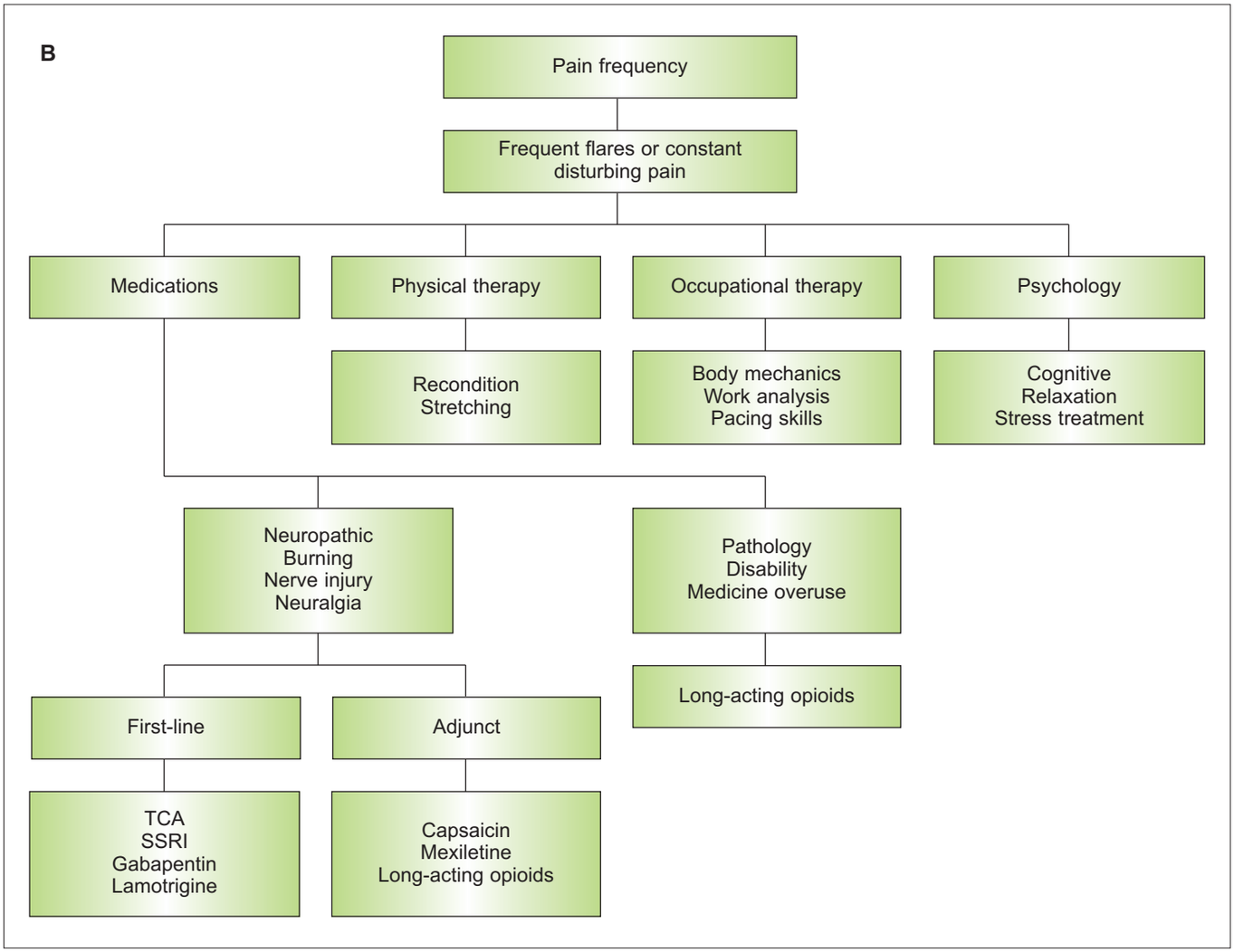
Disabling chronic low back pain is typically best managed with multidisciplinary treatment, involving a combination of medical treatments, psychological training, physical therapy, and occupational therapy focused on the restoration of physical functioning (**5.21**). A systematic review of 10 randomized clinical trials assessing multidisciplinary treatment for chronic low back pain reported positive benefits for improving short- and long-term work participation and quality of life, without benefit for significant pain reduction[17]. A more positive effect was shown with pain reduction for studies using more intensive therapy, requiring at least 30 hours of training per week. Therefore, patients with recalcitrant pain complaints and associated disability will often require intensive, multidisciplinary treatment, with a primary target goal of return to work rather than pain reduction. In addition, inclusion of psychological pain management skills, such as relaxation, biofeedback, and cognitive behaviour therapy, in



5.20 Algorithm for treating acute low back pain. Acute back pain without neurological deficits will typically resolve with conservative, symptomatic treatment. Patients with neurological deficits often benefit from a short course of steroids and muscle relaxants. Surgery should be considered when a motor deficit or bowel/bladder impairment is present. NSAID: nonsteroidal anti-inflammatory drug.



5.21 A, B Chronic back pain management. Selection of specific therapies is initially guided by the frequency of disabling pain flares. Individual therapies can target unique pain features, such as the presence of neuropathic pain, deconditioning, work disability, and depression. Patients without significant depression or anxiety benefit from psychological intervention that focuses on training in pain management techniques. SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressant.



a multidisciplinary treatment programme can maximize reduction in pain interference and functional disability[18].

Patients with myofascial dysfunction and restricted spine mobility will require targeted physical therapy. Occupational therapy may also be beneficial. Patients with ankylosing spondylitis may require anti-inflammatory therapy (e.g. NSAIDs and tumor necrosis factor-alpha antagonists).

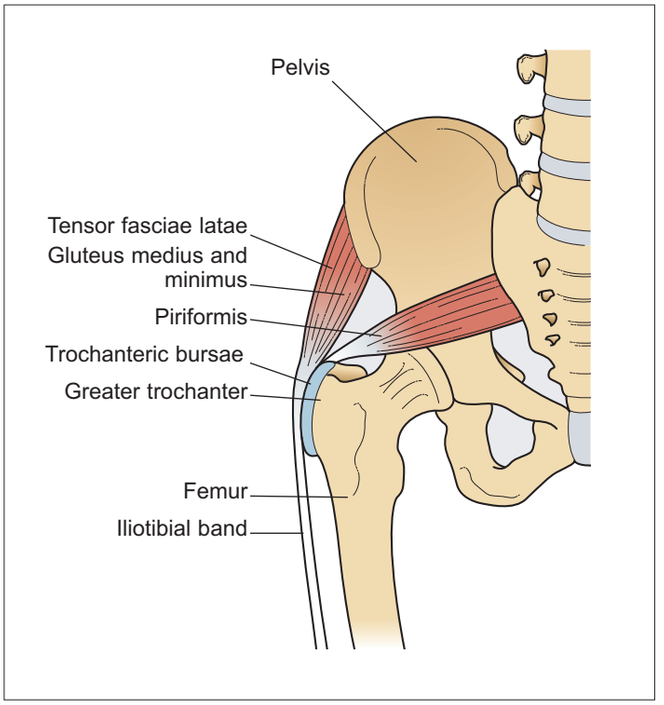
Opioids provide limited effectiveness for chronic back pain, with misuse/abuse behaviours reported in up to 24% of patients[19]. A meta-analysis of pooled data from comparative studies with opioids in chronic back pain patients showed no significant difference in pain reduction with opioids compared with nonopioid analgesics or placebo.

A systematic review of invasive procedures and surgery, using data from the Cochrane reviews and European management guidelines, determined that facet joint, epidural, and trigger point injections had not clearly demonstrated efficacy for chronic low back pain[20]. Benefit from targeted injections is often improved when using fluoroscopic guidance. For example, in a prospective study, accurate placement of sacroiliac joint injections was successful using traditional anatomical landmarks without fluoroscopy in only 12% of patients[21]. Evidence was conflicting for the benefit of radiofrequency denervation for lumbar facet pain, and limited evidence suggested radiofrequency denervation was ineffective for discogenic low back pain. In degenerative disc disease, nondenervating pulsed radiofrequency offers treatment at the lumbar dorsal root ganglion without nerve injury. Unpublished data showed relief (measured by reduced pain, disability, and

medication use) lasting several months in about 60% of over 100 patients with severe nonradicular degenerative disc pain when treated with pulsed radiofrequency stimulation (unpublished data from author DKC). Surgical discectomy provides effective relief for carefully selected patients with sciatica from herniated discs that have failed to respond to conservative therapy. Surgical outcome is best in patients with associated lower extremity pain and clear neurological deficits. Prior to surgery, most patients should be treated with the combination of cognitive behavioural therapy and active physical therapy exercises.

Chronic hip pain

Chronic pain in the hip often accompanies low back pain. Patients reporting hip pain should be asked to point to the area of pain to clarify if the pain is localized to the hip or other areas, such as the low back or buttocks. Hip pain is often located over the greater trochanter (**5.22**). The incidence of trochanteric pain in primary care is about 2 cases per 1,000 patients per year, with most cases persisting >5 years[22]. Pain over the greater trochanter may be caused by arthritis or bursitis. Chronic sacroiliitis or lumbar radiculopathy often mimics true degenerative hip pain, with MRI showing relatively normal hip joint anatomy in these patients.



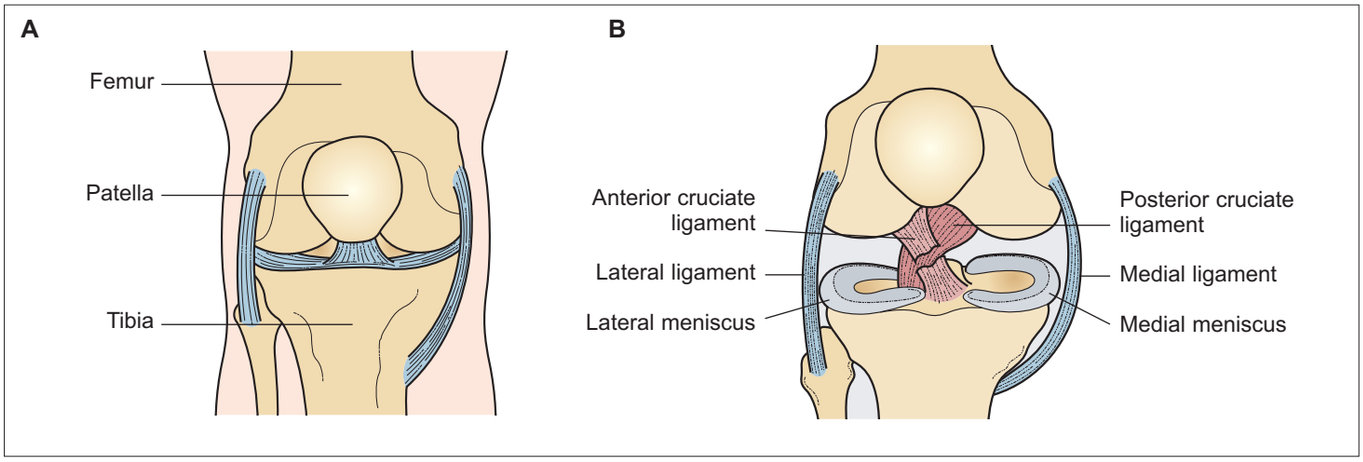
5.22 Hip anatomy. The tensor fasciae latae, gluteal, and piriformis muscles attach to the greater trochanter and provide hip stability. The tensor fasciae latae and gluteal muscles perform hip abduction and internal rotation, while the piriformis muscle produces external rotation. Four fluid-filled bursae sacs help reduce friction as muscles and their attachments move over the greater trochanter. The fibrous iliotibial band extends from the crest of the ilium to the lateral condyle of the tibia, providing lateral knee stability.

Trochanteric bursitis

Inflammation of trochanteric bursae may occur due to trauma, overuse, or associated chronic pain conditions, like arthritis. Pain is located over the lateral hip and may radiate into the thigh. Pain may be aggravated by palpation of the greater trochanter, climbing steps, rising from a chair, or prolonged standing. Treatment typically includes rest, measures to reduce inflammation (such as ice and anti-inflammatory drugs), physical therapy, and possibly local corticosteroid injections. Postural abnormalities that may aggravate trochanteric bursitis should be corrected, such as insertion of shoe inserts to correct leg length discrepancies.

Chronic knee pain

The knee is a complicated structure, with joints formed by the long bones and patella and structural support provided by ligaments and tendons (**5.23**). Injuries to the ligaments, tendons, and meniscus often result in acute knee pain, while chronic knee pain is commonly attributed to bony changes from rheumatoid or osteoarthritis and patellofemoral syndrome. Fluid-filled bursae surround the joint and help reduce friction with joint movement. Inflammation of the bursa, or bursitis, is another common cause of acute or subacute knee pain. The most commonly affected bursa is the prepatella bursa above the kneecap, typically affected by occupations and activities that require excessive kneeling, such as carpet laying, plumbing, mining, roofing, gardening, and housework.



5.23 Anatomy of the knee. **A**: Bony anatomy. The knee is formed by joints between the femur and tibia and femur and patella; **B**: soft tissue anatomy. Strength and stability are added to the joint by the collateral (lateral and medial) and the cruciate ligaments. The cartilaginous lateral and medial menisci provide a surface for smooth movement of the joint.

Patellofemoral syndrome

Patellofemoral syndrome is one of the most common sports-related chronic pain complaints, affecting about 20% of adolescents and young adults[23]. Patellofemoral syndrome typically affects younger adults. Patients >50 years old with knee pain should have radiographic evaluations to ensure the absence of symptomatic arthritis.

Pain behind or around the patella characterizes patellofemoral syndrome. Pain and stiffness are aggravated by prolonged sitting, walking down steps or hills, and weight-bearing impact exercise, like running. Patellofemoral syndrome should be distinguished from patellar tendonitis, which is associated with pain and focal tenderness over the patellar tendon below the knee cap.

Patellofemoral syndrome is treated conservatively, with reduction in knee activities, especially avoiding high-impact exercise. Patients may continue aerobic conditioning with low-impact exercise, such as swimming or using an elliptical machine. Therapeutic exercises should include strengthening of the quadriceps and stretching of the iliotibial band, hip, hamstring, and calf. Ice and anti-inflammatory medications may be helpful. Arch supports and orthotics may also reduce patellar pain. Running shoes should be switched every 300 miles (500 km) after resuming impact sports. Patellar bracing and taping are typically not helpful.

Chronic foot pain

Chronic foot pain can usually be diagnosed by identifying pain location and manoeuvres that worsen or improve the pain (**5.24**, *Table 5.7*). Nerve conduction and EMG testing are typically reserved for patients with atypical symptoms for whom mononeuropathies (such as radiculopathy or

Case presentation

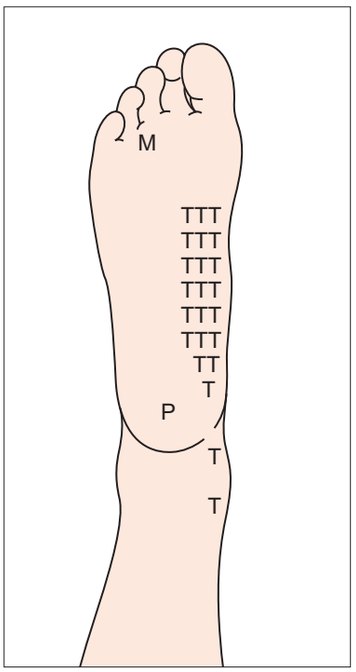
A 43-year-old obese hair stylist is requesting a foot X-ray because she believes she has a fracture of her heel bone. For the last several months, she has experienced excruciating pain in her heel. The pain is so severe in the morning, that she has started to crawl to the bathroom, since putting pressure on her foot is unbearable. Curiously, her foot pain is much better during the work day when she is on her feet. In the evenings, though, the pain returns once she begins to relax and watch television.

Plantar fasciitis is a common and agonizingly painful cause of chronic foot pain. Patients with plantar fasciitis may insist they have a fracture because of the pain intensity and point tenderness over the heel. Good response to stretching exercises, however, clarifies the diagnosis and provides effective treatment.

Table 5.7 Common causes of foot pain

Diagnosis	*Pain location*	*Typical complaints*	*Pain response with ambulation*	*Treatment*
Plantar fasciitis	Heel of foot	Exquisite pain with first morning steps or after rest	Improves after taking several steps	Stretching with foot dorsiflexion
Tarsal tunnel syndrome	Diffuse pain and numbness over medial ankle and foot	Diffuse pain worsens with activity; tapping behind medial malleolus gives electric shock	Worsens with walking	Orthotics, NSAIDs, stretching exercises, local steroid injections, surgical release
Morton's neuroma	Ball of foot	Pain with every step when pressure is on foot	Worsens with walking; electrical and tingling sensations in toes with walking	Avoid tight shoes; use orthotics, NSAIDs, local steroid injections
Peripheral neuropathy	Bilateral burning below ankles	Tingling and numbness in toes; aggravated by light touch	May worsen or improve with walking	Antidepressants, antiepileptics
Peripheral vascular disease	Diffuse cold with rest, pain with exercise	Cold, discoloured feet	Aching and cramping with walking	Reduce smoking, hypertension, and high cholesterol; consider antiplatelets, cilostazol, revascularization surgery

NSAIDs: nonsteroidal anti-inflammatory drugs



5.24 Location of typical painful foot syndromes. M: Morton's neuroma; P: plantar fasciitis; T: tarsal tunnel syndrome.

compressive neuropathy) or peripheral neuropathy is suspected. Treatment is targeted to pathology for specific diagnoses (*Table 5.7*). In most cases, patients will require long-term treatment for chronic foot pain to avoid recurrence of disabling pain.

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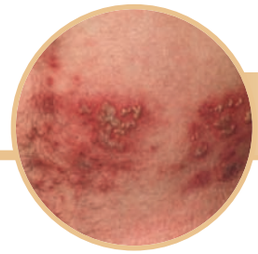


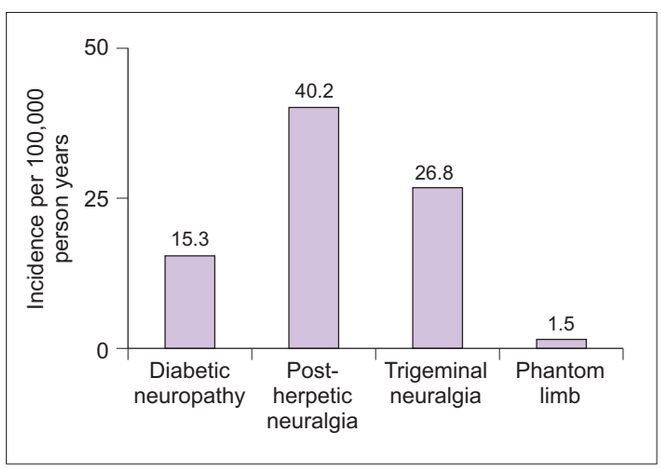
Chapter 6

Neuropathic pain

Prevalence

Neuropathic pain is estimated to affect about 1.5–3% of people worldwide[1,2]. The incidence of neuropathic pain varies among different pain syndrome categories (**6.1**)[3]. Diabetes mellitus is the most common medical condition resulting in neuropathy. Polyneuropathy occurs in one of every 4–5 patients with diabetes[4,5]. Painful neuropathy more commonly occurs in diabetics with long-duration illness and older age.

Painful neuropathies constitute a diverse collection of individual disorders, including conditions associated with direct nerve compression or trauma, such as mononeuropathy, radiculopathy, deafferentation pain, and reflex sympathetic dystrophy, and neuropathies related to other medical illnesses, such as peripheral polyneuropathy (*Table 6.1*). Several common unique neuropathic pain conditions are postherpetic neuralgia (PHN), trigeminal neuralgia, and complex regional pain syndrome (CRPS).



6.1 Incidence of painful neuropathies. A survey of 686 primary care practices in the United Kingdom identified the incidence of common painful neuropathies. (Based on Hall GC, *et al.*, 2006[3].)

Table 6.1 Diverse neuropathic pain syndromes

- Mononeuropathy
  - Carpal tunnel syndrome
  - Postmastectomy syndrome
- Radiculopathy
  - Herniated nucleus pulposus
- Polyneuropathy
  - Diabetes
  - Thyroid disease
  - Paraneoplastic syndrome
  - Alcoholism
  - Chemotherapy
  - HIV infection
- Deafferentation syndrome
  - Phantom pain
  - Spinal cord injury
  - Poststroke pain
- Complex regional pain syndrome (CRPS)
  - Reflex sympathic dystrophy (CRPS Type I)
  - Causalgia (CRPS Type II)

Postherpetic neuralgia

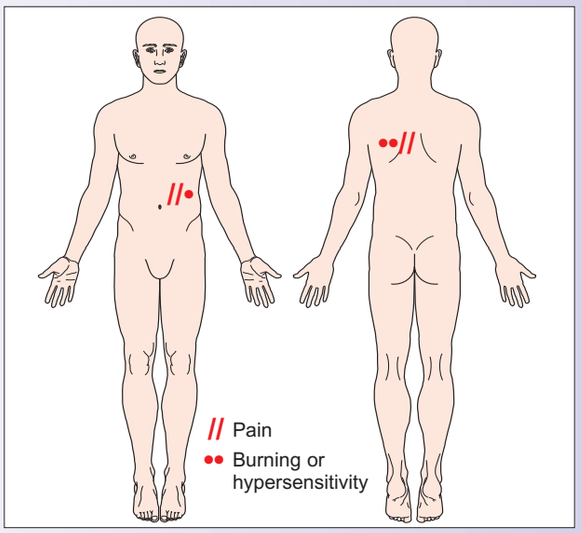
Herpes zoster characteristically begins with dermatomal pain or sensory disturbance, followed within hours to days by a painful papular rash in a dermatomal distribution (**6.2**). Papules change to vesicles and then become crusted. The acute zoster rash typically heals within 3–4 weeks. PHN is defined as pain that persists for >1 month after the onset of herpes zoster.

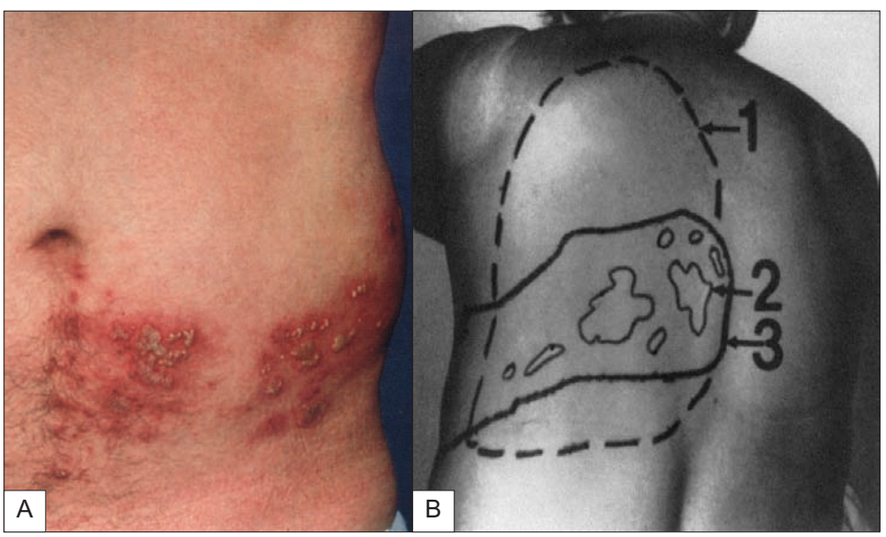
PHN occurs in about 30% of patients following acute zoster, and lasts 1 year in about 10% (**6.3**)[6]. The prevalence of PHN by dermatomal region and likelihood of improvement by region are shown in **6.4**[7]. PHN most commonly affects the trunk or face. Among patients with trigeminal distribution PHN, the ophthalmic division is usually affected. Risk factors for the development of PHN include female gender, older age, experiencing pain or sensory disturbance before the development of the rash, greater pain severity during acute herpes zoster, and larger distribution for zoster rash[8]. Persistent PHN increases in patients with older age and greater pain severity.

Case presentation

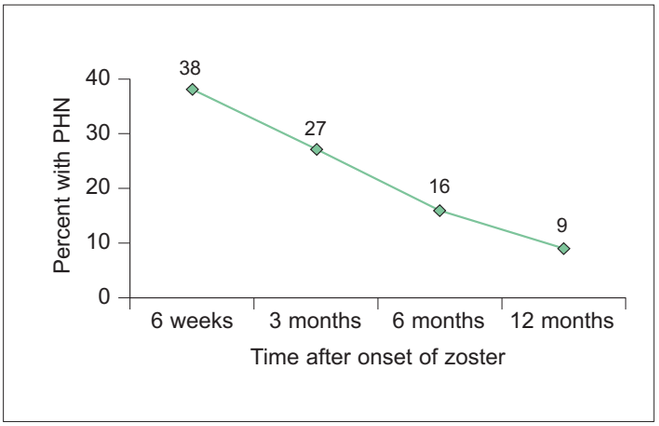
A previously active 75-year-old woman reports feeling depressed and hopeless due to pain over her left chest. Four months ago, she developed a small band of itchiness around her left chest under her breast. After a couple of days, she noticed small blisters that quickly crusted over, which she assumed was a heat rash. This was followed by a searing, unbearable pain in this same area that has persisted. Her pain drawing is shown. She reports, "I feel silly complaining about a little pain when my health is so good, but I can't stand it anymore. If anyone touches my back or chest, I just want to scream."

This case of PHN was effectively treated with a low-dose antidepressant and a 5% lidocaine patch, which reduced her pain and provided protection from inadvertent touch over the painful area. Despite the often small area involved in PHN, the pain is frequently intolerable and is the leading cause of suicide in elderly patients with chronic pain.

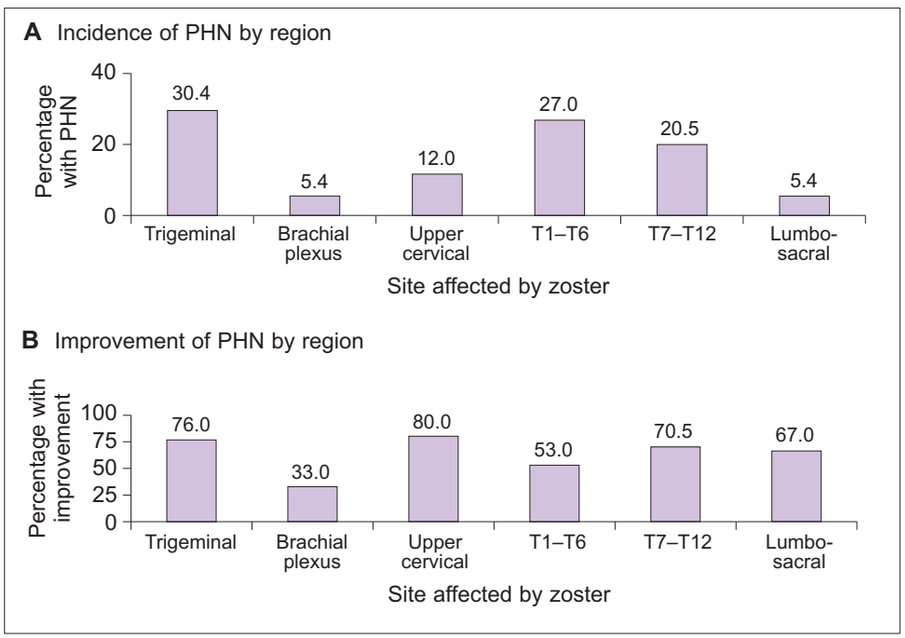




6.2 Typical thoracic herpes zoster. Acute lesions are shown in **A**. In patients developing postherpetic neuralgia (**B**), areas of allodynia (1), residual scarring (2), and sensory loss (3) may be identified.



6.3 Prevalence of PHN in patients with herpes zoster. A total of 204 primary care patients with acute shingles of ≤7 days with the diagnosis confirmed by laboratory testing were followed for up to 1 year in a prospective, observational study. Optimal antiviral therapy was started within 72 hours of symptom onset in 54% of patients, and delayed until after 72 hours in 25% of patients, usually due to delayed presentation to the family doctor. Antiviral therapy was predominantly with acyclovir (91% of treated patients). Patients >50 years old and those with moderate–severe pain at presentation were significantly more likely to develop PHN. (Based on Scott FT, *et al*., 2003[6].)



6.4 Epidemiology of PHN after herpes zoster. Pain features were retrospectively reviewed in 191 consecutive PHN patients, with a mean age of 68 ± 11 years. PHN most typically affected trigeminal and thoracic dermatomes (**A**), with pain right-sided in 52% of patients. Improvement by 75% or better (**B**) depended on pain location, with the best outcome for patients with pain in the face (especially the jaw), neck, and trunk. (Based on Bowsher D, 1996[7].)

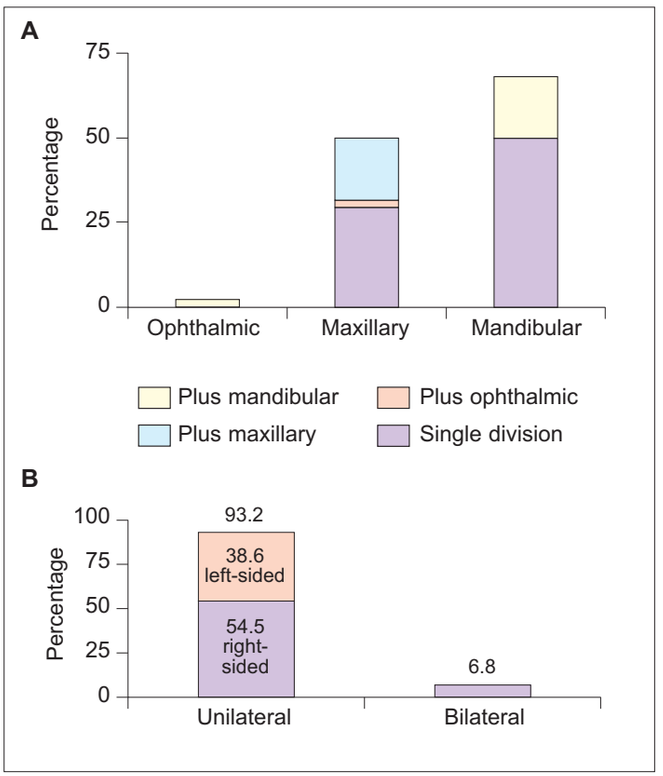
Case presentation

A 37-year-old homemaker presented with severe pain in her lower jaw and teeth. She was referred by her dentist due to persistent pain despite repair of dental caries. She comes to the office holding her face and limiting verbal responses. With each verbal response, she winces in pain, reporting jolts of pain with talking, brushing her teeth, or touching the jaw. Her only previous medical complaints were two remote episodes of arm and hand numbness that resolved over several weeks and an episode of vertigo. Her examination is limited due to her refusal to permit full examination of the face and jaw. She does endorse a small area of numbness over her jaw and chin and has positive Babinski's.

Although her current pain complaint was typical of trigeminal neuralgia, this patient's relatively young age, history of neurological episodes, and abnormal neurological examination warrant further evaluation. An imaging study of the brain revealed white matter abnormalities consistent with multiple sclerosis.

Trigeminal neuralgia

Trigeminal neuralgia is experienced as a unilateral, intermittent, electric-shock-like jolt of pain into one or more of the divisions of the trigeminal nerve, usually over the cheek or jaw (**6.5**). Interestingly, pain more commonly affects the right side of the face[9,10]. Pain is typically triggered by activating a discrete trigger point on the face, such as with touching, shaving, talking, or chewing, often limiting the patient's cooperation with a careful examination of the face and mouth. Curiously, patients with trigeminal neuralgia, as in the case presentation, will often sit holding the painful side of the face, possibly to prevent stimuli from activating their trigger point. In between pain episodes, some people experience a residual low level of pain over the face or jaw. Trigeminal neuralgia generally affects adults after age 40. Younger patients and patients with bilateral symptoms should be evaluated for multiple sclerosis. Although sensory loss occurs in a minority of patients with idiopathic trigeminal neuralgia, identifying sensory loss warrants evaluation with neuroimaging studies.



6.5 Location of trigeminal neuralgia pain. **A**: Nerve division affected; **B**: side of face affected. Pain distribution was evaluated in 44 patients treated at university settings in Singapore and Malaysia. There were no cases of trigeminal neuralgia pain affecting the ophthalmic division alone (**A**). Ophthamic plus maxillary pain occurred in one patient (2.3%). Most patients had mandibular pain (68.2%), with pain limited to the mandibular distribution for 50% of trigeminal neuralgia patients. Pain affected the maxillary division alone for 29.5% of patients and maxillary plus mandibular regions for 18.2%. Most patients had unilateral pain, more often affecting the right side of the face (**B**). (Based on Loh HS, *et al.*, 1998[9].)

Table 6.2 Epidemiology of CRPS

	United States	*Netherlands*
Incidence per 100,000		
CRPS I	5.46	25.4
CRPS II	0.82	0.77
Mean age at diagnosis, years	46.9	52.7
Female:male ratio	4:1	3.4:1
Extremity affected	Twice as often upper	59% upper
Precipitating event (%)		
Fracture	46	44
Sprain	12	18
Other	42	38

(Based on Sandroni P, *et al.*, 2003[11]; de Mos M, *et al.*, 2007[12])

Complex regional pain syndrome

CRPS is a neuropathic pain that develops following limb injury or a period of limb immobilization (e.g. casting). CRPS may be divided into Type I (occurring in the absence of a nerve injury; formerly called reflex sympathetic dystrophy) and Type II (occurring after injury to a specific large nerve; formerly called causalgia). CRPS is characterized by excessive splinting and guarding of the painful extremity. Sympathetically-maintained pain and sympathetically-mediated pain are also terms formerly used to describe this syndrome. Failure of relief from sympathetic blocks, particularly in patients with long-standing complaints, led to the discontinuation of these terms.

The incidence of CRPS differs between the United States and Europe, although other epidemiological features are similar (*Table 6.2*)[11,12]. In the United States sample, symptoms resolved in 74% of cases, with a mean symptom duration of 1 year and a range of 1–60 months. Most patients rated treatment effectiveness good for physical therapy (87%), sympathetic blocks (79%), and prescription medication (80%).

CRPS patients typically report pain, hyperalgesia, restricted range of motion, and autonomic changes in the affected limb (*Table 6.3*). Chronic CRPS may also be associated with changes in hair and nail growth and tremor. Autonomic changes are generally transient and often elicited by history but not seen on physical examination. Edema and temperature changes frequently vary during the course of

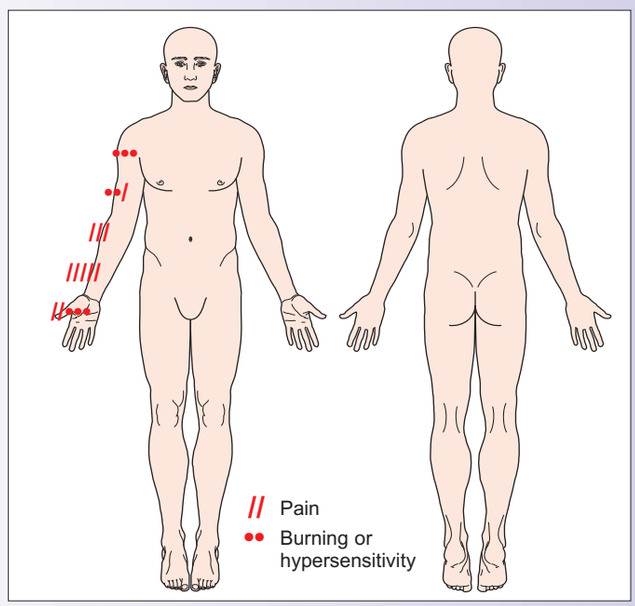
Table 6.3 Patient-reported symptoms in CRPS I

- Allodynia – 54%
- Colour change – 77%
- Motor deficits – 57%
- Sensory abnormalities – 46%
- Sweating abnormality – 28%
- Swelling – 97%
- Temperature change – 62%

(Based on Sandroni P, *et al*., 2003[11])

Case presentation

A 45-year-old woman arrived at the clinic on a hot summer day with a wool shawl draped across her shoulders and right arm. She held her arm in a flexed position, splinted to her body. The nails on her left hand were clipped close, while those on the right were long and abnormally angled. She reported severe pain in the right upper extremity for the last 8 months, following removal of a cast for a seemingly uncomplicated wrist fracture after a skating accident. She claimed to wear the shawl because her arm was always cold and sometimes sweaty. She also reported being unable to clip her nails due to their abnormal shape and pain while attempting to cut them. She had already seen three other doctors, each of whom referred her to psychiatry with a diagnosis of malingering or conversion disorder. Another doctor refused to see her because he assumed she was planning litigation from the skating accident and fracture repair. Her pain drawing is shown.



This patient's presentation is typical of CRPS Type II, with seemingly exaggerated and persistent pain after a period of limb immobilization. Efforts to protect the extremity, such as by splinting and covering the arm with a heavy shawl, are characteristic of this disorder. Extreme complaints, often in the absence of objective pathology during examination, frequently result in the false perception of symptom magnification or fictitious disorders.

CRPS, with patients typically reporting excessive extremity warmth and edema during early CRPS and excess coldness with less edema during later stages (**6.6**)[13].

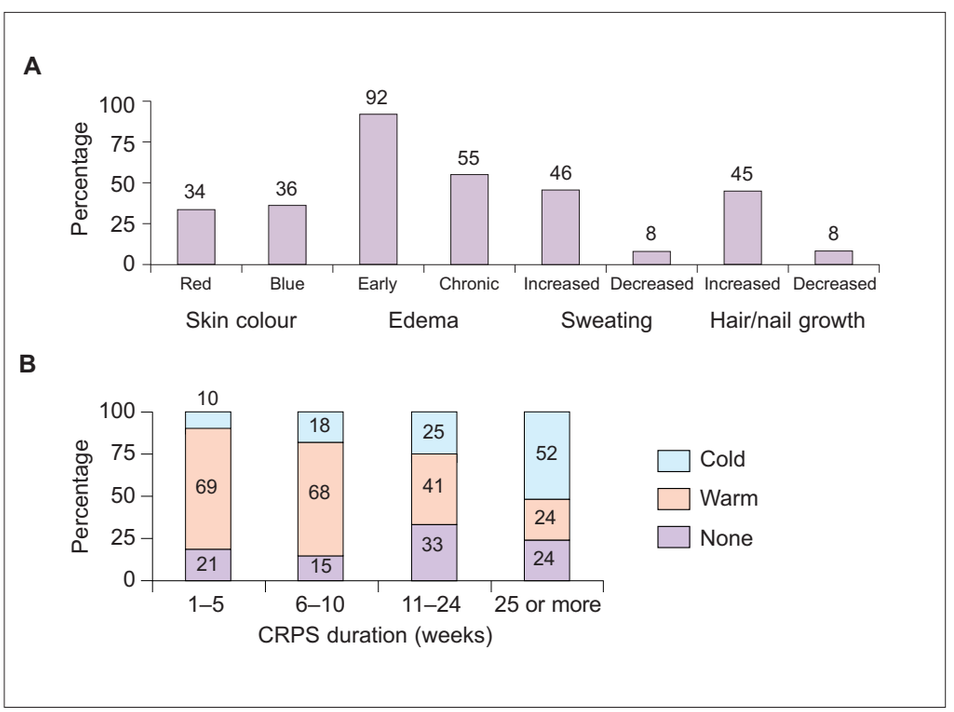
Interestingly, patients' subjective reports of CRPS changes (allodynia, edema, sweating/colour/temperature abnormality) have greater diagnostic sensitivity and specificity than relying on objective clinical examination findings for the same conditions[14]. For example, in a survey of 389 patients with CRPS, reports of altered sensation were recorded for 46% of patients, while objective sensory findings were noted in only 19%[11].

Objective motor findings are rarely present in CRPS, but may include restricted range of motion, weakness, or tremor. Motor findings typically are seen with very long-standing, untreated CRPS. Ten or twenty years ago, it was common to see patients with end-stage CRPS, with contracted joints, as well as abnormal skin, hair, and nail growth. Better identification of this syndrome and an emphasis on early rehabilitation and maintaining function of the painful limb have resulted in current patients typically displaying only early, more reversible disease stages, such as colour and temperature changes and avoidance of movement by voluntary splinting.

Assessment strategies

Neuropathic pain can be distinguished from other types of chronic pain by a history of nerve injury, description of pain as burning or electrical, and symptoms or signs of neural deficits, such as hypesthesia or allodynia (*Table 6.4*)[15]. Hypesthesia describes sensory loss or numbness, while allodynia represents a perception of innocuous, tactile stimuli as painful. A simple, 6-item questionnaire called the ID Pain Questionnaire was developed and validated as an effective screening tool for neuropathic pain (**6.7**)[16].

The distribution of neuropathic pain complaints can help clarify the specific pain diagnosis. Sensory deficits typically



6.6 Autonomic changes in CRPS. Symptoms were evaluated prospectively in 145 patients with CRPS (N=122 CRPS type I and N=23 CRPS type II). Hyperalgesia was similarly reported in response to lowering the extremity (60% and 56%), striking the extremity (61% and 52%), and physical effort (43% and 61%) for patients with CRPS I and II, respectively. CRPS II patients were more likely to report pain amplification with exposure to cold compared with CRPS I patients (61% *vs*. 32%, $P<0.04$). Autonomic changes occurred in 98% of patients (**A**). Excessive skin warmth and edema were more likely to occur with acute CRPS, while long-standing CRPS was more often associated with excessive skin coldness and a lower prevalence of edema (**B**). (Based on Birklein F, *et al*., 2000[13].)

Table 6.4 Percentages of patients endorsing pain descriptors: neuropathic vs. non-neuropathic pain

Pain descriptor	*Neuropathic pain*	*Non-neuropathic pain*
Burning	54	29
Electric shock	53	21
Tingling	48	25
Pricking	37	18
Itching	33	9
Cold	22	10

These 6 pain descriptors are more commonly used by neuropathic pain patients ($P<0.05$)
(Based on Boreau F, *et al.*, 1990[15])

ID Pain questionnaire (Portenoy 2006)

Answer the following questions about your pain over the past week:

	Yes scores	***No scores***
Did the pain feel:		
Like pins and needles	1	0
Hot or burning	1	0
Numb	1	0
Like electric shocks	1	0
Is the pain worse with touching by clothes or bed linens?	1	0
Is the pain limited to your joints?	-1	0
Total yes score		

Add scores from all "yes" answers to get the total yes score. Scores ≥3 suggest likely neuropathic pain

6.7 Pain questionnaire. (Based on Portenoy R, 2006[16].)

affect dermatomes for radicular pain, patterns of individual nerve roots for mononeuropathy, and a stocking–glove distribution for most polyneuropathies (**6.8**).

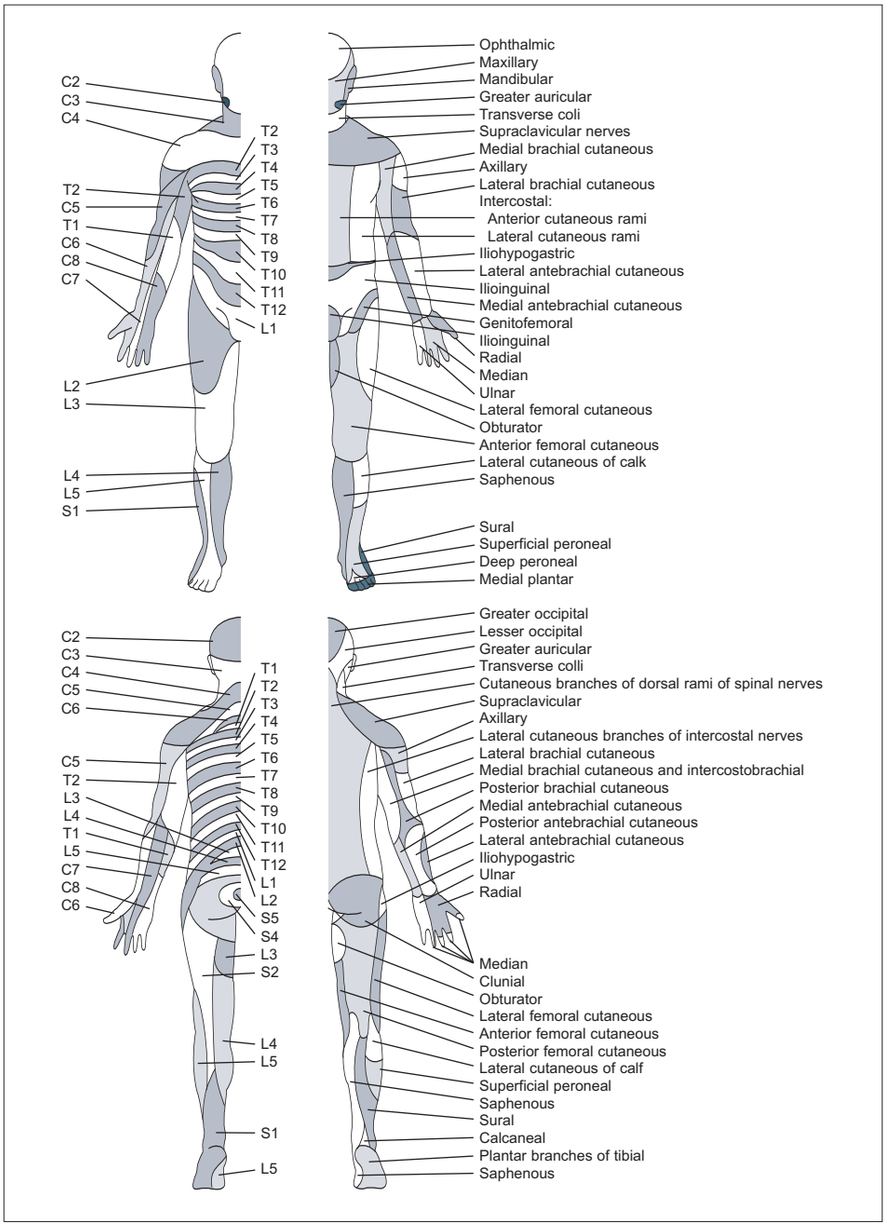
CRPS

CRPS is distinguished by reports of seemingly exaggerated pain severity and protective behaviours (such as splinting and guarding the affected extremity) and patient reports of autonomic changes. Specific diagnostic criteria rely heavily on patient history (*Table 6.5*). Changes in colouration, moisture, temperature, skin, hair, and nails may be seen on physical examination (**6.9**). Failure to confirm symptomatic reports of autonomic changes on physical examination should not preclude this diagnosis, since symptoms are often transient.

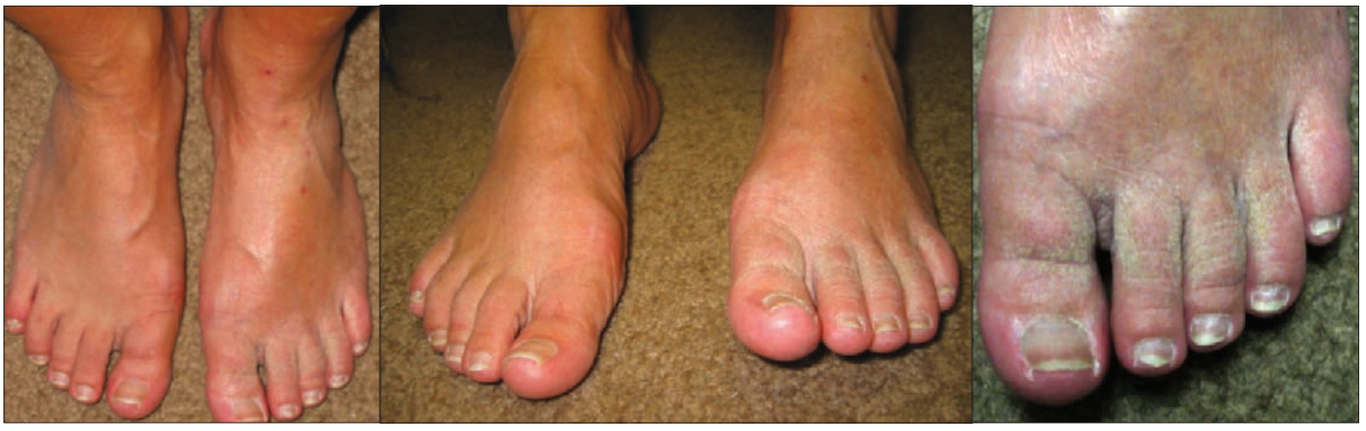
Table 6.5 Diagnostic criteria for CRPS

- Identification of inciting event or history of immobilization
- Persistent pain, allodynia, or hyperalgesia with severity in excess of expectations from inciting event
- History of changes in swelling, temperature, colour, or sweating in the painful area

(Based on Merskey H and Bogduk N, 1994[17])



6.8 Sensory patterns: comparison of nerve roots and peripheral nerves. Dermatomal areas served by spinal nerve roots are shaded and numbered on the left of the drawing. Good landmarks for thoracic dermatomes are the nipples for T4 and the umbilicus for T10. Sensory areas supplied by individual peripheral nerves are shaded and labelled in the drawing on the right. Carefully mapping areas of sensory disturbance or loss can help distinguish between radicular neuropathy and mononeuropathy.



6.9 Complex regional pain syndrome. Notice characteristic CRPS changes with swelling and abnormalities in the skin and nails in this patient's left foot.

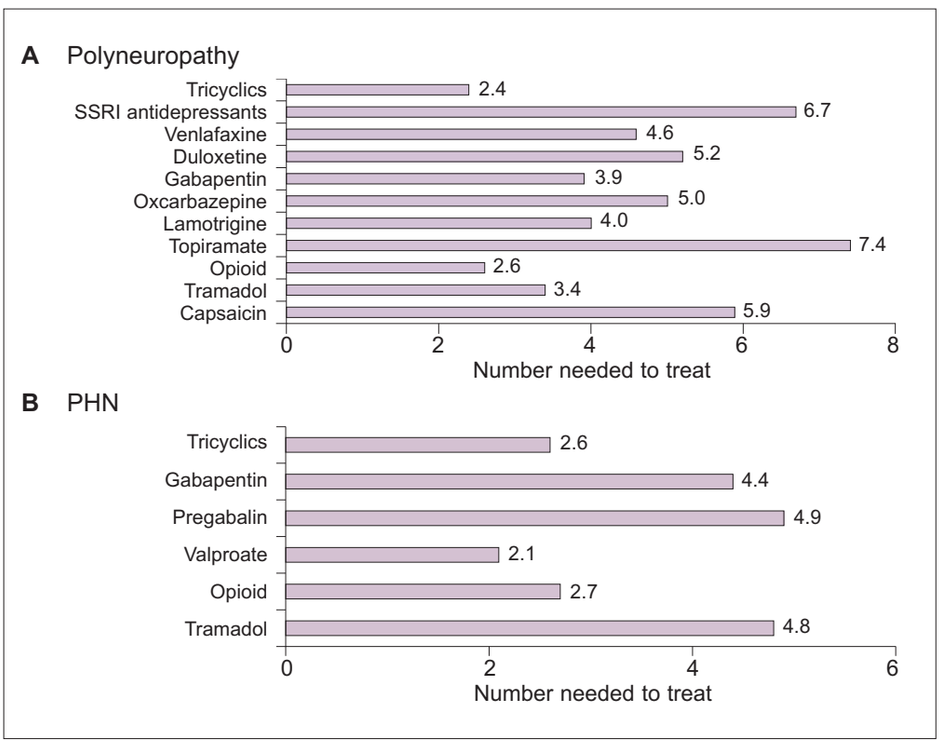
Treatment

Neuropathic pain is typically treated with correction of the underlying condition resulting in neuropathy (such as surgical release of compression, normalization of blood sugar in diabetics, and nutritional supplementation in alcoholics) and use of medications. A variety of medications can be used to reduce neuropathic pain (*Table 6.6*), although the most effective therapies are tricyclic antidepressants and gabapentin (**6.10**). A survey of a university pain practice in Thailand reported that oral medication was used by 79% of patients with neuropathic pain, most commonly tricyclic antidepressants (77%), gabapentin (35%), carbamazepine (34%), and tramadol (24%)[18].

Table 6.6 Neuropathic pain treatment armamentarium

- Antidepressants
- GABA agonist anticonvulsants
- Sodium channel blockers
- NMDA antagonists
- Alpha-2 agonists
- Topical agents (lidocaine, capsaicin)

Painful polyneuropathy, such as diabetic and nondiabetic peripheral neuropathy, is best treated with antidepressants and gabaminergic antiepileptics (**6.10**, *Table 6.7*). Tricyclic antidepressants are most effective, with moderate efficacy from serotonin-noradrenaline reuptake inhibitors venlafaxine and duloxetine and only modest relief with selective serotonin reuptake inhibitors[19,20].



6.10 Number of patients needed to be treated to obtain one patient with ≥50% pain reduction. In patients with polyneuropathy (**A**), tricyclic antidepressants provide the best efficacy, with the fewest number of patients needing to be treated to achieve relief. SSRI (selective serotonin reuptake inhibitor) antidepressants are less effective than tricyclics. Gabapentin and pregabalin (not shown) also offer good efficacy with excellent tolerability. Analgesics may provide effective adjunctive therapy, although fewer studies have evaluated their benefits than those of tricyclics and gabapentin. Medication misuse or abuse is a potential concern with opioids for long-term neuropathic pain treatment. **B**: PHN similarly responds well to tricyclic antidepressants and antiepileptics. Although valproate also demonstrates good efficacy, this number is based on data from a single trial. (Based on Coluzzi F, Mattia C, 2005[19]; Attal N, *et al*., 2006[20].)

Table 6.7 Medication recommendations for neuropathic pain

Neuropathy type	*First-line treatment*	*Alternative therapies*
Polyneuropathy	Gabapentin Pregabalin Tricyclic antidepressants	Lamotrigine Opioids SNRI antidepressants Tramadol
PHN	Gabapentin Pregabalin Topical lidocaine Tricyclic antidepressants	Capsaicin Opioids Tramadol Valproate
Trigeminal neuralgia	Carbamazepine Oxcarbazepine	Phenytoin Surgery

SNRI = serotonin and noradrenaline reuptake inhibitors
(Based on guidelines from the European Federation of Neurological Societies. Attal N, *et al*., 2006[20])

PHN

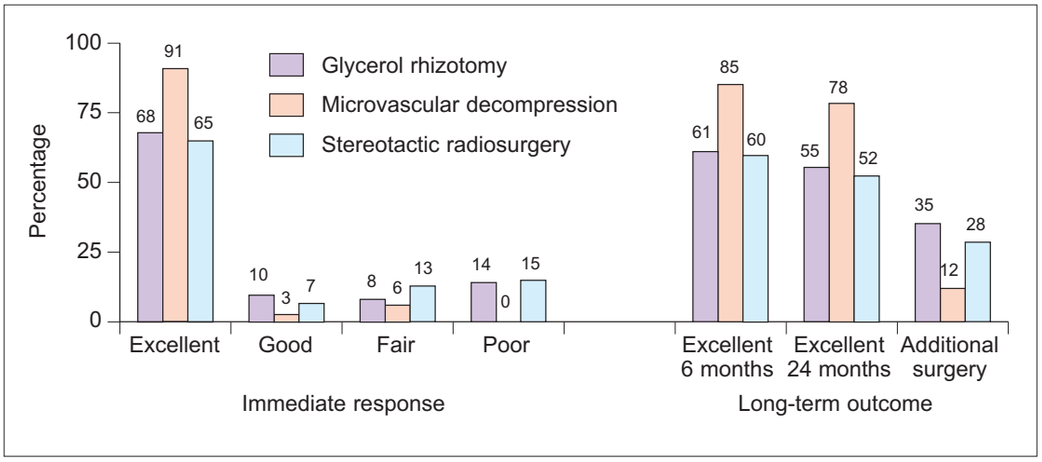
Although not affecting the incidence of PHN, PHN duration may be effectively reduced by early and aggressive treatment of herpes zoster with antiviral therapies. In a double-blind, placebo-controlled study, famciclovir administered within the first 72 hours of appearance of herpes zoster lesions resulted in a two-fold decrease in the duration of PHN[21]. Among all adults in the study, average PHN duration decreased from 119 days with placebo to 62 days with antiviral therapy. Among patients >50 years old, PHN duration decreased from 163 days to 63 days. Early intervention with other antivirals may similarly reduce PHN duration. Brivudin, valacyclovir, and acyclovir similarly reduce duration of PHN; however, the incidence of PHN is higher with acyclovir[22–24]. Vaccination of adults ≥60 years old with varicella-zoster vaccine in a double-blind, placebo-controlled study resulted in a 51% decrease in the incidence of herpes zoster and 66% decreased incidence of PHN[25].

Once PHN has developed, typical neuropathic medications are often helpful (*Table 6.7*). An evidence-based consensus statement from the American Academy of Neurology recommended tricyclic antidepressants, gabapentin, pregabalin, lidocaine patch, and opioids as the most effective therapies for PHN[26].

Trigeminal neuralgia

Antiepileptics are the preferred therapy for trigeminal neuralgia. The number-needed-to-treat to produce 50% pain relief with carbamazepine is 1.8[20]. Oxcarbazepine is also considered first-line therapy for trigeminal neuralgia. While oxcarbazepine is generally less effective than carbamazepine, tolerability is typically superior. Phenytoin is less well tolerated; however, patients can achieve effective blood levels more quickly by using initial loading doses. Baclofen is likewise consistently effective for trigeminal neuralgia. Other antiepileptics (such as lamotrigine, valproate, and gabapentin) may be tried in patients failing to achieve benefit or failing to tolerate carbamazepine, phenytoin, or baclofen. Patients often experience pain-free periods lasting months to years, so medication taper may be attempted after the patient has been pain-free for several months. Over time, medication efficacy usually decreases. Patients failing to respond or achieve a maintained response with medication therapy may be treated with rhizotomy, microvascular decompression, or stereotactic (gamma knife) radiosurgery (**6.11**). Rhizotomy typically produces good acute pain relief, although surgery is often complicated by post-operative facial numbness and recurrence is common[28].

Retromastoid microvascular decompression cushions the trigeminal nerve by placing a pad between the trigeminal nerve near its root and nearby blood vessels. Microvascular decompression offers the most complete and persistent pain relief and should be considered first-line surgical treatment for patients able to receive general anesthesia[27].

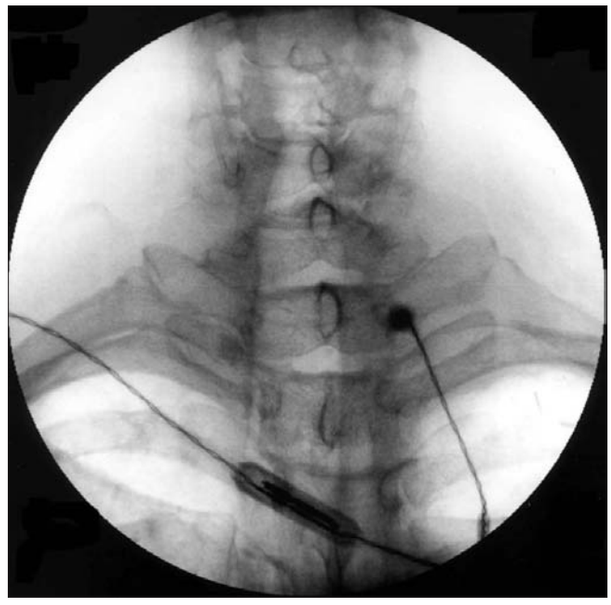


6.11 Surgical response with trigeminal neuralgia. Postoperative outcome was directly compared in 126 patients undergoing a total of 153 separate surgical procedures for trigeminal neuralgia: glycerol rhizotomy (N=51), stereotactic radiosurgery (N=69), or microvascular decompression (N=33). Treatment assignment was based on preference by the treating clinician. Patients selected for glycerol rhizotomy were older and less likely to have had previous trigeminal surgery. Patients were followed for an average of 2 years after surgery. Postoperative response was termed excellent (no pain and no medications), good (no pain with low-dose medication), fair (>50% pain reduction), and poor (≤50% pain reduction). An excellent outcome was more likely to be achieved and maintained at 6 and 24 months after microvascular decompression compared with the other two surgeries (P<0.01). (Based on Pollock BE, Ecker RD, 2005[27].)

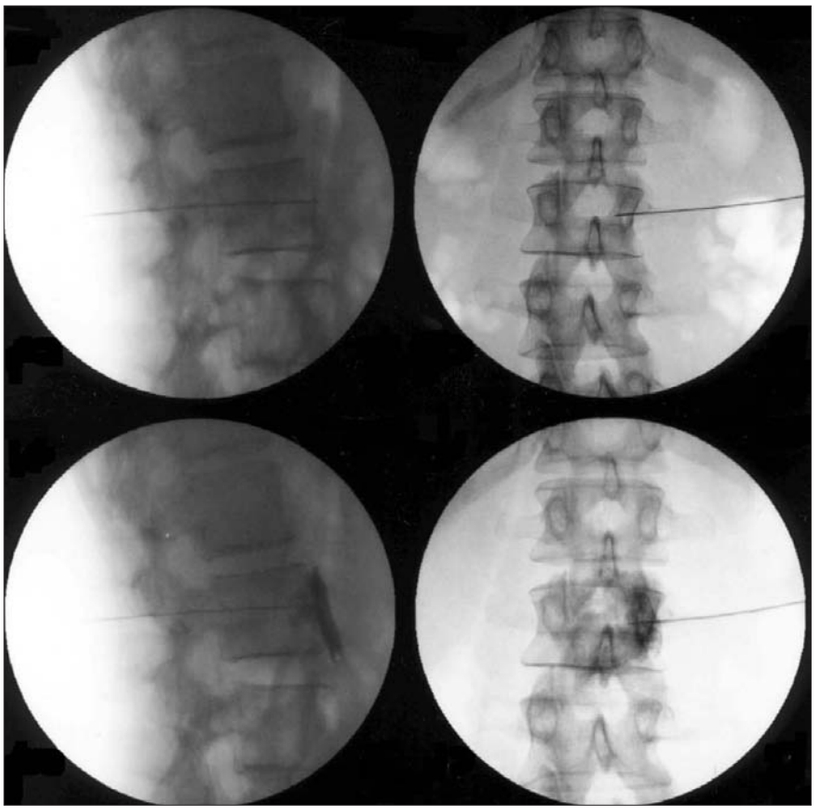
CRPS

CRPS is treated with a combination of symptomatic reduction and aggressive physical rehabilitation. Treatment of the very early stages of CRPS includes sympathetic blocks (**6.12, 6.13**). Response to stellate ganglion blocks is superior in younger patients with early CRPS symptoms (**6.14**)[29]. Blocks typically have minimal benefit for long-standing or later symptoms of CRPS.

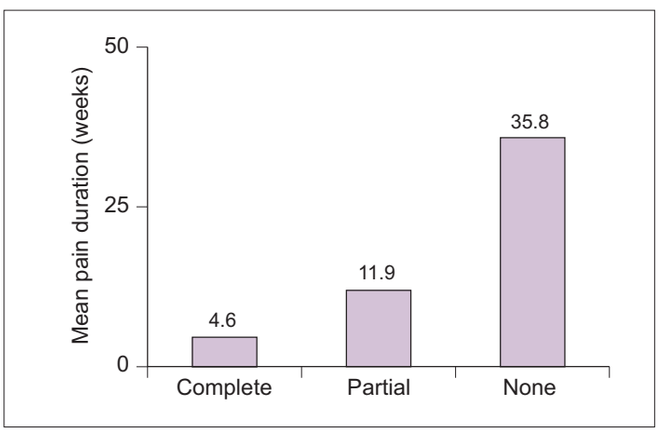
Symptomatic relief with spinal cord stimulation combined with physical therapy has also demonstrated both early and long-term relief in a small, prospective, controlled study[30,31]. Interestingly, superior benefit with the addition of spinal cord stimulation to physical therapy versus physical therapy alone was shown both short term and after 2 years; this benefit was no longer evident 3–5 years post-treatment[32]. These important data confirm the clinical impression that symptomatic treatments offer early benefits for CRPS patients and can help maximize therapeutic response to physical therapy and disruption to the pathological process of CRPS. Long-term benefits are achieved and maintained with rehabilitative treatment, such as aggressive physical and occupational therapies. Selected patients with well-established CRPS may benefit from intrathecal ziconotide[33,34].



6.12 The cervicothoracic ganglion (stellate) is a fusion of the lower cervical ganglion and the first thoracic ganglion. Usually this block is performed at C6 to avoid pneumothorax or vertebral artery compromise. Radiofrequency ablation is performed in a pulse modality at 42°C for 120 seconds, which preferentially modulates transduction of the vulnerable sympathetic fibres over larger sensory or motor fibres. Pain relief and vasodilation in the upper extremity can last for months or longer.



6.13 Lumbar sympathetic nerve blocks are a direct, immediate way to reverse vasoconstriction and sympathetic hyperactivity in lower extremity CRPS. On the left, the needle position in the lateral view is at the anterior margin of L2 with contrast shown below. On the right, the appropriate needle position is shown over the facet line on the affected side. If the needle were too lateral, the local anesthetic solution would be injected in the psoas muscle; if too medial, the sympathetic chain would not be blocked. Symptomatic relief of allodynic pain, restoration of colour symmetry, and preferentially increased temperature on the injected side demonstrate a positive response to a correctly placed sympathetic nerve block. If there is a clear increase in temperature postprocedure but no pain relief, the pain may not be primarily sympathetically mediated but neuropathic or somatic pain. Therefore, this procedure may be used diagnostically as well as therapeutically.



6.14 Response to stellate ganglion blocks. Twenty-five patients with CRPS of one hand were treated with 3-weekly fluoroscopically-guided stellate ganglion blocks. After treatment, patients were divided into those achieving complete, partial, and no relief. Demographics and most pretreatment pain characteristics were not related to subsequent treatment outcome. Mean CRPS duration before blocks ranged from 3–84 weeks, with an average duration of 15 weeks. Mean pain duration before blocks was linked to treatment outcome, with significantly better relief in patients with shorter symptom duration ($P<0.05$). (Based on Ackerman WE, Zhang JM, 2006[29].)

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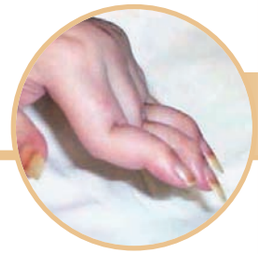


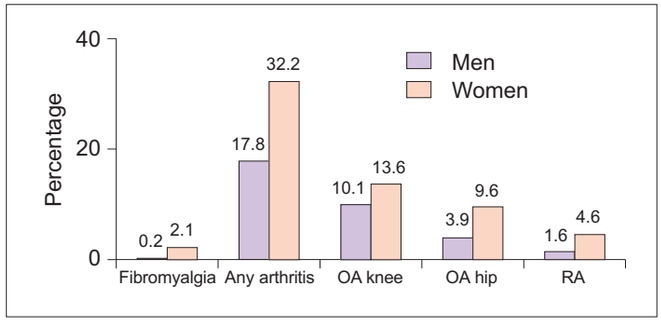
Chapter 7

Fibromyalgia and arthritis

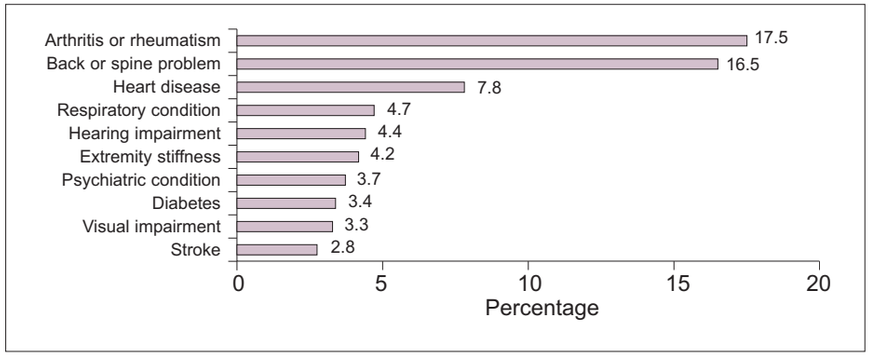
Introduction

Fibromyalgia and arthritis are common musculoskeletal conditions causing chronic pain (**7.1**)[1]. A survey of 99 general practitioners in Italy showed that 32% of all visits were for pain, with 47% for acute and 53% for chronic pain[2]. In this survey, joint-related pain comprised the most common individual diagnostic category (23%).

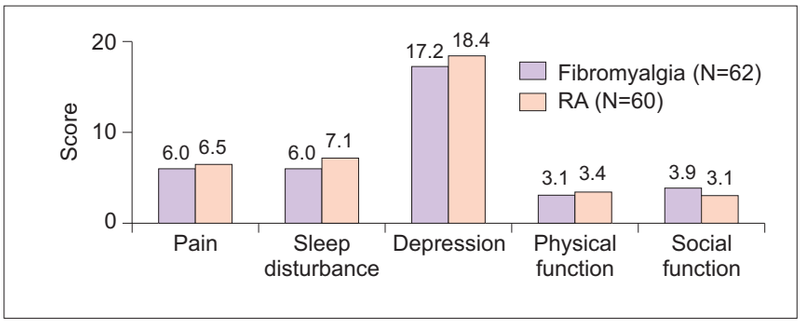
Chronic rheumatologic conditions are a major cause of disability[3]. Of all medical problems resulting in a disability, arthritic conditions are the most common (**7.2**). Almost 18% of adults with a disability attribute their disability to arthritis or rheumatism. Interestingly, despite lack of joint damage in fibromyalgia, disease impact is similar for patients with fibromyalgia or rheumatoid arthritis (**7.3**)[4].



7.1 Prevalence of fibromyalgia and arthritis. The prevalence of self-reported fibromyalgia and arthritis was determined for a Dutch population-based sample. Both fibromyalgia and arthritis were more common in women. OA: osteoarthritis; RA: rheumatoid arthritis. (Based on Picavet HJ, Hazes JW, 2003[1].)



7.2 Health conditions resulting in disability in the United States. Using surveillance data, the Centers for Disease Control reported that 22% of adults in the United States have a disability, defined as having a functional limitation, restrictions for work, use of an assistive device, or receipt of federal disability benefits. The most commonly reported health conditions resulting in disability are arthritis or rheumatism, followed by back or spine problems, each affecting slightly less than one in five persons with a disability. (Based on CDC, 2001[3].)

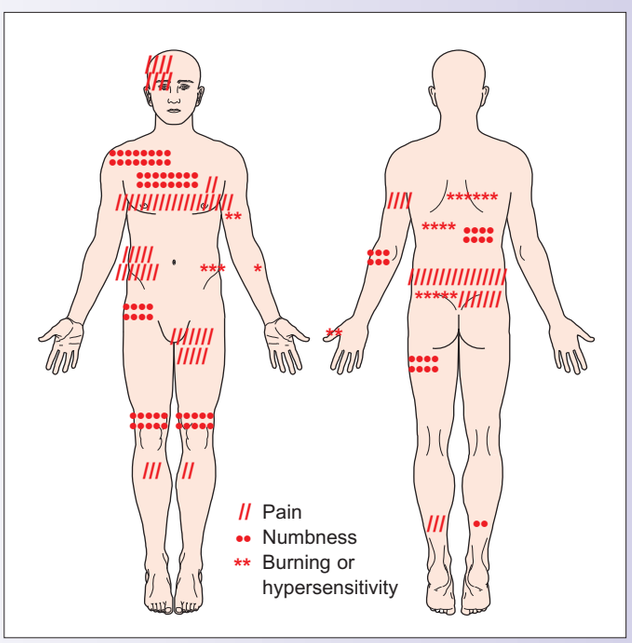


7.3 Impact of fibromyalgia and arthritis. Symptoms and quality of life were compared in female outpatients in Istanbul with fibromyalgia or rheumatoid arthritis. Pain and sleep disturbance were measured using a visual analogue scale (0=none; 10=severe). Depression was measured using the Beck Depression Inventory, with a score >17 indicating depression. Quality of life was measured with the Arthritis Impact Measurement Scale II subscales, with scores ranging from 0 (best) to 10 (worst). Symptom severity, depression, and quality of life were similar for patients with either condition. (Based on Ofluoglu D, *et al*., 2005[4].)

Fibromyalgia

Case presentation

A 43-year-old corporate attorney complains of a 4-year history of diffuse pain. She began having back pain without any obvious trauma and progressively developed pain in her shoulders, chest, and legs over the next 6–8 months. Pain intensity would fluctuate among the pain areas on different days. Radiologic testing was unremarkable. She also reported extreme fatigue, difficulty concentrating, migraine headaches, anxiety, bowel irregularities, and frequent urination. Her complaints resulted in impaired work performance and she was asked to reduce her commitment to part-time. Her physical examination shows her to be bright and articulate, with good muscle strength and joint motion. At this point, she has had numerous, unremarkable blood tests and imaging studies and spends several days each week visiting doctors or attending different therapy appointments. Her frustration is evident when she verbalizes, "Every doctor tells me how great I look and that my physical examination is perfect. I know people think I must be exaggerating." Her pain diagram is shown.



Fibromyalgia is recognized as a condition resulting in both chronic, widespread pain and a variety of somatic complaints. Like this patient, fibromyalgia patients typically have unremarkable musculoskeletal and neurological examinations, with normal laboratory and radiographic tests. Despite normal function for bedside testing, disability and psychological impairment are often substantial in fibromyalgia patients.

Epidemiology of fibromyalgia

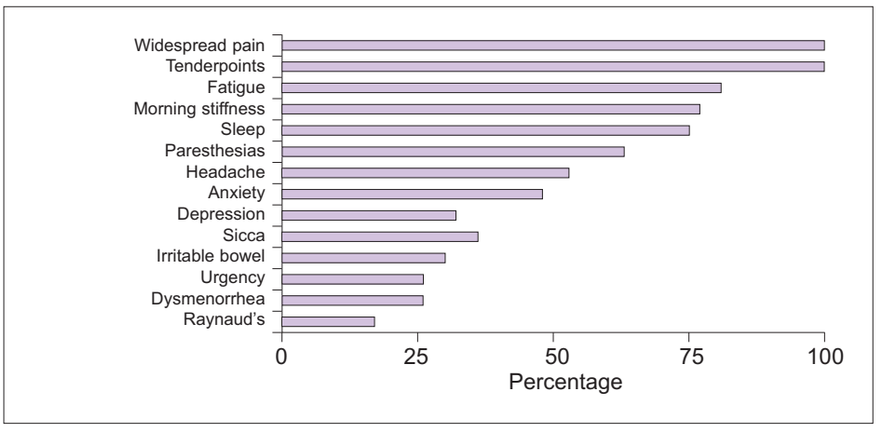
Fibromyalgia is defined as diffuse, chronic pain associated with tender body areas and somatic complaints (*Table 7.1*). Most patients with fibromyalgia experience a wide variety of fluctuating symptoms in addition to body pain (**7.4**)[5]. Fibromyalgia patients are also more likely to be experience a number of other rheumatologic, medical, and psychological conditions, contributing to the burden of this condition (**7.5**).

Fibromyalgia affects 2% of adults, predominantly women (**7.6**). Incidence rate increases with age for both genders, with women more likely to be affected throughout their lifetimes[6].

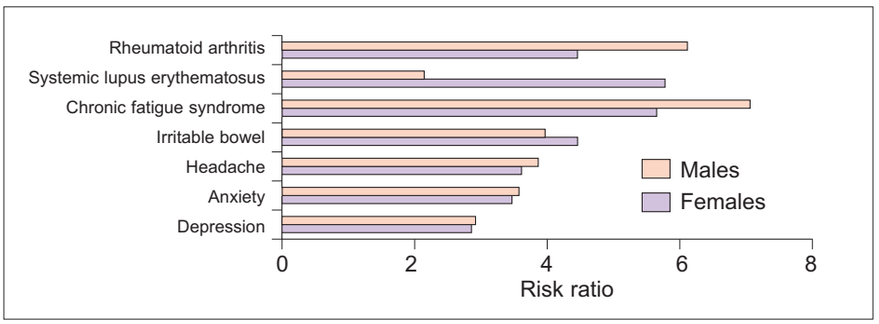
Table 7.1 Diagnosis of fibromyalgia

- Widespread body pain
  - Pain on both left and right sides of the body
  - Pain above and below the waist
  - Axial pain present
- Pain persisting ≥3 months
- ≥11 of 18 tenderpoints painful to 4 kg pressure

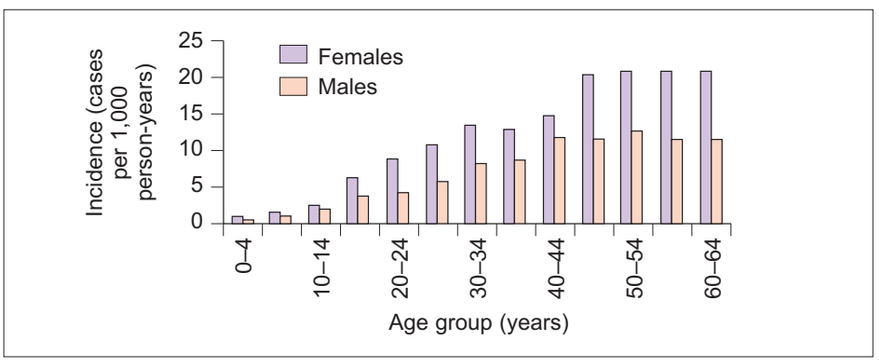
(Based on American College of Rheumatology criteria. Wolfe F, *et al.*, 1990[5])



7.4 Constellation of symptoms in fibromyalgia patients. (Based on Wolfe F, *et al.*, 1990[5].)

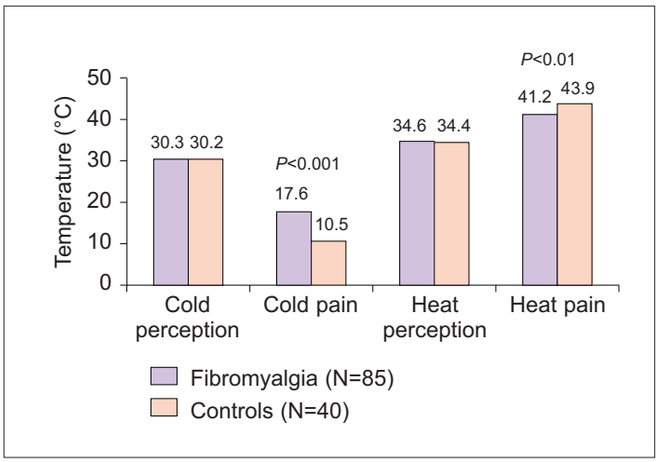


7.5 Comorbid conditions and fibromyalgia. Using a large insurance claims database in the United States, the prevalence of concomitant illnesses was compared between patients with and without fibromyalgia. Risk ratios >1 were used to identify illnesses occurring with greater than expected prevalence (comorbid) among fibromyalgia patients. All of the conditions in the graph were comorbid with fibromyalgia, except for lupus in men, which failed to achieve statistical significance due to wide data variability (95% confidence interval=0.29–15.74). (Based on Weir PT, *et al.*, 2006[6].)



7.6 Epidemiology of fibromyalgia. Fibromyalgia incidence rate was calculated using 1997–2002 data from a large insurance claims database serving about 62,000 members annually. Fibromyalgia incidence peaked at about 13 cases per 1,000 person-years for males and 21 cases per 1,000 person-years for females. (Based on Weir PT, *et al.*, 2006[6].)

As highlighted by the case presentation, fibromyalgia patients typically have unremarkable examinations. Despite lack of physical or laboratory abnormalities, research studies show that fibromyalgia patients experience a variety of changes in the nervous system that result in increased pain sensitivity. In comparison to healthy controls, fibromyalgia patients experience a lower pain threshold, increased sensitivity to painful stimuli (hyperalgesia) and simple touch (allodynia), enhanced temporal summation, and prolonged after sensations[7,8]. These studies show that the nervous system is activated to produce a stronger response to pain than in nonfibromyalgia persons (**7.7**)[9].



7.7 Enhanced perception of hot and cold pain. Quantitative sensory testing was performed at nonpain locations in fibromyalgia patients and healthy, matched controls. Nonpain perception thresholds were similar between groups, with nearly equivalent cold and hot temperatures required to result in perception of cold or heat. Fibromyalgia patients, however, reported experiencing unpleasant pain with cold and heat stimuli before controls, i.e. fibromyalgia patients reported a pain response before cold stimulation reached the same low temperature required to produce a pain signal in controls and before the heat temperature was as hot as needed to produce a hot pain signal in controls. Therefore, fibromyalgia patients experienced significantly lower thresholds for pain response to both cold and heat stimuli. Tolerance to cold pain was severely reduced by 66%. (Based on Desmeules JA, *et al.*, 2003[9].)

Assessment of fibromyalgia

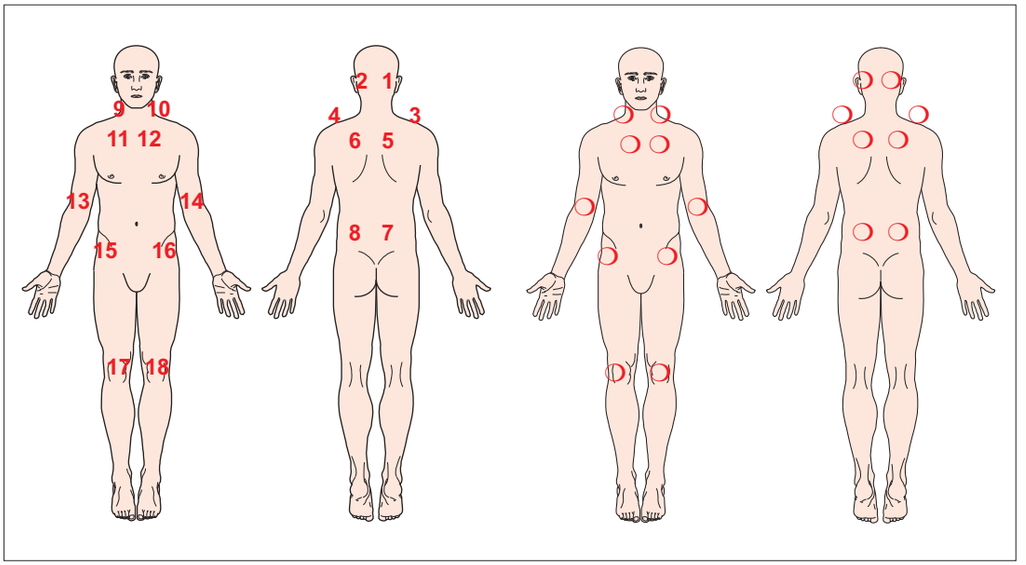
Diffuse pain may occur with a plethora of medical conditions (*Table 7.2*). Patients presenting with generalized pain complaints require a careful history and examination to ensure the absence of potentially correctable or treatable medical conditions.

The diagnosis of fibromyalgia requires documentation of widespread pain and 11 of 18 painful tenderpoints, using a standardized tenderpoint examination (**7.8**). Documentation of the number and pain severity of tenderpoints can provide a tool to monitor progress with treatment at follow-up visits. Disability may be monitored using the Fibromyalgia Impact Questionnaire (**7.9**)[11]. In addition, treatment selection depends on identifying those symptoms typically most responsive to symptomatic improvement (**7.10**). Identifying disabling symptoms helps to clarify the most important treatment targets.

Table 7.2 Common causes of generalized pain

- Ankylosing spondylitis
- Chronic hepatitis C
- Diabetes
- Fibromyalgia
- Hyperparathyroidism
- Hypothyroidism
- Lyme disease
- Metastatic cancer
- Multiple myeloma
- Osteoarthritis
- Osteomalacia
- Polymyalgia rheumatica
- Rheumatoid arthritis
- Sjögren's syndrome
- Systemic lupus erythematosus

7.8 Fibromyalgia tenderpoint examination. Test each labelled spot by exerting 4 kg of pressure with the thumb (watch for the nail bed to blanch). Record pain severity at each spot in the circles from 0 (none) to 10 (excruciating). Determine the tenderpoint count (number of painful tenderpoints scored >0) and tenderpoint severity (sum of all recorded scores). (Based on Marcus DA, 2005[10].)



Question 1: Rate how frequently you were able to perform each task during the PAST WEEK. Choose NA for not applicable if you would not normally perform this task.

	Always = 0	Mostly = 1	Occasionally = 2	Never = 3	NA
Shopping					
Laundry					
Prepare meals					
Wash dishes					
Vacuum					
Make beds					
Walk several blocks					
Visit friends/relatives					
Do yard work					
Drive a car					
Climb stairs					

Question 2: How many days did you FEEL GOOD in the PAST WEEK (0–7)_____

Question 3: How many days did you MISS WORK (including housework) in the PAST WEEK (0–7)_____

Question 4: Rate how you felt for each symptom over the PAST WEEK from 0 (none) to 10 (severe):
How much did fibromyalgia interfere with work: 0 1 2 3 4 5 6 7 8 9 10
How bad has your pain been: 0 1 2 3 4 5 6 7 8 9 10
How tired have you been: 0 1 2 3 4 5 6 7 8 9 10
How poorly rested have you felt when you got up in the morning: 0 1 2 3 4 5 6 7 8 9 10
How bad has your stiffness been: 0 1 2 3 4 5 6 7 8 9 10
How nervous or anxious have you been: 0 1 2 3 4 5 6 7 8 9 10
How depressed or blue have you felt: 0 1 2 3 4 5 6 7 8 9 10

Scoring the FIQ: possible score ranges from 0 (no impact) to 100 (severe impact)
Question 1: add the numbers for each checked item in Question 1 and divide by the number of scored items. Number of scored items will be 11 unless some are not applicable. Multiply this average score by 0.33
Question 2: score items in Question 2 in reverse order: 7=0, 6=1, 5=2, etc. Multiply the score for the selected items by 1.43
Question 3: multiply selected number by 1.43
Question 4: add all numbers together

Add numbers obtained for scoring Questions 1–4 for the total FIQ score. Scores >70 represents severe impact

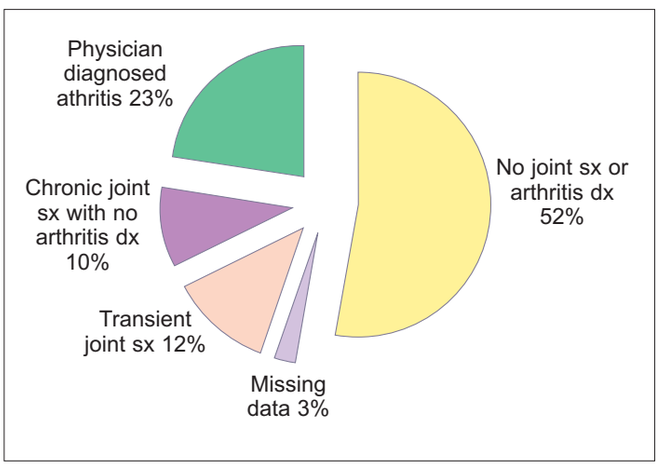
7.9. Fibromyalgia Impact Questionnaire. (Based on Burckhardt CS, *et al*., 1991[11].)

Which of the following problems limit your daily activities?			
Problem	*Not a problem*	*Problem occurs but does NOT limit daily routine*	*Problem limits daily routine*
Fatigue			
Sleep disturbance			
Frequent constipation			
Frequent diarrhea			
Depressed or blue mood			
Anxiety or nervousness			
Headache			

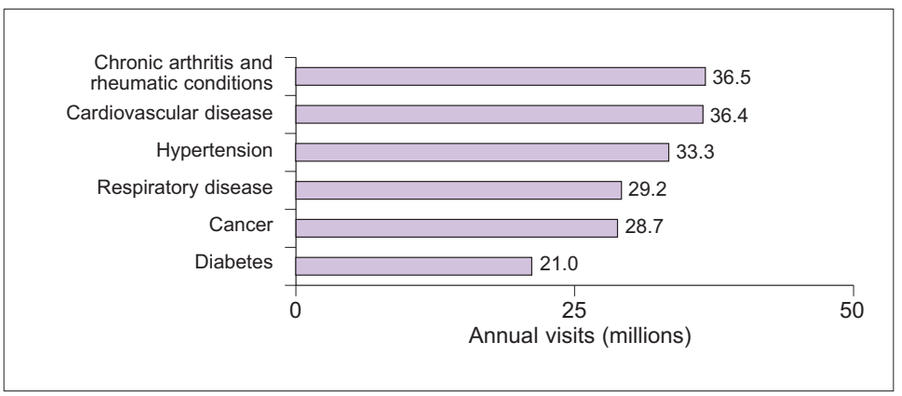
7.10 Assessment of disabling symptoms. (Based on Marcus DA, 2005[10].)

Arthritis

Arthritis or chronic joint pain, aching, stiffness, or swelling affects 1 in 3 adults (**7.11**)[12]. Chronic arthritis is a major cause of outpatient visits. Using data from two large, national surveys in the United States, arthritis or other rheumatic conditions were the primary diagnosis for 44 million of the total 959 million annual ambulatory care visits (**7.12**)[13]. The rate of arthritis visits increased with age, and women accounted for almost twice as many arthritis visits as men. Most arthritis visits were made to primary care health providers (53%), with only 16% made to rheumatologists. The most common individual arthritic conditions were osteoarthritis (OA) (20%) and rheumatoid arthritis (RA) (11%).



7.11 Prevalence of joint pain. A total of 212,510 adults ≥18 years old were questioned about joint pain, aching, stiffness, or swelling in a national survey in the United States and its territories (dx: diagnosis; sx: symptoms). (Based on Feinglass J, *et al.*, 2005[12].)



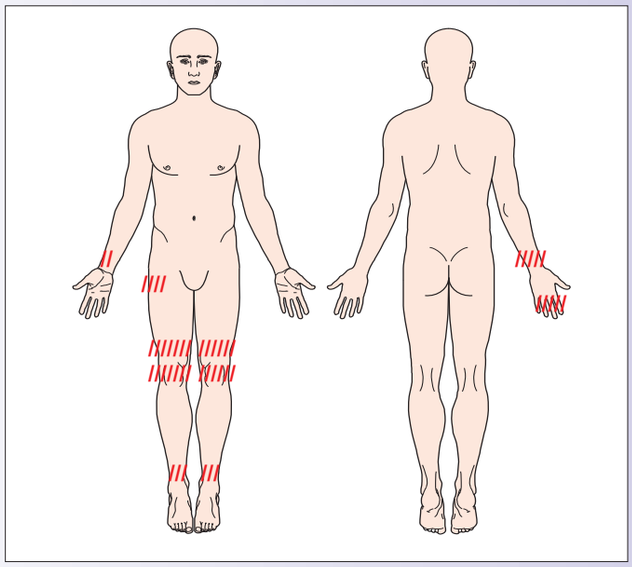
7.12 Reasons for ambulatory care visits. Number of ambulatory care visits was determined for different primary diagnoses, using data from the National Ambulatory Medical Care Survey/National Hospital Medical Care Survey in 1997. (Based on Hootman JM, *et al.*, 2002[13].)

Osteoarthritis

Case presentation

An overweight, 54-year-old hotel maid reports pain in her right hand, right hip, both knees, and both ankles for the last 8 months. "All of my joints are so stiff when I first wake up in the morning. After I've moved around for about 20 minutes, they begin to move better." She has been able to continue her work, although occasionally her joints seem to lock and she is also very stiff for about 15–20 minutes after her lunch break. "My knees creak and groan like I'm an old lady whenever I walk." Resting in the evening helps relieve her pain. Her pain drawing is shown.

Asymmetric pain of weight-bearing joints is characteristic of OA. Joint stress from excess weight and physical labour can aggravate degenerative arthritis. Patients typically report brief periods of morning stiffness that improve with using the joints. Pain often improves with rest. Joint crepitus and locking are characteristic of OA.



Epidemiology of osteoarthritis

OA is characterized by morning joint stiffness, bony enlargement, and pain with activities that improves with rest (*Table 7.3*). Nonjoint symptoms may occur from associated muscle spasm, nerve root impingement, or spinal canal stenosis. Systemic symptoms are not expected.

As adults age, the prevalence of OA increases. Hand OA occurs in about 10–30% of young adults and about 75% of adults 60–70 years old[14]. Knee OA is less common, but still affects 1 in 3 adults ≥75 years old. As the worldwide population ages, the impact of OA on society and clinical practices is expected to increase. Advancing age, female gender, obesity, and frequent joint stress from occupation or other activities may all increase risk for developing symptomatic OA.

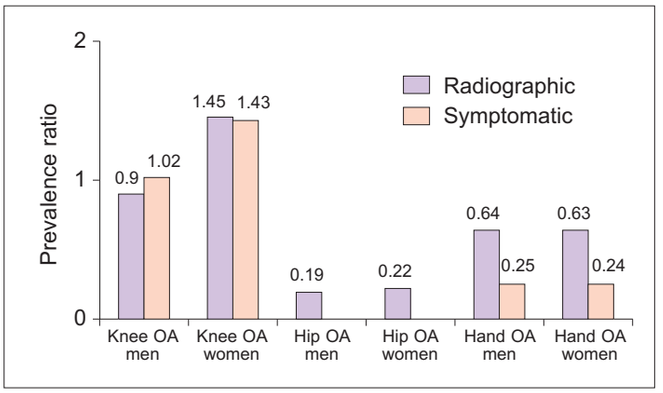
The prevalence of OA varies among countries. Comparison of data from the Beijing OA Study and several United States samples showed a generally lower prevalence of OA among Chinese, including the prevalence of hand OA, which can be considered a marker of generalized OA risk (**7.13**)[15–17].

Assessment of osteoarthritis

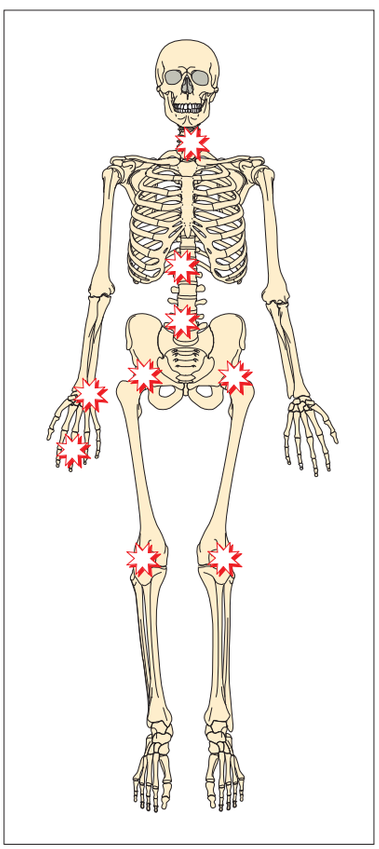
The diagnosis of possible OA requires identification of characteristic joint involvement patterns, physical examination findings, and radiographic abnormalities. OA typically affects high-use, weight-bearing joints in an asymmetric pattern (**7.14**). Characteristic physical examination findings are depicted in Figure **7.15**.

Table 7.3 Diagnostic features of OA

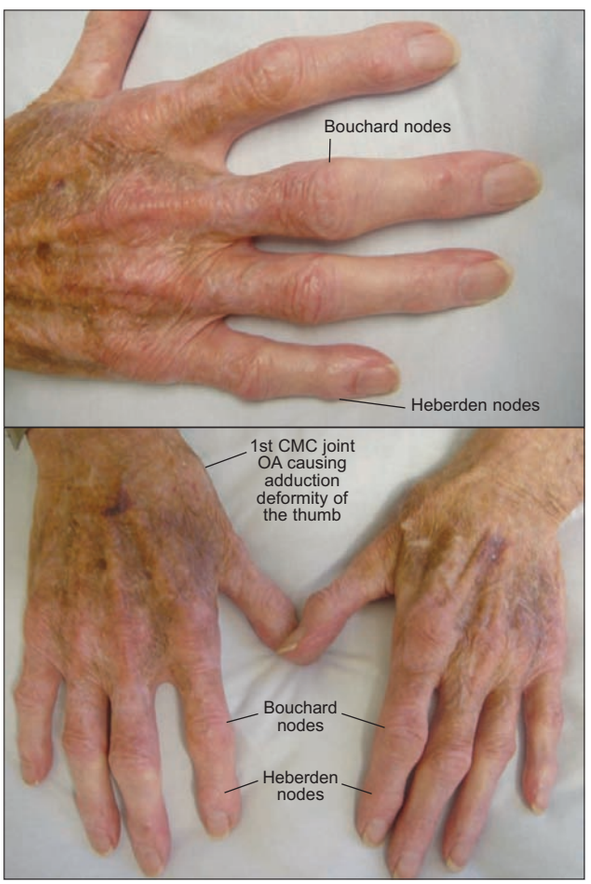
- Joint pain
- Morning stiffness
- Joint changes on radiographs
- Crepitus with joint movement



7.13 Age-standardized OA prevalence ratio Chinese:US Caucasians. Prevalence of OA in community-dwellers 60 years and older was compared in samples of Chinese adults in Beijing and Caucasian adults in the United States in three studies. Diagnosis was made based on radiographic evaluations and/or symptom reports. After adjusting for differences in age, prevalence ratios were calculated to describe OA occurrence in Chinese compared with Caucasian adults. Ratios for all three studies are depicted in the graph. Ratios >1 describe a higher prevalence in Chinese. Only female knee OA (diagnosed by either clinical symptoms or radiographic appearance) occurred more commonly in Chinese participants. Hip and hand OA were less prevalent in Chinese adults. Researchers in Thailand linked the increased prevalence of knee OA in Asians with habitual use of stressful knee positions, including squatting, lotus position, and side-knee bending[18]. (Based on Zhang Y, *et al*., 2001[15], 2003[17]; Nevitt MC, *et al*., 2002[16].)



7.14 Typical patterns of joint involvement in OA. Stars denote typical joints involved in OA, which characteristically affects overused and large weight-bearing joints. Joint involvement is often asymmetrical.



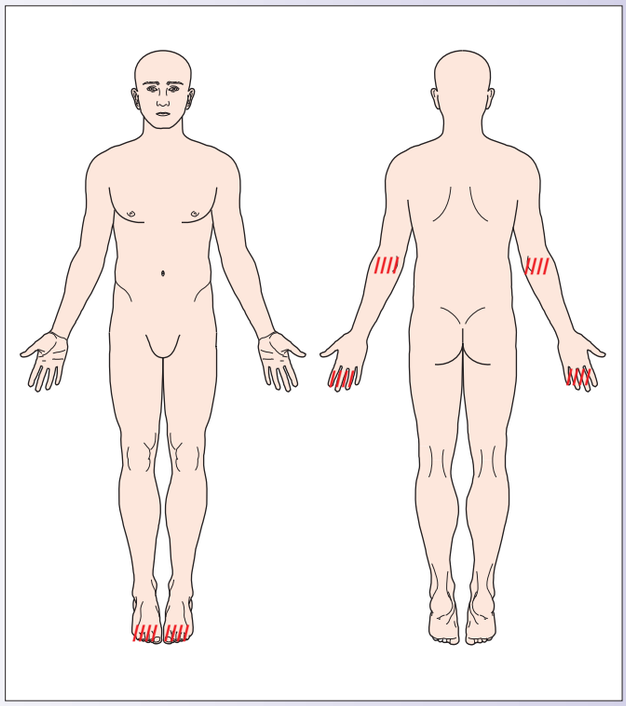
7.15 Characteristic changes in OA. These two photographs from the same patient show typical features of OA in the hands. Bony nodules (osteophytes) are called Bouchard nodes at the proximal interphalangeal joints and Heberden nodes at the distal interphalangeal joints. Note the sparing of the metacarpophalangeal joints, which would typically be involved in patients with RA. This patient also has OA of the right 1st carpometacarpal (CMC) joint, leading to an adduction deformity in the thumb. Also note the wasting of the interossei muscles because of hand pain leading to disuse.

Rheumatoid arthritis

Case presentation

A 37-year-old homemaker has noticed pain and stiffness in her elbows, hands, and feet that began about 6 months ago and seems to wax and wane. The morning is very bad and she has a lot of trouble getting her children ready for school. About 1–2 hours after the children have left for school, the pain and stiffness usually start to improve. The pain is still there, even if she doesn't use her hands. She is otherwise in good health, although she has had some low-grade fevers over the last few months with no other signs of systemic illness. Her pain drawing is shown. Physical examination shows swelling and tenderness of her metacarpophalangeal joints on both hands and restricted range of motion in her shoulders and elbows bilaterally. Blood work reveals mild anemia and an elevated CRP. Synovial fluid analysis confirms inflammatory arthritis, without evidence of infection or gout.

Symmetrical swelling, pain, and stiffness of joints in the hand and other nonweight-bearing joints are characteristic of RA. RA treatment focuses on preventive therapies to minimize long-term joint destruction and disability.



Epidemiology of rheumatoid arthritis

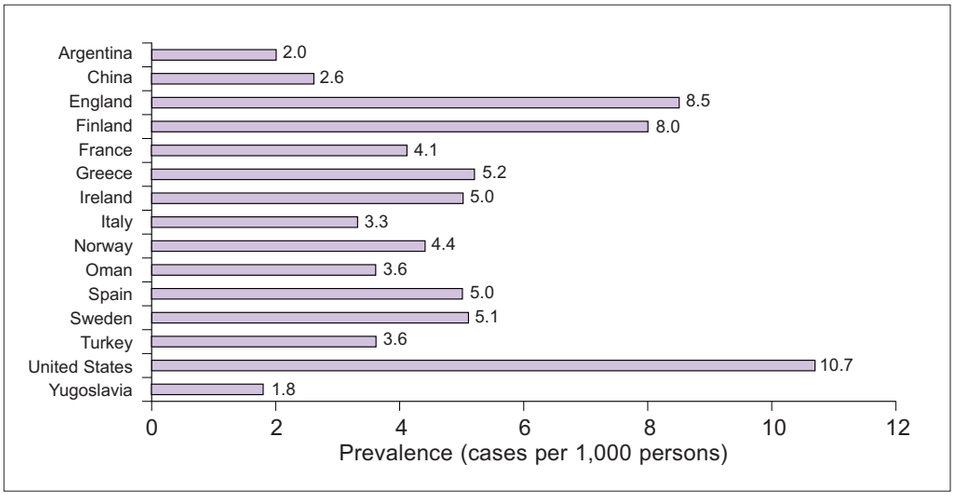
Rheumatoid arthritis (RA) is characterized by pain, swelling, and prolonged morning stiffness of small joints, especially the hands (*Table 7.4*). Joints are typically affected in a symmetrical distribution. Systemic symptoms are common in RA.

RA affects about 1% of people worldwide, with a female: male preponderance of about 2.5 to 1 (**7.16**)[20,21]. Risk factors for developing RA include both genetic and environmental factors. Estrogen, cigarette use, diet, and occupation have all been linked to RA risk[22].

Table 7.4 Clinical features suggesting inflammatory arthritis

- Historical features
  - Pain and/or swelling in several joints
  - Significant joint stiffness in the morning or after rest
  - Progressive loss of joint function
  - Symmetrical joint involvement in hands and feet
  - Good response to NSAIDs
- Physical examination features
  - Joint inflammation (soft tissue swelling around joints, warmth, tenderness)
  - Restricted joint range of motion

NSAID: nonsteroidal anti-inflammatory drug. (Based on Gormley GJ, *et al.*, 2003[19])



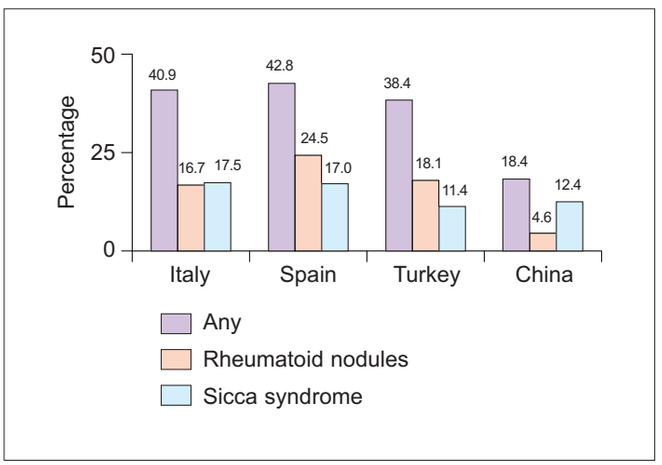
7.16 Worldwide prevalence of RA. The prevalence of RA was estimated in several world regions, with data from cross-sectional and retrospective studies using American College of Rheumatology diagnostic criteria. Median prevalence by region per 1,000 persons was 5.0 for northern Europe, 3.3 for southern Europe, and 3.5 for developing countries. Researchers postulate that genetic and environmental factors, such as increased consumption of fish and olive oil, may contribute to the decreased RA prevalence in southern Europe. (Based on Alamanos Y, *et al.*, 2006[21].)

A wide assortment of extra-articular symptoms occurs in RA (*Table 7.5*). The most commonly reported extra-articular manifestations are rheumatoid nodules and sicca or Sjögren's syndrome. Extra-articular or systemic symptoms in RA correlate with RA severity and high rheumatoid factor titers and predict higher mortality. The prevalence of extra-articular symptoms varies by region, with a particularly low prevalence reported in Chinese patients with RA (**7.17**)[23–26]. Furthermore, patients with RA have a significantly increased risk of cardiovascular disease, including myocardial infarction, stroke, and cardiovascular-related deaths (**7.18**)[27].

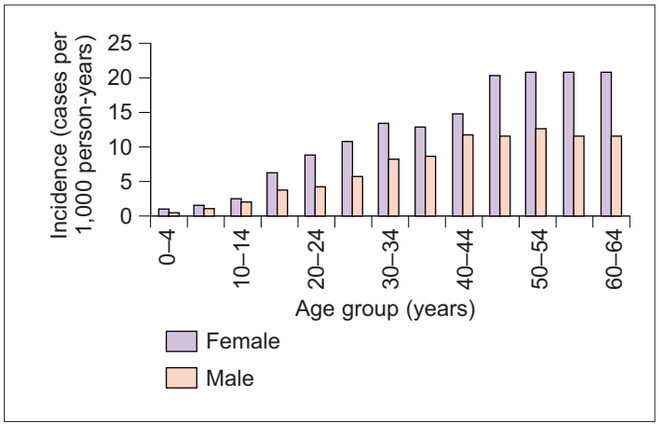
Overall mortality is increased twofold in adults with RA compared with the general population[28]. Risk is greatest in the first 5 years after initial hospitalization for RA. In general, causes of death are similar for patients with RA and

Table 7.5 Extra-articular manifestations of RA

- Osteoporosis
- Scleritis and episcleritis
- Rheumatoid nodules
- Sicca syndrome (dry mouth and eyes)
- Pleuropulmonary disease
- Raynaud's phenomenon
- Cutaneous vasculitis
- Peripheral neuropathy
- Lymphadenopathy
- Splenomegaly
- Felty's syndrome
- Amyloidosis

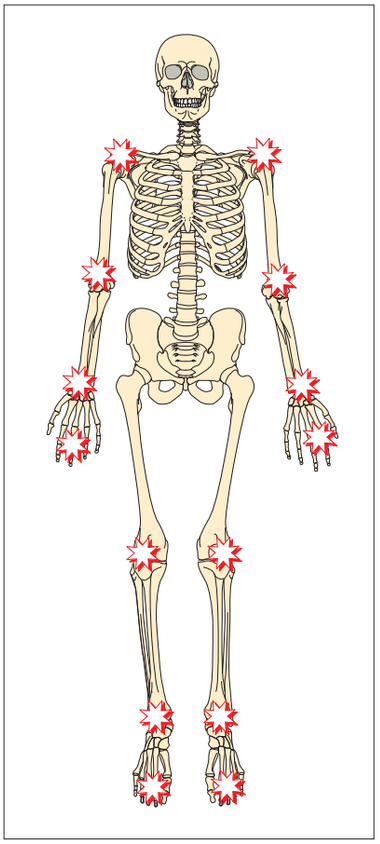


7.17. Occurrence of common extra-articular manifestations of RA by region. Occurrence of extra-articular manifestations identified in RA patients in Italy (Cimmino MA, *et al.*, 2000[23]), Spain (Carmona L, *et al.*, 2003[24]), Turkey (Calgüneri M, *et al.*, 2006[25]), and China (Cohen MG, *et al.*, 1993[26]).



7.18 Incidence rates of cardiovascular events. Data from a Canadian healthcare database were used to compare cardiovascular disease in adults receiving at least three diagnoses of RA within 2 years and age-matched controls with at least three doctor visits within 2 years and no RA diagnosis. Overall cardiovascular event rate (defined as events per 1,000 person-years) was 14.8 among subjects with RA and 9.1 among controls. (Based on Solomon DH, *et al.*, 2006[27].)

7.19 Typical pattern of joint involvement in RA. Stars denote typical joints involved in RA, which generally produces symmetrical inflammatory changes in small joints.



the general population, although death occurs prematurely in RA patients. Causes of death with increased risk in RA patients include lung and hematologic cancers, cardiovascular disease, respiratory infections, chronic obstructive pulmonary disease, and renal failure.

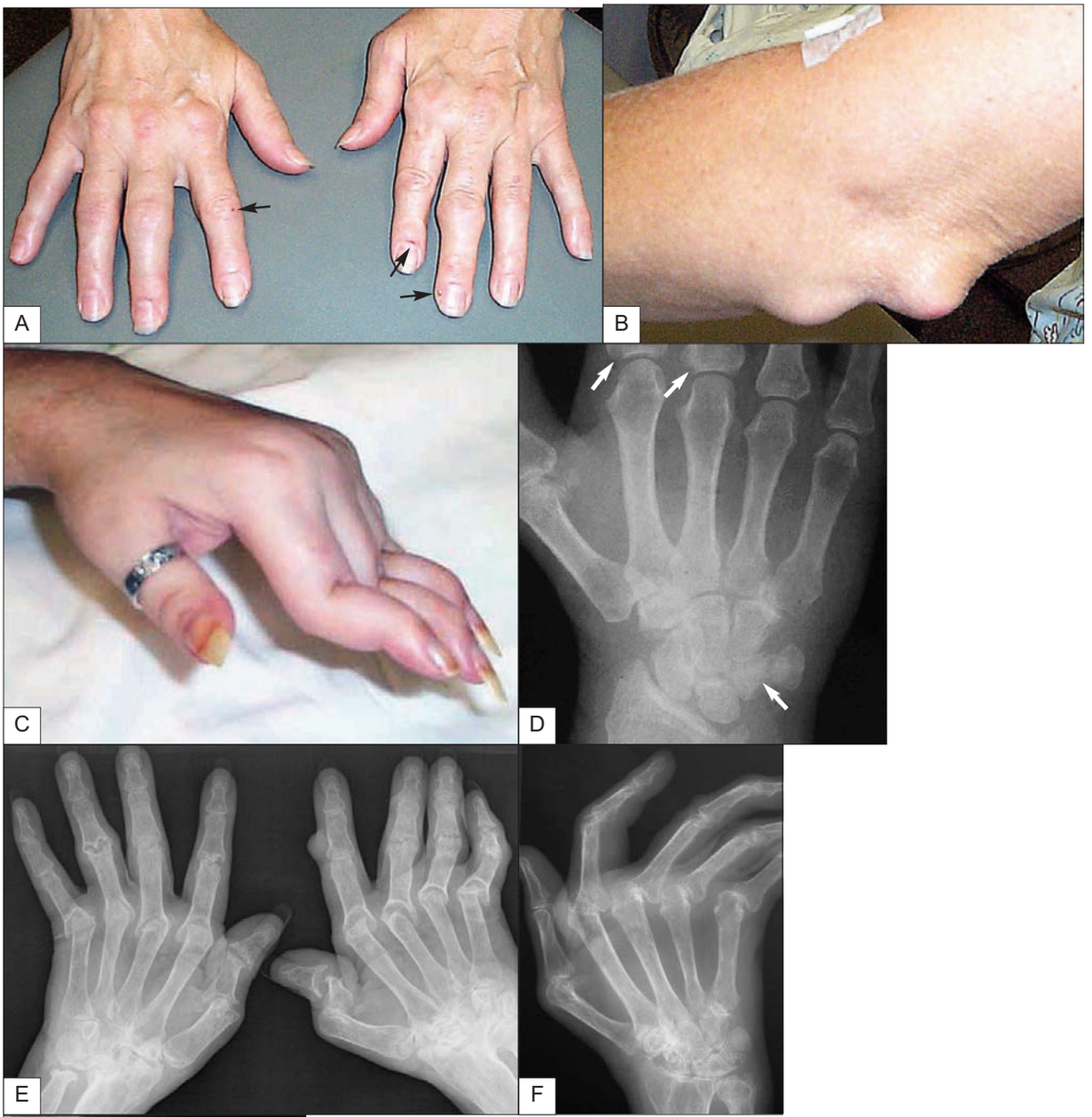
Assessment of rheumatoid arthritis

The diagnosis of RA is made when patients have characteristic patterns of joint involvement, physical examination findings, and radiographic abnormalities. RA usually affects small, nonweight-bearing joints in a symmetrical fashion (**7.19**). Symmetrical swelling of the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints is seen in early RA (**7.20**). Typical fusiform or spindle-shaped enlargement of the PIP joints is usually seen, accompanied by tenderness and restricted range of motion. As RA progresses, joint destruction occurs with characteristic deformities in the hands, such as the boutonnière, the swan neck, and the unstable PIP joint by joint synovitis. Ulnar deviation, MCP joint subluxation, and rheumatoid nodules are characteristic changes seen with progressive disease.

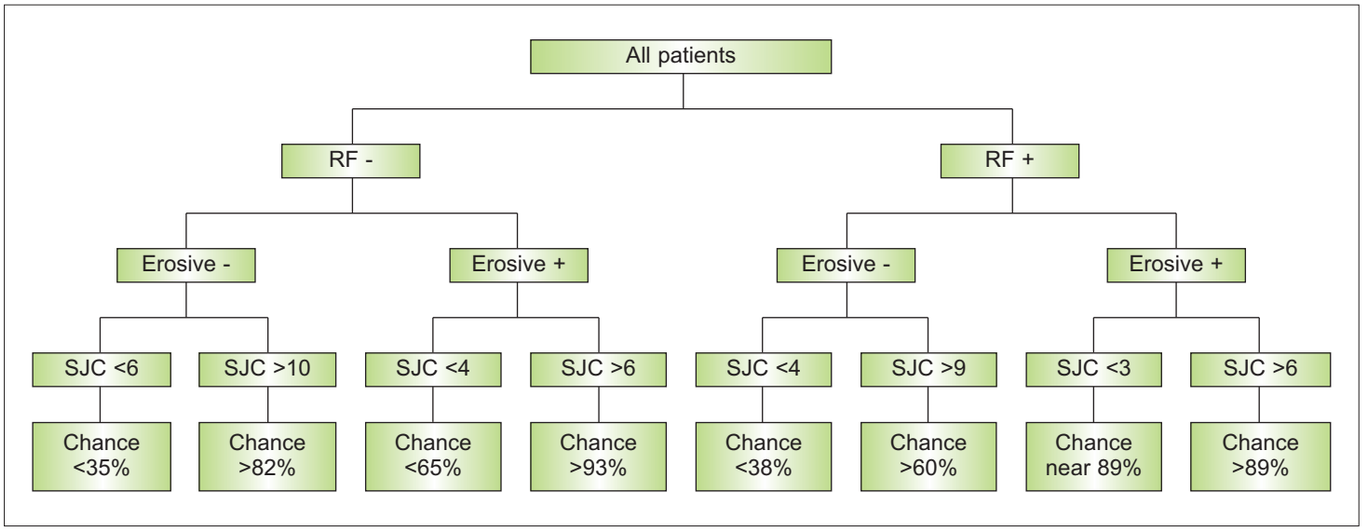
Patients with RA need to have pretreatment assessments of blood work (*Table 7.6*), a synovial fluid analysis to rule out other conditions, and radiographs of affected joints, as well as of hands and feet. Physical examination recordings should also be made of severity of pain, stiffness, fatigue, disability, and systemic symptoms. The number of swollen and tender joints, joint deformities, and motion restrictions should be documented. Symptomatic severity and physical

Table 7.6 Baseline laboratory tests in RA patients

- Erythrocyte sedimentation rate or C-reactive protein
- Rheumatoid factor
- Antibodies to cyclic citrullinated peptide (anti-CCP)
- Complete blood count
- Electrolytes, creatinine, and liver functions
- Urinalysis



7.20 Features of RA. Characteristic physical examination findings in RA patients are shown in **A**. Bilateral swelling and deformities characteristically affect metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. Small vessel vasculitis, as marked by the arrows, is an extra-articular RA manifestation that affects a small minority of patients with severe RA. Rheumatoid nodules may also be present over extensor surfaces and pressure points in patients with severe, seropositive RA (**B**). Swan neck deformity affecting the PIP occurs most commonly in RA patients, although it can also occur in other types of arthritis (**C**). Chronic inflammation of the PIP joint stretches supportive ligaments, resulting in chronic hyperextension. Radiographic changes also characteristically affect the proximal joints in the hand and wrist (**D**), with more severe bony erosions developing with more advanced disease (**E**–**G**). Arrows in **D** and **G** demonstrate areas of joint erosion. (Images **E–G** courtesy of Dr. Donald Sauser.)



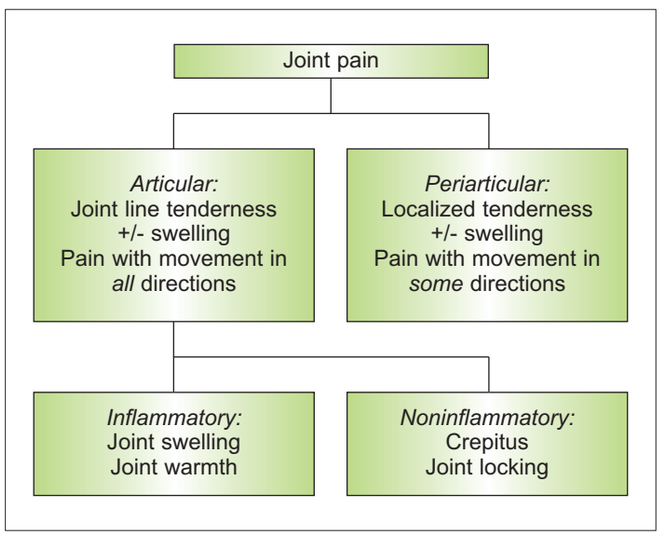
7.21 Algorithm predicting long-term outcome in RA patients. A total of 112 female RA patients with symptoms <5 years at the time of enrolment were followed for 12 years to identify factors related to long-term disability. An algorithm was developed to predict outcome, based on clinically-available disease measures. Rheumatoid factor (RF), the presence of radiographic erosions, and swollen joint count (SJC) were used to predict the probability of severe disability (chance). (Based on Drossaers-Bakker KW, *et al*., 2002[29].)

examination measures can be used at follow-up visits to assess treatment benefits. In addition, long-term prognosis can be predicted using information from laboratory, radiographic, and physical examination findings (**7.21**)[29].

Differentiating among arthritis diagnoses

Musculoskeletal pain can be divided into arthritis, periarticular pain, nonarticular pain, and referred pain. Periarticular pain includes bursitis, tendonitis, tenosynovitis, and ligament-related pain. Nonarticular pain includes abnormalities of the muscle (e.g. myofascial pain) or bone and fibromyalgia. Referred pain includes visceral and neurological pain. Differences in pain characteristics and physical examination findings can distinguish among these pain categories (*Table 7.7*).

Patients with joint-area pain may have articular or periarticular pain. These categories can be distinguished by identifying areas of tenderness and response to joint movement (**7.22**). Once arthritis has been diagnosed, patients should be categorized with either inflammatory or noninflammatory arthritis (**7.23**). Inflammatory arthritis is typically rapid in onset, with a waxing and waning course and profound and prolonged morning stiffness. Pain occurs with activity or rest. Patients often report having hot, red



7.22 Distinguishing articular from periarticular pain.

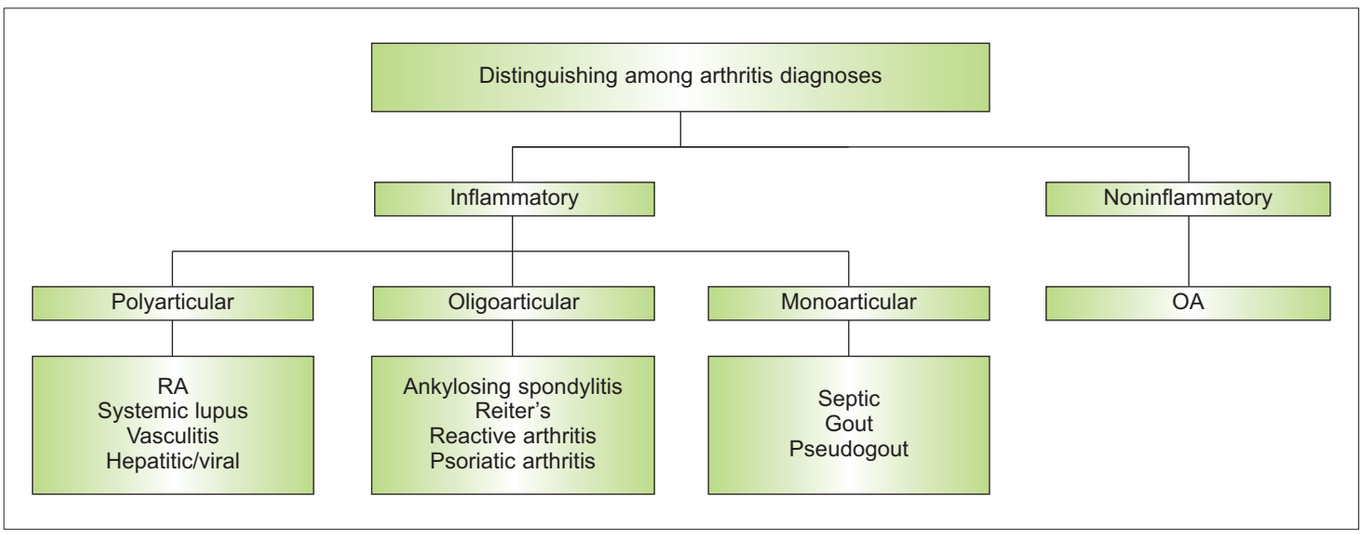
Table 7.7 Identifying arthritis

	Arthritis	*Periarticular*	*Nonarticular*	*Referred*
Pain location	Joint	Near joint	Diffuse; not tied to joint(s)	Visceral or nerve distribution pain. Regional pain pattern
Pain aggravation	Pain occurs with movement in *all* directions	Pain occurs with *some* movements	Pain unrelated to specific joint movements	Pain unrelated to specific joint movements
Examination	Swelling and tenderness of entire joint; ROM limited in *all* directions. Pain similar with passive and active ROM	Swelling and tenderness over part of joint and surrounding joint; ROM limited in *some* directions; pain worse with active ROM than passive ROM	Tenderness over muscle areas or nonjoint bony areas	Lack of joint swelling and tenderness; passive ROM normal; numbness and weakness occur with neurological pathology

ROM: range of movement

joints. Systemic symptoms are also common. Noninflammatory arthritis, conversely, usually has a slow onset and steadily progressive course. Pain usually increases with joint use and decreases with rest. Morning stiffness is milder and shorter in duration and systemic symptoms are absent. On examination, crepitus is often present in addition to joint swelling and tenderness. Synovial fluid analysis reliably differentiates between inflammatory and noninflammatory arthritis (*Table 7.8*). Septic arthritis is distinguished by a positive synovial fluid culture.

Distinguishing between diagnoses of OA and RA depends on differences in patterns of joint involvement, symptoms, and examination findings (**7.24**, *Table 7.9*). Hands are typically involved in both common types of arthritis.



7.23 Differentiating among arthritis diagnoses.

Table 7.8 Comparison of synovial fluid analyses

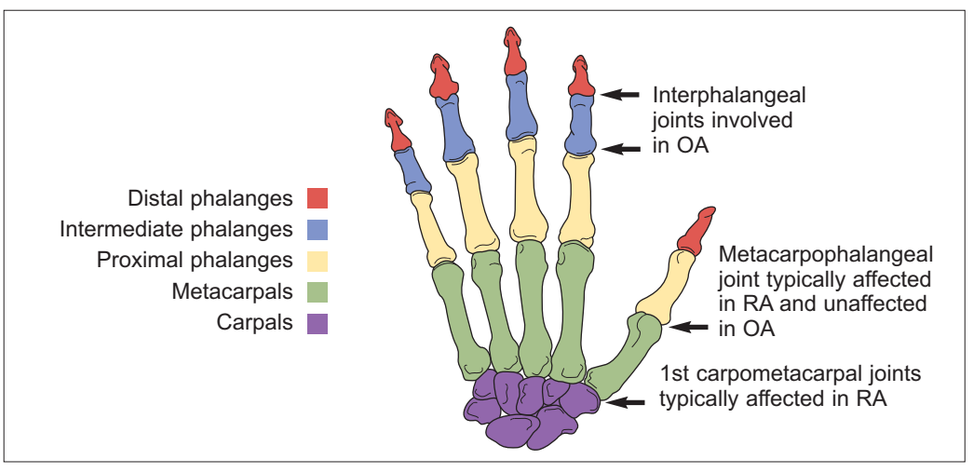
	Normal	***Arthritis***		
		Noninflammatory	*Inflammatory*	*Septic*
Volume	Low	High	High	High
Appearance	Clear	Clear	Cloudy	Cloudy
Viscosity	High	High	Low	Low
WBC (%PMN)	<200 (<25%)	200–2,000 (<50%)	2,000–75,000 (>75%)	>50,000 (>90%)

PMN: polymorphonuclear leukocyte; WBC: white blood count

Table 7.9 Comparison of osteoarthritis (OA) and rheumatoid arthritis (RA)

	OA	*RA*
Onset	Gradual	May be acute or insidious
Affected joints	PIP & DIP joints of fingers, hips, knees, feet	Metacarpophalangeal joint, wrist, elbows, ankles
Symptoms	Pain worse with activities, improves with rest Stiffness after inactivity	Morning stiffness usually longer than 1 hour Systemic symptoms (low-grade fever, fatigue, malaise)
Physical examination	Deformities, bony overgrowth, crepitus, reduced range of motion, associated muscle spasm	Joints swollen, tender, and warm Hands held in flexion to avoid distention of joint capsules
Radiographic pattern	Asymmetrical joint involvement Nonuniform joint space loss, osteophytes, subchondral cysts and sclerosis	Symmetrical joint involvement No new bone formation Uniform joint space loss, erosions, decreased bone density Swan neck, boutonnière, and ulnar deviation deformities common

DIP: distal interphalangeal; PIP: proximal interphalangeal



7.24 Joint involvement in hand in arthritis. OA: osteoarthritis; RA: rheumatoid arthritis.

Treatment

Fibromyalgia

No single treatment manages all of the possible variety of symptoms occurring in fibromyalgia patients. Treatments are generally selected to target individual symptom complexes (**7.25**). The most effective therapies for fibromyalgia include aerobic exercise and psychological pain management techniques. Antidepressants are the most effective group medications for fibromyalgia, although only about 1 in 3 fibromyalgia patients benefits[30]. Antidepressants are most beneficial for patients with additional somatic complaints. The good news for fibromyalgia patients and their healthcare providers is that improvement generally occurs with long-term management (**7.26**).

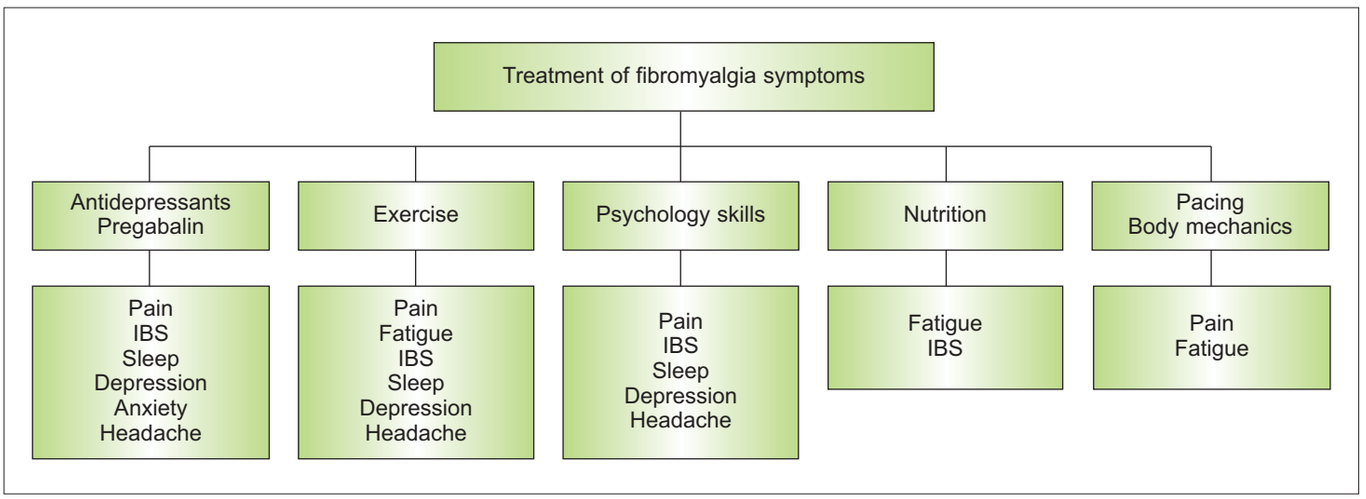
Arthritis

Arthritis treatment varies, depending on the type of arthritis. Among arthritic conditions, NSAIDs, analgesics, and steroids are most commonly prescribed (**7.27**)[13]. A survey of patients with arthritis or fibromyalgia showed that NSAIDs were perceived as more effective than acetaminophen[31]. This difference in perceived effectiveness and tolerability was greatest among RA patients, with less of a preference for patients with either OA or fibromyalgia ($P<0.001$).

Nonpharmacologic treatments are also important, including weight control, exercise, and pain management techniques. Obesity has been linked to the development of OA in the hands, hips, and knees, as seen in the case presentation[32]. Both strengthening and aerobic exercise significantly reduce pain and disability in patients with OA or RA[33,34]. Twice weekly, high-intensity exercise was shown to reduce long-term joint destruction in RA patients[35]. Radiographic joint damage progression occurred in 11% of RA patients treated with exercise versus 22% treated with physical therapy over 2 years ($P<0.05$).

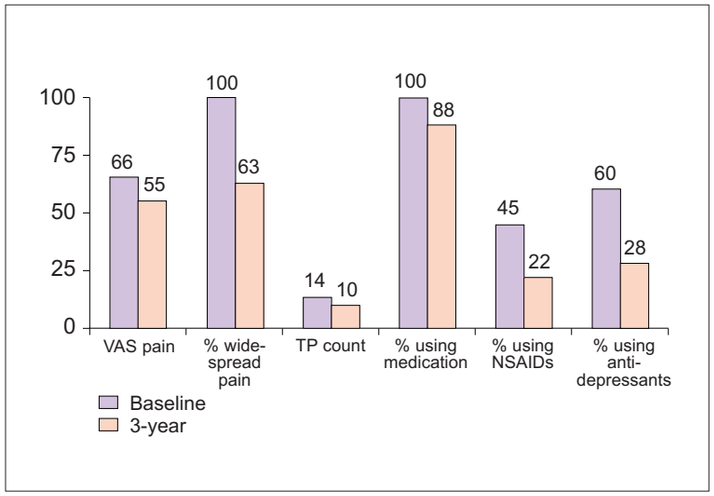
Treating OA

Acetaminophen is the first-line medication therapy for noninflammatory, degenerative OA (**7.28**). The added side-effects from NSAIDs are undesirable in patients who do not need the additional anti-inflammatory component from this medication class. OA patients failing to respond to acetaminophen may require additional medication therapies. In addition, medication response to NSAIDs may differ, depending on arthritis location (**7.29**)[36].

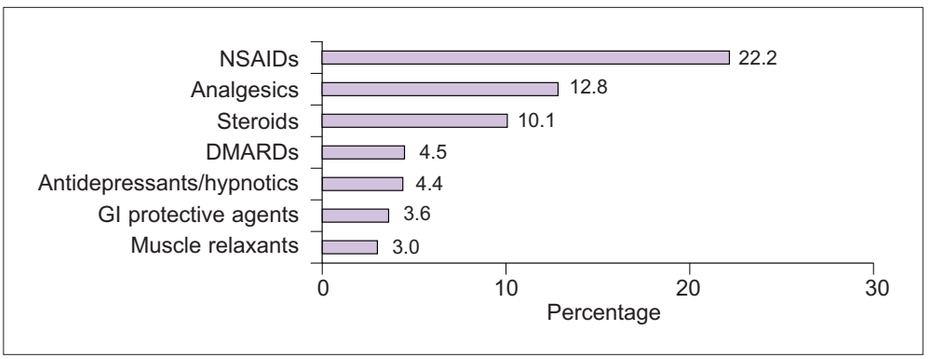


7.25 Targeting symptoms for fibromyalgia treatment. Treatment options are chosen, based on symptom complexes. Generally, fibromyalgia patients respond best when treated with multidisciplinary treatment rather than monotherapy. Among medication options, pregabalin and the serotonin and noradrenaline uptake inhibitors, duloxetine and milnacipran, provide the best symptomatic relief. IBS: irritable bowel syndrome.

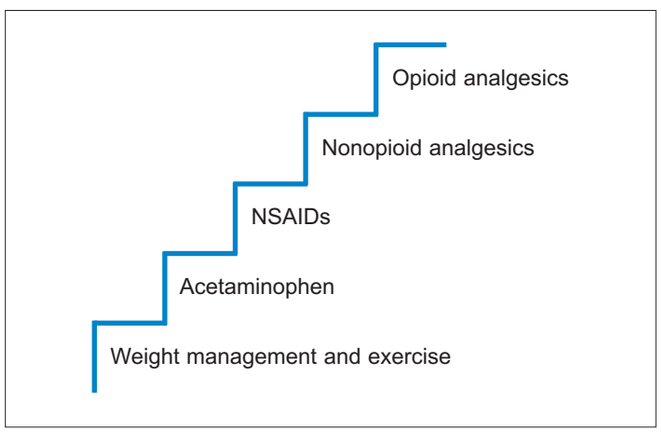
7.26. Three-year follow-up of treated fibromyalgia patients. This longitudinal study followed 59 fibromyalgia patients treated in university or community settings for 3 years. Visual analogue scale (VAS) pain scores (ranging from 0 mm=no pain to 100 mm=severe pain) and tenderpoint (TP) counts decreased significantly after 1 year (P<0.05) and remained significantly decreased for the full 3 years of evaluation (P<0.01). Use of antidepressants, nonsteroidal anti-inflammatory drugs (NSAIDs), and muscle relaxants was each significantly decreased after 1 and 3 years of follow-up (P<0.05). (Based on Pöyhiä R, *et al*., 2001[30].)

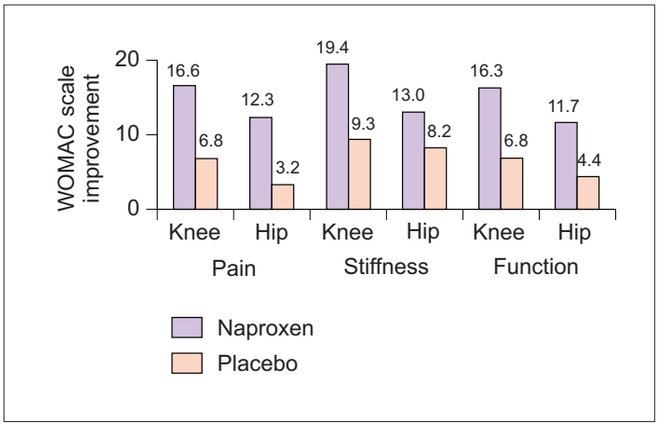


7.27 Treatments prescribed for arthritis and rheumatic conditions. Among drugs prescribed or continued at ambulatory care visits for arthritic conditions in two surveys in the United States, nonsteroidal anti-inflammatory medications (NSAIDs) were most commonly prescribed, followed by nonopioid, opioid, and topical analgesics. Disease-modifying antirheumatic drugs (DMARDs) were most commonly prescribed for patients with rheumatoid arthritis or autoimmune connective tissue diseases. GI: gastrointestinal. (Based on Hootman JM, *et al*., 2002[13].)



7.28 Steps for OA treatment. OA patients should initially be treated with weight management and exercise. Acetaminophen is the first-line therapy in patients requiring medication. Patients failing to respond to these therapies may need to move up the steps to alternative medications. NSAIDs: nonsteroidal anti-inflammatory drugs.





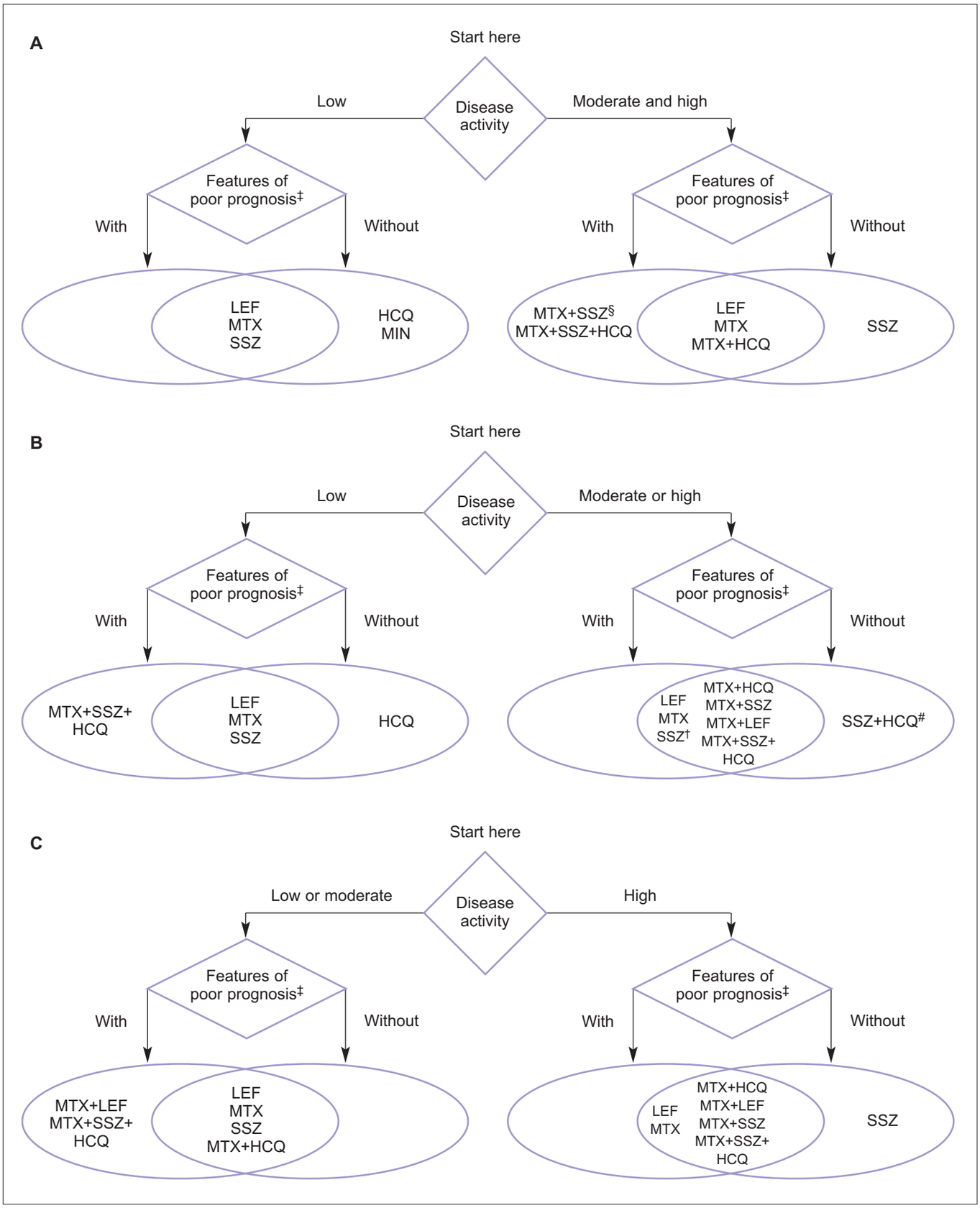
7.29 Differential treatment response of OA to naproxen. Adults aged 40–75 with chronic knee (N=75) or hip (N=33) OA were treated with naproxen 500 mg or placebo twice daily, in a double-blind, 6-week study. Post-treatment response was evaluated using the Western Ontario and McMaster Universities (WOMAC) subscales. After treatment with naproxen, improvement on all scales was significantly better for patients with knee OA (P<0.05). Numerical differences between knee and hip OA patients receiving placebo were not significant. (Based on Svensson O, *et al*., 2006[36].)

Treating RA

The diagnosis of RA should be established early, with initiation of DMARDs within 3 months of RA diagnosis (**7.30, 7.31**)[37]. Although both NSAIDs and DMARDs can effectively reduce joint pain, only DMARDs retard joint destruction. Among DMARDs, hydroxychloroquine or sulfasalazine are often selected as initial therapy in milder cases of RA, although methotrexate is becoming the initial DMARD of choice in the United States. Sulfasalazine is often preferred over hydroxychloroquine due to faster onset of action and better reduction of joint destruction. Disease activity and progression should be measured periodically. If the response to DMARD treatment is inadequate after 3 months of maximum therapy, therapy should be altered by adding or changing DMARDs. In patients with suboptimal response to methotrexate (MTX), biologic DMARDs can be used as monotherapy or in combination. Surgery may become necessary in patients with symptomatic or structural joint damage failing to respond to multiple DMARDs.

DMARDs influence important inflammatory pathways in RA (**7.32**). Despite reduction in inflammation and joint symptoms, bony changes often occur over time in treated patients. A 10-year study conducted in the United Kingdom evaluated clinical symptoms and radiographs in RA patients treated with DMARDs[38]. Average joint tenderness, morning stiffness, and grip strength remained relatively stable over the 10 years, while radiographic scores showed deterioration. At 10 years, 19% of patients received joint surgery, with 15% having at least one large joint replacement. Joint replacement was significantly more common in women than men (18.6% *vs*. 6.5%; P=0.02).

7.30, 7.31 American College of Rheumatology 2008 guidelines for using disease-modifying antirheumatic drugs (DMARDs). Establishing early diagnosis of RA is of paramount importance since early aggressive treatment is known to prevent irreversible joint damage that may occur by treatment delays. All patients with RA should receive DMARDs at diagnosis. It is good clinical practice to give patients a full disclosure on risks/benefits of all agents being considered for treatment. Use of NSAIDs, local corticosteroid injections and referral to physical and occupational therapies is recommended, depending on individual patient needs. **7.30** Recommendations for management of RA with nonbiologic DMARDs in patients who have never received DMARDs, and with disease duration of <6 months (**A**), 6–24 (**B**), and >24 months (**C**). **7.31** (*see page* 124) Recommendations for management of RA with biologic DMARDs in patients with disease duration <6 months (**A**), ≥6 months who failed prior MTX therapy (**B**), and ≥6 months who failed prior MTX combination therapy or sequential treatment with other nonbiologic DMARDs (**C**). ‡ Poor prognosis features include functional limitations and extra-articular disease (e.g. rheumatoid nodules, secondary Sjögren's syndrome, vasculitis, Felty's syndrome, and lung disease), rheumatoid factor positivity, positive anticyclic citrullinated peptide antibodies, or bony erosions on xray); § only recommended for patients with high disease activity with features of poor prognosis; † only recommended for patients with moderate disease activity, regardless of prognostic features or patients with high disease activity without features of poor prognosis; # only recommended for patients with high disease activity without features of poor prognosis. HCQ: hydroxychloroquine; LEF: leflunomide; MIN: minocycline; MTX: methotrexate; SSZ: sulfasalazine; TNF: tumor necrosis factor. (Based on Saag GK, *et al*., 2008[37].)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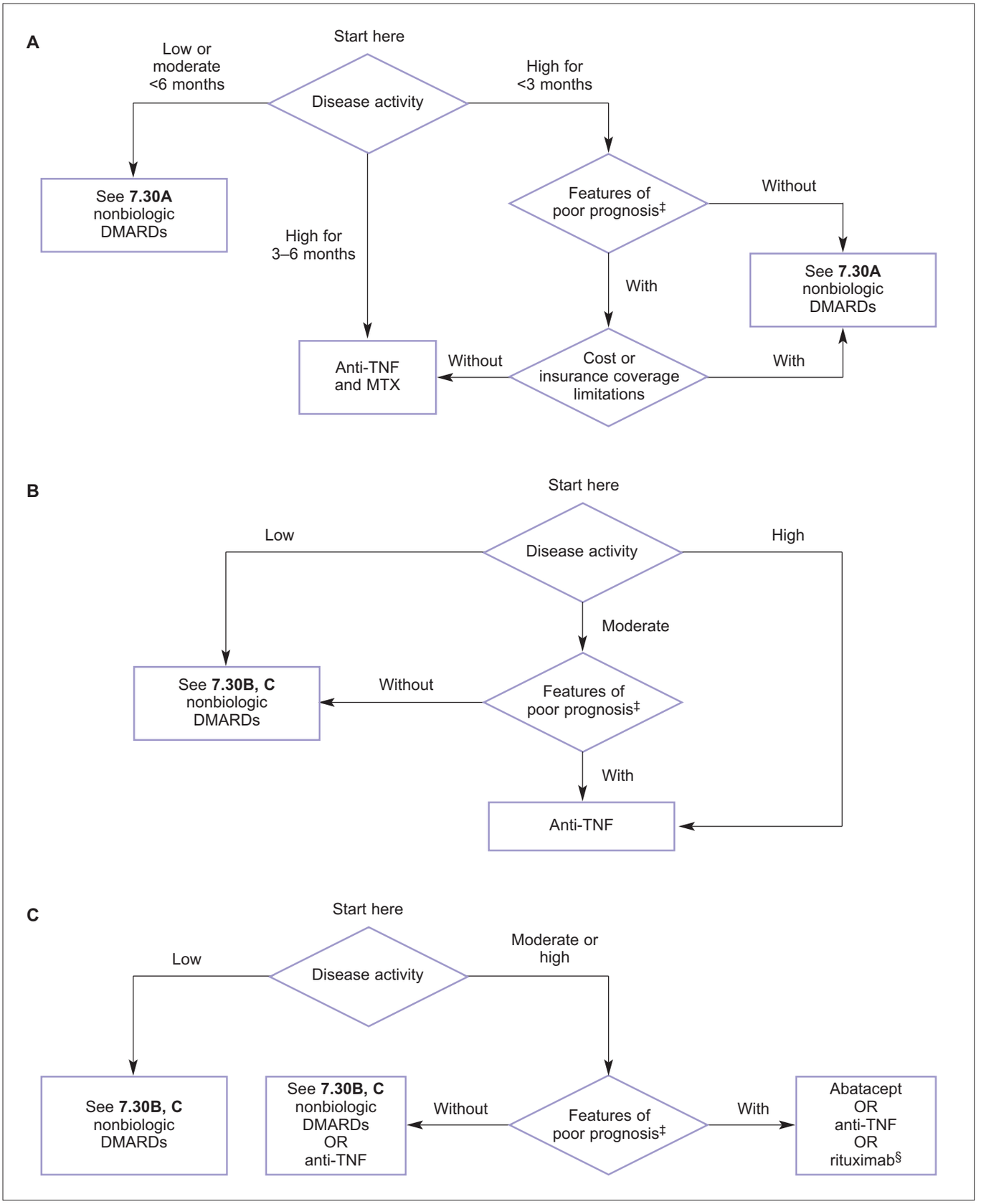
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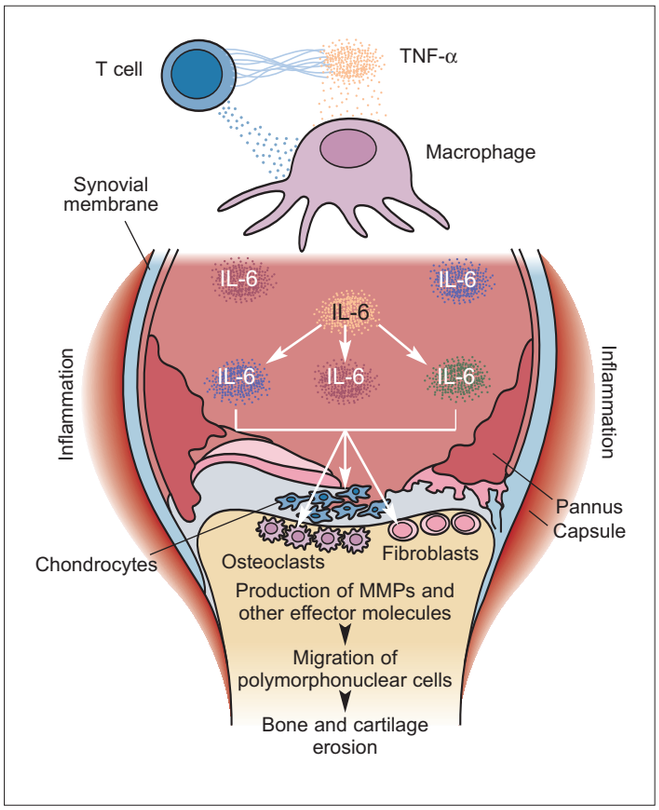

7.32 Inflammatory pathways in rheumatoid arthritis (RA). In RA, the interaction between antigen presenting cells (such as macrophages) and T cells lead to release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukins (IL). IL activates chondrocytes, osteoclasts, and fibroblasts that release matrix metalloproteinase (MMP) enzymes, ultimately leading to the erosion of bone and cartilage.

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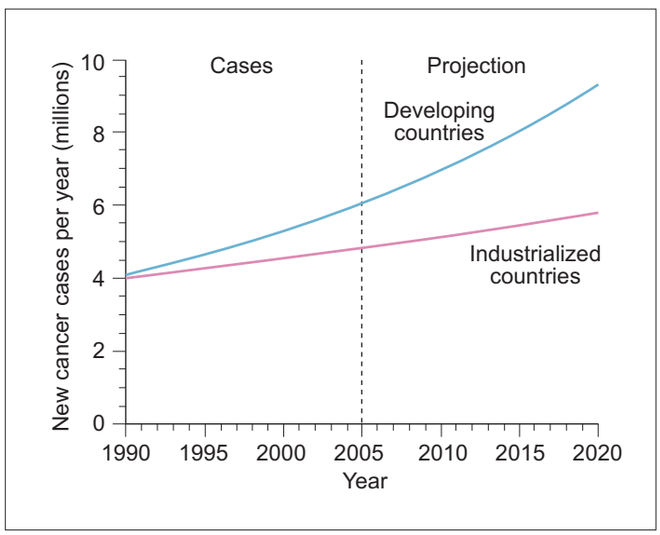
Chapter 8

Cancer pain

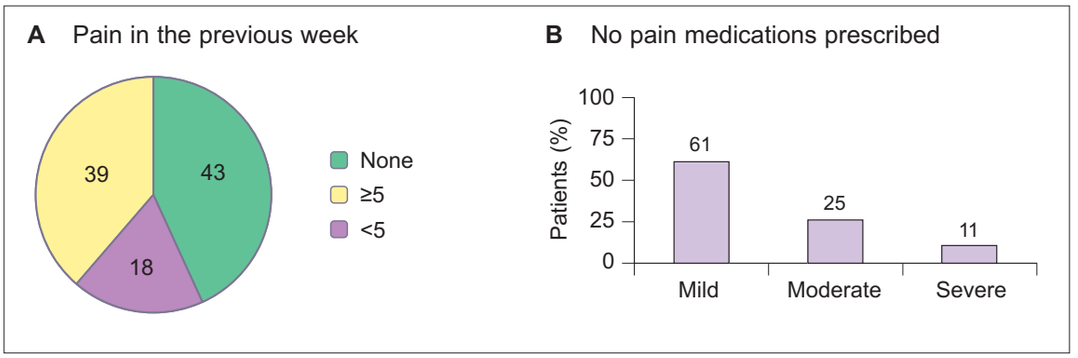
Introduction

Cancer prevalence is increasing in both industrialized and developing countries, with a marked increase among developing countries (**8.1**)[1]. Pain occurs in the majority of patients with cancer, especially among patients with metastatic disease (**8.2**)[2]. A recent meta-analysis of 52 studies of adult cancer pain reported pooled prevalence of pain of 53% in cancer patients overall, including 64% among those with advanced, terminal, or metastatic disease, 59% of those undergoing cancer treatment, and 33% after curative treatment[3]. Pain was rated as moderate to severe by 31% of all cancer patients and 45% with advanced, terminal, or metastatic disease.

Similar to nonmalignant chronic pain, pain in cancer patients has also been linked to disablity and psychological distress. A survey of 219 hospitalized cancer patients in Taiwan identified pain during the preceding week in 38%[4]. Patients with pain were more likely to have metastatic disease compared with nonpain cancer patients (82% *vs*. 41%). Cancer patients with pain also reported a poorer functional status and higher prevalence of anxiety and depression. A multivariate analysis controlling for metastatic disease and functional status showed that pain was an independent predictor of depression.



8.1 Worldwide cancer incidence prediction. Cancer incidence was recently estimated for industrialized and developing countries. Although the incidence was similar between country categories in 1990, the incidence in developing countries currently surpasses that in industrialized nations, with a prediction for almost 2 of every 3 new cancer patients in 2020 to be residing in a developing country. (Based on Salminen E, *et al*., 2005[1].)



8.2 Prevalence and under-treatment of cancer-related pain. A representative sample of 601 cancer patients was collected in 20 treatment settings in France, including 5 cancer treatment centres, 4 university hospitals, 5 state hospitals, 5 private clinics, and one home care setting. Patients were not recruited from speciality pain or palliative care practices. **A**: Pain during the preceding week was reported by 57% of cancer patients, with the majority of these reporting at least moderate severity pain (≥5 on a 0 [no pain] to 10 [unbearable pain] severity scale). Metastatic disease was present in 65% of patients reporting pain. **B**: One in three cancer patients reporting pain was receiving no pain medication prescriptions. Using the World Health Organization ladder to determine appropriate treatment, 51% of patients were considered to be under-treated for their pain complaints. (Based on Larue F, *et al*., 1995[2].)

Assessment

Cancer pain may be caused by cancer directly, cancer treatment, or noncancer conditions (*Table 8.1*). Cancer patients are also at higher risk for developing painful herpes zoster and PHN. In most cases, cancer-related pain is a direct result of cancer, although about one in four patients experience pain related to cancer treatment (**8.3**)[5].

Cancer pain may be caused by musculoskeletal, neurological, and visceral abnormalities. Musculoskeletal pain syndromes may be caused by direct effects on bones and muscles or severe joint deconditioning due to pain or neurological loss of surrounding structures. Bony metastases are more likely to be related to pain and functional disability when lesions are lytic (**8.4**)[7]. Neuropathic pain may be caused by direct invasion, surgery or postsurgical scarring, or by radiation or chemotherapy.

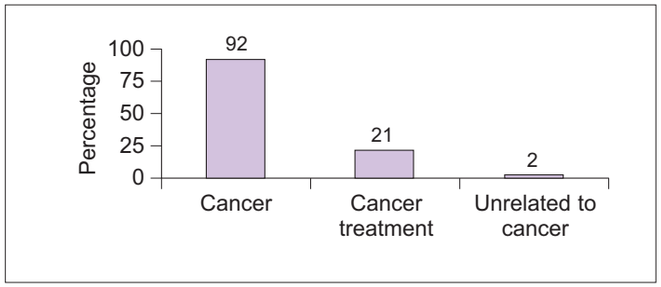
Identifying factors contributing to pain is important to allow appropriate understanding of pain complaints and subsequent development of treatment recommendations. For example, common pain syndromes in breast cancer include pain related to bony metastases, postmastectomy pain, and brachial plexopathy related to tumor or radiation (Case 1). While the pain in Case 1 was primarily neuropathic, Case 2 illustrates cancer pain related to a combination of both somatic and neuropathic pain conditions.

Table 8.1 Common causes of pain in cancer patients

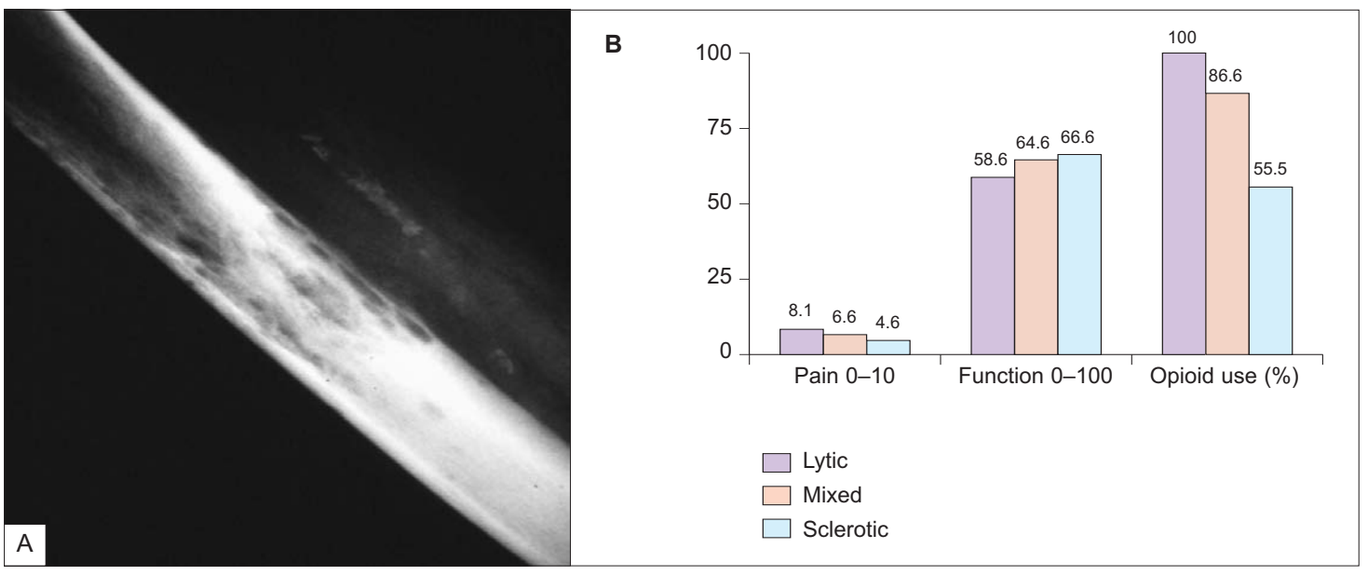
Cancer
- Bony erosion or metastasis
- Mucous membrane ulceration
- Nerve impingement
- Soft tissue infiltration
- Visceral distention

Cancer treatment
- Chemotherapy
  - Peripheral neuropathy
  - Avascular necrosis hip
  - Plexopathy with interarterial infusion
- Radiation
  - Plexopathy or myelopathy
  - Radiation enteritis and proctitis
  - Osteoradionecrosis
- Surgery
  - Postoperative pain
    Postmastectomy pain
    Post-thoractomy pain
  - Phantom pain

Nonmalignant pain conditions
- Musculoskeletal pain



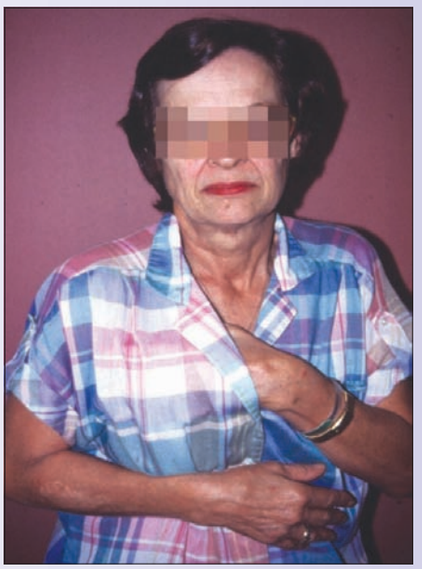
8.3 Causes of pain in cancer patients worldwide. Cancer-pain specialists in 21 countries in 5 continents (North and South America, Europe, Asia, and Australia) collected data on 1,095 consecutive patients >16 years old with cancer and chronic pain severe enough to require opioid analgesics. Primary cancer pain sites varied across most body regions among patients, and 70% of patients were diagnosed with metastatic disease. Most patients experienced pain as a direct result of their cancer, with one in five patients reporting a pain condition related to cancer treatment. A minority of patients reported pain complaints unrelated to cancer or its treatment. Average pain severity was rated as moderate (4.7 on a scale from 0 [no pain] to 10 [unbearable pain]). Sixty-five percent of patients also reported additional breakthrough pain, although reporting was significantly higher in English-speaking countries (Australia, Canada, New Zealand, and the United States) compared with Asia, Europe, and South America[6]. The authors speculated that terminology differences may have resulted in under-reporting of breakthrough pain by non-English-speaking country participants. (Based on Caraceni A, Portenoy RK, 1999[5].)



8.4 Lytic bone metastases. **A**: Radiograph showing characteristic lytic bone metastases. **B**: Comparison of pain and disability by type of bony metastasis. Adult patients with solid tumors and bone metastases (N=80) were evaluated in a prospective study. Pain severity was rated from 0 (no pain) to 10 (unbearable pain). Functional status was assessed with the Karnofsky performance status index, scoring function from 0 (dead) to 100 (normal). Analgesic consumption was also recorded. Patients with lytic bone metastases had significantly greater pain, disability, and opioid use than patients with sclerotic or mixed metastases ($P<0.05$). Pain and opioid use were also significantly higher in patients with mixed metastases compared with sclerotic lesions ($P<0.05$). Mean daily morphine-equivalent opioid dosage was 221 mg in patients with lytic metastases versus 192 mg with mixed lesions and 171 mg with sclerotic lesions. (Based on Vassiliou V, *et al.*, 2007[7].)

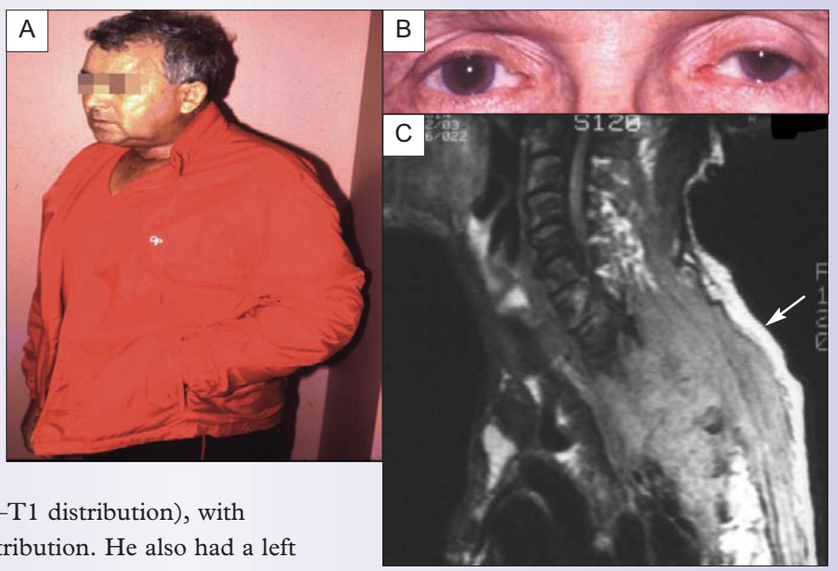
Case presentations

Case 1



This 67-year-old woman reported hyperalgesia and allodynia over her chest and in her armpit 1 month after a right mastectomy. The pain was a severe, knife-life and burning pain that would abate only with avoiding any movement of her right upper extremity. Consequently, she held her right upper extremity in a splinted position and avoided using it. This resulted in marked disability, frustration, and despair. She was eventually diagnosed with postmastectomy pain, which occurs in up to one in five women following mastectomy. Although postmastectomy syndrome may occur even after lumpectomy, it is most common following mastectomy with axillary lymph node dissection. In some cases, there may be associated nerve damage. Postmastectomy syndrome is distinguished from brachial plexopathy, which typically has prominent arm swelling, evidence of cervical root dysfunction, arm burning, and possibly a Horner's syndrome. This patient was treated with multidisciplinary treatment, including neuropathic pain medications, psychological pain management strategies, physical therapy to avoid developing a frozen shoulder, and occupational therapy to assist in resuming more normal function.

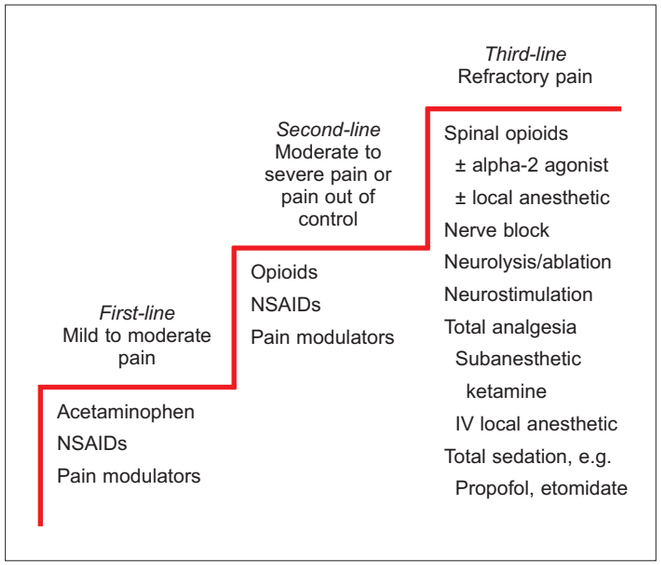
Case 2



This 78-year-old man was diagnosed with an apical lung tumor. He refused surgical resection and chemotherapy and was treated with radiation. One month later, he was referred for severe chest wall and left upper extremity pain that prevented any activities using the left arm. Although he was seen on a particularly hot summer day, he wore a jacket because his hand and arm felt cold and using the jacket pocket resulted in arm splinting and prevented accidental touching of the hyperalgesic hand (**A**). Examination revealed decreased sensation to touch over the medial aspect of the left hand (C8–T1 distribution), with hyperalgesia to pin prick over this same distribution. He also had a left Horner's syndrome, with ptosis and miosis (**B**). Imaging studies revealed an enlarging Pancoast tumor invading bone, the ipsilateral brachial plexus, and the spinal epidural space (**C**, arrow). Treatment included steroids, radiation, neuropathic medication, opioids, psychological pain management, and both physical and occupational therapies to improve functional status.

Treatment of cancer-related pain

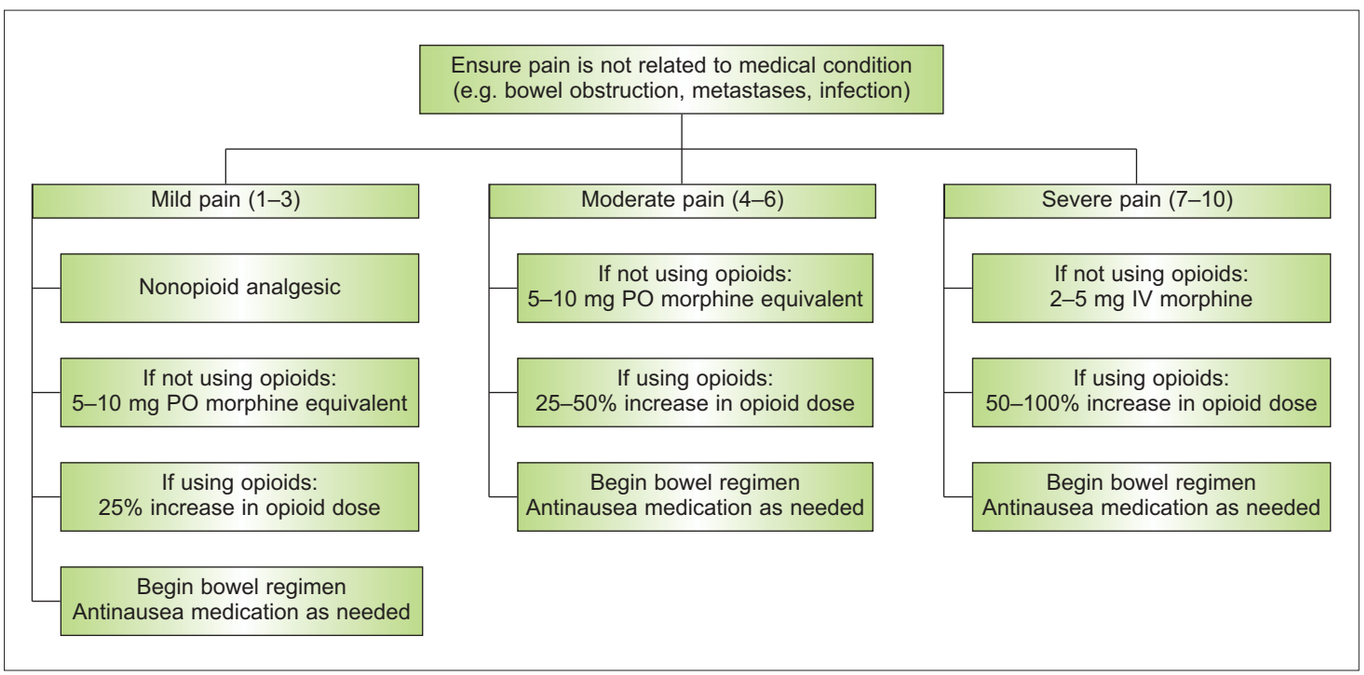
The same principles that guide chronic nonmalignant pain therapy are also used for cancer pain, including use of therapies matched to pain severity and multidisciplinary treatment to address pain, functional impairment, and psychosocial factors. Modifications to medication dosing, route of administration, and implementation of interventional therapies may be needed, especially in patients with refractory cancer pain (**8.5**)[8]. Unfortunately, both doctors treating cancer patients and hospice nurses tend to underestimate pain severity among cancer patients, which can result in inadequate treatment[2,9].



8.5 The modified World Health Organization pain management step ladder for cancer pain considers additional therapies often necessary to control chronic cancer pain effectively. Interventional therapies and higher-dose medications may be appropriate for malignant pain, particularly in patients with limited life expectancy. IV: intravenous; NSAIDs: nonsteroidal anti-inflammatory drugs. (Based on Fine PG, 2005[8].)

Medication

Opioids are often necessary in patients with cancer-related pain (**8.6**)[10]. Typical starting doses are provided in *Table 8.2*. As in nonmalignant pain, cancer pain patients rarely achieve complete pain relief with opioid therapy. A survey of inpatients and outpatients with cancer pain in South Africa noted that 94% were treated with prescription medications, with two in three patients considered to be adequately medicated[11]. Only 21% of patients, however, achieved complete pain relief.



8.6 Opioid therapy for cancer pain. PO: oral; IV: intravenous. (Based on National Comprehensive Cancer Network recommendations[10].)

Table 8.2 Typical opioid starting doses for cancer pain

Opioid	*Typical starting dosage*
Short-acting opioids	
Codeine	60 mg PO every 3–4 hours
Hydrocodone	10 mg PO every 3–4 hours
Oxycodone	50 mg PO every 6 hours
Morphine	30 mg PO or 10 mg IV every 3–4 hours
Hydromorphone	4–6 mg PO every 3–4 hours
Fentanyl	100–400 µg/unit for breakthrough pain
Long-acting opioids	
Morphine	30 mg PO every 12 hours
Oxycodone	20 mg PO every 12 hours
Fentanyl	50 µg/hour every 72 hours
Methadone	20 mg PO or 10 mg IV every 6–8 hours
Levorphanol	2–4 mg PO every 6–8 hours

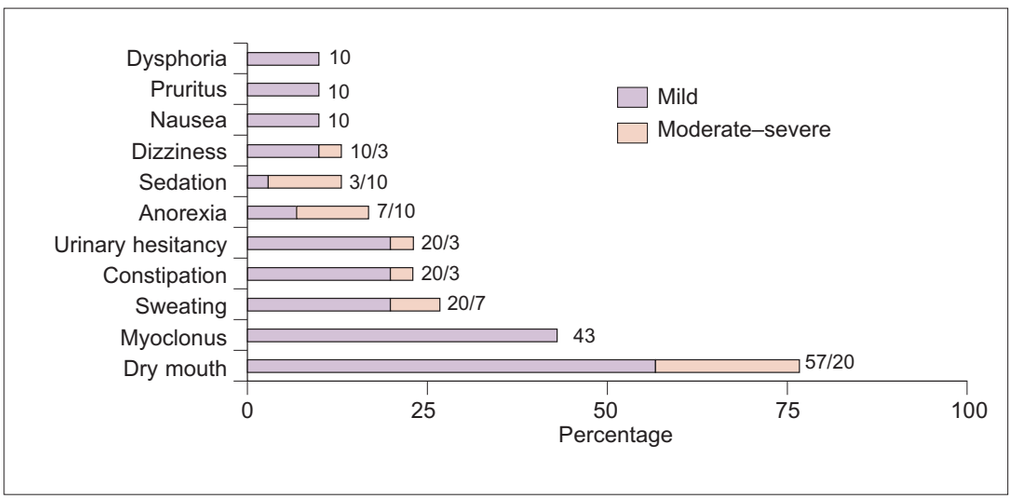
PO: oral; IV: intravenous

Achieving effective analgesia with opioids may be limited by intolerable side-effects (**8.7**, *Table 8.3*)[12,13]. In a survey of hospitalized cancer-pain patients treated with opioids, three in four experienced impaired mental status at least once during a prospective, 1-week assessment[14]; however, cognitive impairment is reported in 20–44% of cancer patients admitted to palliative care and 80–90% before death, and may be related to additional factors besides opioid therapy[14,15]. One study of 130 consecutive cancer

Table 8.3 Prevalence of common opioid-related side-effects

- Constipation – 40–70%
- Myoclonus – 63%
- Sedation – 20–60%
- Nausea and vomiting – 15–30%
- Pruritis – 2–10%

(Based on Cherny N, *et al*., 2001[13])



8.7 Prevalence and severity of opioid-related side-effects. Forty-two consecutive cancer inpatients and outpatients treated by palliative care with morphine repeatedly were asked to report on the occurrence and severity of 27 symptoms that were frequently attributed to morphine over 1 month of use. Symptoms endorsed by ≥10% of patients are shown. Attributing symptoms directly to morphine is limited due to concomitant medication use (steroids/nonsteroidal anti-inflammatory drugs/tricyclic antidepressants in 80% and benzodiazepines/phenothiazines in 36%) and comorbid illnesses. Despite these limitations, this study supports that, while many side-effects occur frequently among cancer patients treated with morphine, moderate to severe side-effects occur infrequently. (Based on Glare P, *et al*., 2006[12].)

patients showed greater impairment on neuropsychological testing from uncontrolled pain than chronic opioids[16]. It is important to recognize that adverse events frequently occurring from opioid use may also occur from common cancer or cancer-treatment comorbid conditions (*Table 8.4*). Opioid-related side-effects may be managed through symptomatic treatment or opioid adjustment (*Table 8.5*)[13].

Table 8.4 Side-effects that commonly reduce opioid use in cancer patients and possible nonopioid contributors

Common opioid side-effect	*Possible nonopioid cause*
Cognitive impairment	Cerebral metastases Cerebrovascular accident Chemotherapy Dehydration Electrolyte imbalance Hypoxia Infection Liver failure Nonopioid medications
Constipation	Nonopioid medications
Myoclonus	Liver failure Renal failure
Nausea and vomiting	Bowel obstruction Cerebral metastases Chemotherapy Hypercalcemia Nonopioid medications Radiation therapy
Pruritis	Nonopioid medications
Sedation	Cerebral metastases Cerebrovascular accident Chemotherapy Dehydration Electrolyte imbalance Hypoxia Infection Liver failure Nonopioid medications Radiation therapy

When switching between opioids, the physician should consider reducing the dose of the new opioid by 30–50%, as patients are often incompletely cross-tolerant of a new opioid, which may result in unexpectedly increased sensitivity to the new opioid.

Fear of promoting addiction among both healthcare providers and patients often limits effective pain control with opioids. While the prevalence of addiction has been reported in as many as 50% of patients with chronic nonmalignant pain, this number is substantially reduced to only 8% among patients with cancer pain[17].

Break-through pain

Break-through pain (BTP) is defined as a temporary severe pain flare occurring in patients with relatively well-managed baseline pain. An international survey of 1,095 cancer pain patients treated with chronic opioids from 24 countries reported BTP in 64.8%[6]. Evaluation of cancer pain patients in the United States showed that BTP occurred most commonly in cancer patients with bone pain, local tumor

Table 8.5 Strategies for reducing opioid-related side-effects

Side-effect	*Management strategies*
Cognitive dysfunction	Antipsychotic for delirium Benzodiazepine for agitation Switch opioid
Constipation	Laxative and stool softeners Switch to transdermal fentanyl
Myoclonus	Antispasmodic Switch opioid
Nausea and vomiting	Antinausea medications Switch opioid Switch from oral to subcutaneous dosing
Pruritis	Antihistamine
Sedation	Amphetamine psychostimulant Switch opioid Switch from oral to subcutaneous dosing

(Based on Cherny N, *et al.*, 2001[13])

Table 8.6 Characteristics and treatment of BTP

Type of BTP	*Pain characteristics*	*Treatment recommendations*
Incident	Predictable Related to specific event or activity	Preactivity stretching and analgesics Posture correction and pacing techniques
End-of-dose	Predictable Prior to scheduled dose of long-acting opioid Gradual onset, long duration pain	Increasing maintenance daily long-acting opioid dosage and/or shortening dosing interval
Idiopathic	Unpredictable Rapid onset, reaching severe pain in 3–5 minutes Brief pain duration, usually 30 minutes	Lipophilic fentanyl

invasion of soft tissues, and brachial plexopathy[18]. Those with bone pain located in the spine, back, and pelvis were most resistant to pain-relief therapies.

Before diagnosing BTP, it is important to ensure that daily pain is reasonably well controlled. Frequent episodes of BTP (>4 per day) suggest inadequately treated chronic cancer pain[19]. In that case, a reassessment of daily pain and pain management strategies should be employed before initiating treatment for BTP.

BTP can be divided into incident, end-of-dose, and idiopathic pain. Pain diaries can assist in determining the type of BTP to help determine the best treatment options (*Table 8.6*)[20]. In addition to behavioural strategies, predictable incident BTP is often well managed with administration of simple analgesics or short-acting opioids 30 minutes before participation in the activity that tends to cause BTP. Short-acting fentanyl is available in oral transmucosal and buccal tablet forms, both of which provide pain relief in about 15 minutes that lasts at least 1 hour[21]. A survey of cancer patients in the United States revealed that two in three patients responded well to management of BTP, while one in three were nonresponders[18].

Radiation

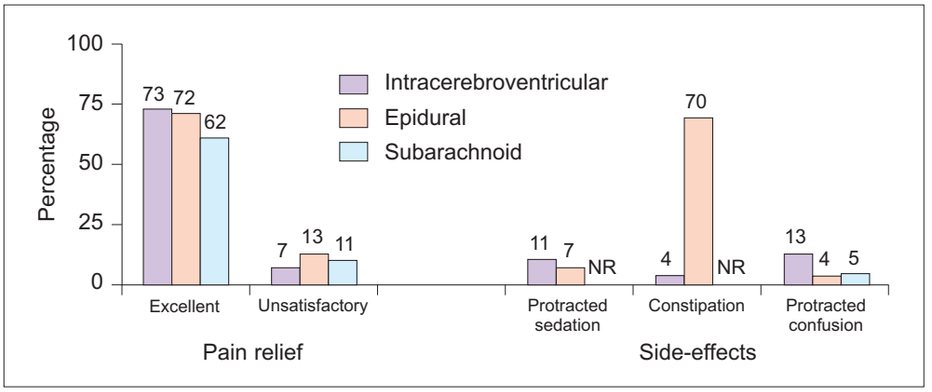
Pain related to bony metastases may be reduced with targeted radiation therapy. Tumor cell death is proportional to the radiation dose administered, with larger doses resulting in greater cell death and pain relief. Large, single dose radiation may be as effective for relieving pain as more frequent, lower dosing fractionation schedules, especially in patients with advanced disease[22].

Intervention

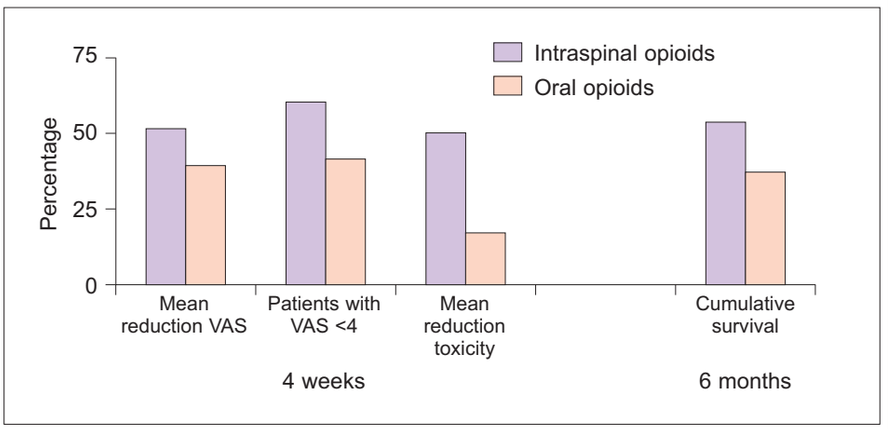
Therapies for cancer pain include several invasive treatments (*Table 8.7*). Activation of spinal cord opioid receptors more effectively reduces pain severity than receptor activation at higher centres using systemic drug administration. Consequently, cancer pain can be managed by using an intrathecal morphine dose that is about 1% of the systemic oral dose needed to achieve similar pain control. Drugs may be delivered through an external pump in patients with limited life expectancy, or an internal pump in patients expected to survive longer than 3 months. A review of uncontrolled studies evaluating pain relief from neuraxial opioids showed excellent results in about three of four patients (**8.8**)[23]. A single randomized, controlled study showed a trend toward superior pain control and survival among cancer patients using intraspinal opioid using an implantable infusion system (**8.9**)[24]. Neurolytic intervention may be considered when symptoms cannot be adequately

Table 8.7 Effective interventional therapies for cancer pain

- Neurolytic blocks
  - Celiac plexus block
- Spinal analgesia
  - Epidural infusion
  - Intrathecal infusion



8.8. Pain relief with neuraxial opioids. Due to the paucity of randomized trials, data were obtained by reviewing uncontrolled studies evaluating intracerebroventricular (72 studies), epidural (31 studies), and subarachnoid (28 studies) opioids in patients with cancer pain. Most patients achieved excellent results. The graph shows a comparison among locations and several side-effects. Protracted sedation and constipation were not reported in studies for patients receiving subarachnoid opioids (NR). Constipation was frequent with epidural and subarachnoid opioids, although reported as easily managed. Persistent nausea, transient and persistent urinary retention, and transient pruritis occurred more frequently with epidural and subarachnoid opioids. Respiratory depression, sedation, and confusion were more common with intracerebroventricular opioids. There were no major infections when pumps were used with epidural or subarachnoid opioids. Major infections occurred in a minority of patients using a reservoir: 4% intracerebroventricular, 2% epidural, and 9% subarachnoid. (Based on Ballantyne JC, Carwood CM, 2005[23].)



8.9 Randomized study of intraspinal opioid for refractory cancer pain. Two hundred patients with advanced cancer and refractory pain were randomly assigned to pain treatment using intraspinal opioids administered through a programmable implantable drug infusion system or oral opioids along with comprehensive medical management. Demographics and disease characteristics were similar between treatment groups. Median daily systemic morphine oral equivalent dose at baseline was 250 mg for those randomized to intraspinal opioids and 272 mg for those randomized to continue oral therapy. Four weeks after study enrolment, median equivalent dose decreased to 50 mg among the intraspinal group and increased to 290 mg in the oral opioid group. Mean reductions in pain visual analogue scale (VAS) at 4 weeks and 6-month survival showed trends toward superiority with intraspinal opioids (P=0.06), while change in composite toxicity scores at 4 weeks was significantly greater with intraspinal opioids (P=0.004). Reduction in drug toxicity was significantly linked to improved survival (P<0.05). The greater reduction in toxicity among intraspinal opioid users may at least partially explain the improved survival in this group. (Based on Smith TJ, *et al*., 2002[24].)

controlled and life expectancy is limited. Neurolytic procedures are generally performed using fluoroscopic guidance after ensuring a desirable result with a local anesthetic block. Neurostimulators have been most widely studied in patients with nonmalignant pain from failed back pain, refractory angina, peripheral vascular disease, and complex regional pain syndrome. Neurostimulation may be helpful for cancer pain related to spinal, radicular, or plexus pathology. Tumor debulking may effectively reduce local impact from impingement on pain-provoking structures.

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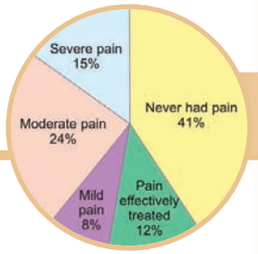
Chapter 9

End-of-life care



Introduction

End-of-life is usually defined as the final stages of a terminal illness, typically when the prognosis is considered to be ≤6 months. A more meaningful and broader definition used by many palliative care programmes defines people to be at the 'end-of-life' when they have a chronic, life-limiting condition (e.g. end-stage renal disease, class IV congestive heart failure, and so on) for which it would not be surprising for death to occur within the next year. Confining end-of-life care to the actively dying may limit important service opportunities for patients and their families who also require care for the final stages of their illness.

End-of-life concerns are varied among patients and healthcare providers, although individual issues often focus on several important themes (*Table 9.1*). Critical end-of-life issues focus on safe and comfortable dying, self-determined life closure, and effective grieving for those left behind. Healthcare providers need to establish open, nonjudgmental communication with both patient and their support network to address end-of-life issues effectively. Healthcare providers need to clearly and caringly inform patients about their terminal condition to allow the patient to have an opportunity for growth during the dying process and achieve closure to his or her life. Healthcare providers also need to ensure that each patient will have a treatment team who will work closely with them throughout the terminal process, available until death for the patient and into the period after death for remaining family members.

In 1997, the Institute of Medicine reviewed end-of-life care practices and determined there were four deficiencies[1]. First, patients suffer needlessly due to failure to administer effective palliative therapy. Second, legal and economic obstacles impair good end-of-life care, including excessive concerns about opioid addiction and difficulties in securing payment for palliative services. Third, healthcare providers

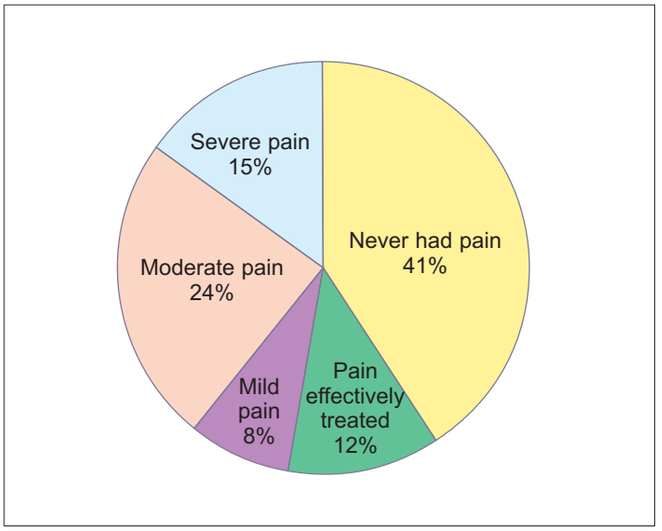
Table 9.1 Common concerns for terminal patients

Questions patients need to ask	*Questions healthcare providers need to ask*
• How long do I have to live?	• What are you most worried about?
• Will my doctor work with me until the very end?	• What are your biggest fears?
• Will you be able to control my pain?	• What do you want to accomplish in your remaining time?
• Can you help keep me comfortable at the end?	• What kind of treatment do you want?
• Can you help me to die at home?	• How can I help your family through this time?
	• Where do you want to spend your last days?
	• Do you wish to include a spiritual leader in your treatment decisions?

are inadequately educated to care effectively for the dying. Finally, insufficient data are available to understand accurately end-of-life experiences. These problems can be corrected with changes in education for healthcare providers, updated guidelines for medical providers and regulatory agencies, increased utilization of palliative and hospice services, and increased research and public discussion about death and dying issues. Since this report, end-of-life care opportunities have improved for patients. For example, palliative and hospice care have recently been recognized as unique medical subspecialities in the United States and a recent survey reported that the number of United States hospitals offering palliative care programmes nearly doubled from 2000 to 2005[2].

Pain as an end-of-life symptom

Pain is a common symptom during the final weeks and days of life, with about one in three patients experiencing untreated or ineffectively treated moderate to severe intensity pain (**9.1**)[3]. A retrospective review of 185 patients dying during a 12-month period in five long-term care facilities in Canada evaluated symptoms during the last 48 hours of life[4]. Patients experiencing sudden, expected



9.1 Pain during the last month of life. Caregivers for 674 patients dying in one of 230 long-term care facilities in four states in the United States (Florida, New Jersey, North Carolina, and Maryland) were interviewed about symptoms occurring during the last month of each patient's life. Nearly 60% of patients experienced pain during their final month of life, with only 20% of those with pain reporting effective pain control. Pain was moderate–severe in 62% of those with pain. (Based on Hanson LC, *et al*., 2008[3].)

Table 9.2 Common symptoms and treatment during the last 48 hours of life

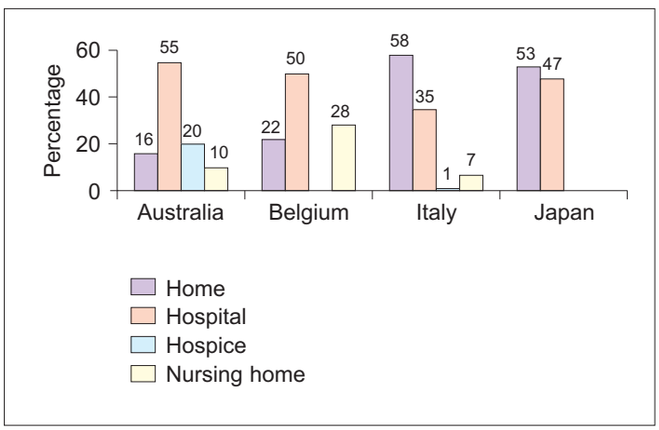
Symptom (%)	*Management (%)*	
	None	*Treatment*
Dyspnea – 62	23	Oxygen – 64 Opioids – 27 Nonpharmacological – 6
Pain – 44	1	Opioids – 72 Nonopioid analgesic – 37
Noisy breathing – 39	49	Hyoscine – 27 Suctioning – 23
Delirium – 29	38	Benzodiazepine – 25 Involving family – 19 Opioids – 17

(Based on Hall P, *et al.*, 2002[4])

deaths were not included. The most common causes of death, each accounting for one in three deaths, were cardiac and respiratory diseases. Cancer accounted for 14% of deaths. The most common symptoms and treatment for each were catalogued (*Table 9.2*). Pain was noted in nearly half of patients, with most treated with analgesics. An earlier prospective study of 200 consecutive hospice patients reported similar symptoms during the last 48 hours before death, with pain reported in 51%, with about half of these patients developing new pains and the remainder experiencing exacerbations of previously controlled pain[5]. Opioids were used by 91% of patients prior to the last 48 hours of life, with the dosage increased during the last 48 hours in 44%, unchanged in 43%, and decreased in 13%.

Meeting patients' end-of-life needs

Nine of 10 cancer patients prefer to die at home in order to continue a 'normal' routine as long as possible and maintain close contact with loved ones[6,7]. Over half of terminal patients rate the importance of dying in their preferred place



9.2 Place of death among cancer patients. Although most terminal cancer patients would prefer to die at home, many die in hospitals or nursing home facilities. Likelihood of dying at home varies by region. Over half of those patients surveyed in Italy and Japan died at home, although the Italian survey reported wide regional differences, with 94% dying at home in southern Italy and the isles, 56% in central Italy, 46% in northwest Italy, and 26% in northeast Italy. (Based on Beccaro M, *et al.*, 2006[7]; Babazono A, *et al.*, 1998[8]; Hunt RW, *et al.*, 2001[9]; Van Rensbergen G, *et al.*, 2006[10].)

to be very important and an additional 20% consider location to be important[6]. Unfortunately, only a minority of terminal patients actually spend their remaining days and hours at home (**9.2**)[7–10]. The likelihood of dying at home increases when a patient lives with a caregiver, has stated a preference to die at home, and has a family physician who makes home visits[11]. Healthcare providers need to identify preferred end-of-life locations for their patients and help facilitate achieving death in their preferred environment.

Epidemiologists in the United Kingdom interviewed 2,074 caregivers about the experiences of the person for whom each cared during the final 12 months of that person's life[12]. Most of the final year of life had been spent at home, with only 10% of the sample spending >3 months in the hospital. This study identified the important role that healthcare providers play and unmet needs for services. One in three caregivers reported that their own personal health problems interfered with caring for the terminal patient. Furthermore, caring for the dying patients resulted in restrictions in caregivers' own activities for 65% of caregivers. Despite this, only 7% of caregivers described their experience as a burden. Healthcare providers eased the burden on caregivers, although many caregivers could have used additional services. General practitioners typically made home visits, with at least one home visit during the last 12 months of life for 93% and during the last one month in

Case presentation

After a previously active and healthy 49-year-old mother of two teenagers failed a brief course of chemotherapy for metastatic cancer, she continued end-of-life care at home during her remaining 3 months of life. Recognizing that cure was unlikely, she wished to spend her final weeks of life in a familiar surrounding close to loved ones. Care initially focused on providing pain medication, respiratory aids, and emotional and spiritual support for the patient. As she became more ill, services were expanded to meet family needs, including meals, afternoons of respite care, and emotional and spiritual counselling for the family. This comprehensive care, providing services directly to both patient and her caregivers, allowed this woman to die comfortably at home.

81%. About one in three caregivers would have liked to have received more home visits and 15% would have liked a night-time visit. Over 80% of those receiving help from visiting nurses rated the care as good to excellent, although 31% reported needing more help with daily activities than was provided. One in three caregivers whose patient had not received help at night thought they would have benefited from night-time care. In addition, one in four patients also needed additional social services to assist with domestic tasks. This study highlights the important role of healthcare service providers in helping patients achieve desirable at-home care (*Table 9.3*).

Palliative care for pain control

Palliative care is defined as the total care of patients for whom curative treatment is not possible[13]. Palliative care includes management of pain as well as psychosocial and spiritual problems (*Table 9.4*). Palliative care provides a support network to help both the patient and their family and friends cope with death as a natural and final stage of the patient's life. Up-to-date information about employing palliative care services in a variety of situations can be obtained at the Center to Advance Palliative Care website (http://www.capc.org/) and http://www.getpalliativecare.org/.

Table 9.3 Services to assist caregivers of terminal patients

Healthcare provider	*Necessary services*
Physician	Make repeated home visits, including night visits Ensure healthcare needs of caregiver are being met
Visiting nurse	Ensure adequate visit duration Consider addition of night-time care Conference with caregiver to ensure ADL needs are sufficiently met
Social services	Provide domestic help to patients living alone Offer domestic help to patients living with caregiver Provide meal services
Spiritual counsellor, clergy	Spiritual needs for patient and family

ADL: activities of daily living

Table 9.4 Common palliative care services

Needs addressed	*Available services*
Physical symptoms (e.g. pain, gastrointestinal, hematologic, and respiratory symptoms)	Medical consultation Nursing care Physical and occupational therapy Medications Adaptive equipment
Emotional symptoms (e.g. depression, anxiety, delirium, and other psychiatric symptoms)	Psychiatry Psychological counselling
Spiritual needs for both patient and family	Chaplain/spiritual leader
Family needs (including caregiver assistance, equipment, and establishing advance directives)	Nursing care, including respite care Social services

Palliative care services should be used to help control unpleasant end-of-life symptoms, including pain. Opioids are generally necessary to relieve moderate to severe pain symptoms. Family members and healthcare providers may be concerned about providing adequate analgesia with opioids, fearful that high-dose opioid treatment may hasten death. A prospective hospice study evaluated the relationship between opioid escalation and survival in 13 hospitals across the United States[14]. While higher opioid doses were linked to shorter survival, opioid dose was one of only several factors in a multivariate analysis linked to reduced time to death, including cancer diagnosis, unresponsiveness, and pain severity. None of these individual factors, however, explained >10% of the variance in time until death. Therefore, while opioid dosing is a factor in patient survival, this association is fairly weak and the authors concluded that opioids should be administered to terminal patients in doses that achieve effective analgesia.

Palliative sedation may be used for refractory, unpleasant symptoms that increase end-of-life distress. A survey of 100 consecutive hospice inpatients reported requirements for sedation in 20 patients. Sedation was required due to delirium (45%), nausea and vomiting (25%), seizures (15%), dyspnea (10%), and pain (5%)[15]. Palliative sedation is distinguished from euthanasia because palliative sedation is designed to provide comfort measures and symptom relief, without hastening death. Sedation is generally achieved with benzodiazepines, although sedating antipsychotics, barbiturates, and general anesthetics may also be used. Nutrition and fluids are generally not provided during palliative sedation. Fluid restriction helps improve comfort by reducing pulmonary, salivary, and gastrointestinal secretions that might otherwise result in coughing, vomiting, or need for suctioning, reducing urinary output to limit incontinence and the need for catheterization, and possibly reducing pain caused by tumor-related edema. Dry mouth should be managed with fluid sips and oral hygiene measures. Although considered controversial, palliative sedation is justified using the doctrine of double effect, which helps clinicians choose between courses of action when neither choice is ideal. The doctrine of double effect distinguishes between intended and unintended effects of treatment, confirming that intentionally causing death is not acceptable but prescribing high doses of sedatives and opioids to relieve pain is, even if the resulting death is foreseen.

Hospice care

Supportive care during the final stages of terminal illness may be provided at the patient's home, in the hospital, or in other healthcare facilities (*Table 9.5*). Hospice services are most commonly performed as routine home hospice level of

Table 9.5 Levels of hospice care

Level of care	*Location of care*	*Typical services*	*When this level is used*
Routine home hospice	Patient's home	Nurse and home aide visits Social worker Dietician Chaplain Palliative medications Home equipment	Continuous nursing care is not necessary
Continuous nursing care	Patient's home	24-hour nursing care Home aide visits Social worker Dietician Chaplain Palliative medications Home equipment	Continuous nursing care is necessary to manage severe symptoms, such as severe pain, nausea and vomiting, bleeding, or respiratory distress

Continued overleaf

Table 9.5 Levels of hospice care (*continued*)

Level of care	*Location of care*	*Typical services*	*When this level is used*
Inpatient care	Hospice or hospital facility	Intense, individualized attention to patient by nursing staff, with ongoing consultation with treating physician to permit frequent therapeutic adjustments, as needed	More acute care is needed to manage symptoms or other aspects of care
Respite care	Hospice or hospital facility	5-day transfer to medical facility	When family caregivers require a break due to exhaustion

care. In the United States, 74% of patients receive hospice services outside of a hospital or hospice facility[16]. While hospice is often associated with cancer care, 56% of hospice services rendered in the United States in 2007 were for a noncancer illness[16]. Staff can assist families in making advance care plans and determining when different levels of care are needed. Advance directive planning to establish end-of-life wishes and power of attorney can be assisted by using documents available on the Caring Connections website (http://www.caringinfo.org/).

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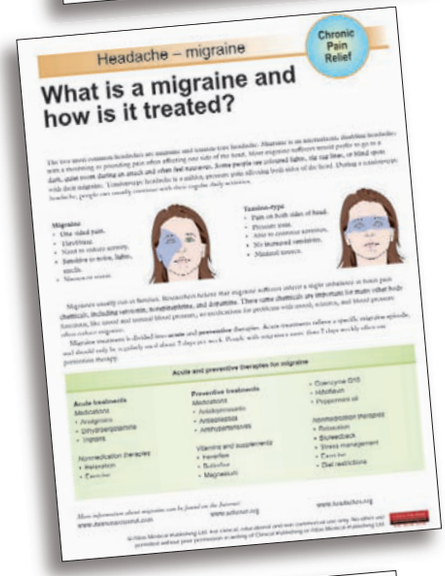

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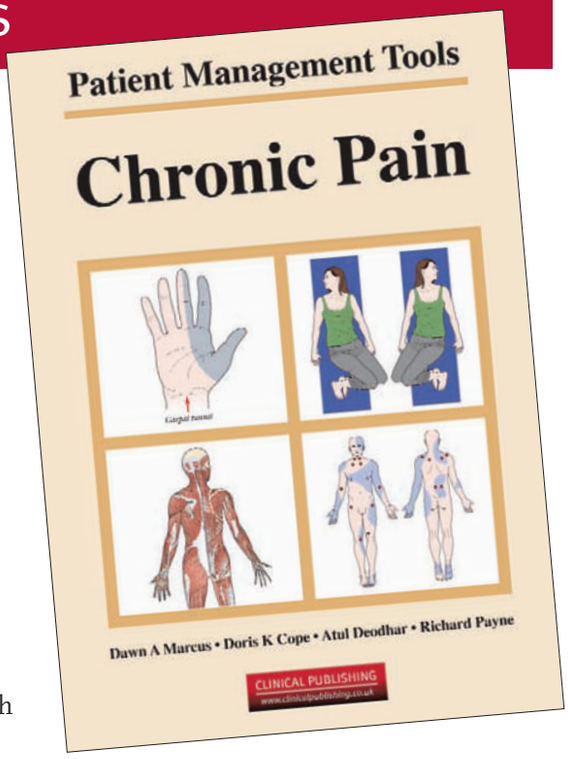

Management Tools include:

- Arthritis
- Osteoporosis
- Carpal tunnel syndrome
- De Quervain's syndrome
- Tarsal tunnel syndrome
- Plantar fasciitis
- Morton's neuroma
- Migraine
- Cluster headache
- Medication overuse headaches
- Trigeminal neuralgia
- Myofascial pain
- Fibromyalgia
- Peripheral neuropathy
- Postherpetic neuralgia
- Ruptured disc or pinched nerve
- Lumbar stenosis
- Complex regional pain syndrome
- Complex regional pain syndrome (CRPS) / Reflex sympathetic dystrophy (RSD)
- Healthy lifestyle tips to reduce chronic pain
- Stretching exercises
- Flare management
- Psychological pain management techniques
- Communicating effectively with your doctor
- Charting documentation with treatment initiation
- Charting documentation to follow treatment progress
- Opioid contract
- Progress weekly logs

Index