

A 50-Year-Old Man With Chronic Low Back Pain

James P. Rathmell, MD, Discussant

DR LIBMAN: Mr S is a 50-year-old man with chronic low back pain. In the mid-1970s he developed persistent right leg pain and was diagnosed by myelogram as having a herniated disk. L5-S1 discectomy was performed in 1977 with modest improvement in his leg pain. He developed low back pain, which was treated with physical therapy and nonopioid and opioid drugs. Over the next decade, his intermittent back and right leg pain caused him to modify his daily activities. It worsened in 1994 after he fell out of a bathtub. He was evaluated in a local pain unit and received local injections with limited benefit. In 1996, Mr S underwent repeat discectomy, which improved his right leg pain but not his back pain. Following surgery, he had a crush injury of his right foot, which slowed his recovery. Between 1996 and 2002, he had facet blocks, epidural injections, and physical therapy, all of which were ineffective. Since 2003, he has been followed up at a pain unit. He takes methadone with oxycodone-acetaminophen for breakthrough pain with modest relief, but he wants better treatment options.

His back pain is a constant dull ache, sometimes throbbing and radiating to both legs. It worsens with sitting and standing. There are no other musculoskeletal or neurologic symptoms.

Mr S also has hypertension, gastroesophageal reflux disease, seasonal allergies, depression, anemia, and hyperlipidemia. In the 1990s, he underwent tonsillectomy and adenoidectomy for obstructive sleep apnea.

He takes clonazepam, 1 mg 3 times per day; cyclobenzaprine, 10 mg by mouth 3 times per day; methadone, 40 mg every morning, 30 mg at noon, and 40 mg at bedtime; naproxen, 500 mg twice per day; and oxycodone-acetaminophen, 5 mg/325 mg (one tablet) 4 times per day as needed. He also takes atorvastatin, fenofibrate, lisinopril/hydrochlorothiazide, omeprazole, ranitidine, sertraline, and verapamil.

Mr S, a former restaurant worker, is now receiving disability benefits and lives with his longtime female partner. He does not smoke cigarettes or use alcohol but occasionally uses marijuana for pain control. There is no other history of drug use.

He is 5 ft, 7 in tall, weighs 209 lb [94 kg], and has a blood pressure of 108/80 mm Hg and a heart rate of 72/min. Per-

Mr S, a 50-year-old man, has long-standing low back pain. His pain began more than 20 years earlier with a lumbar disk herniation and has persisted despite discectomy. He has undergone numerous treatments, but he remains disabled with ongoing pain. His treatment course is used to frame the epidemiology and pathophysiology underlying acute and chronic lumbosacral and radicular pain. The roles of neuropathic pain medications, chronic opioid therapy, physical therapy, spinal manipulation, and multidisciplinary pain treatment programs are reviewed. The indications for and outcomes associated with interventional pain treatments, including epidural steroid injection, facet blocks and radiofrequency treatment for facet-related pain, intradiskal electrothermal therapy, spinal cord stimulation, and intrathecal drug delivery, are discussed. Clinicians are given an evidence-based approach to using available treatment options for low back pain.

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inent physical findings include mild paravertebral tenderness in the lumbar region, 4/5 motor strength in his right lower extremity, and 1+/4+ right ankle jerk. He has pain on straight leg raising on the right side at 60°.

Magnetic resonance imaging of the lumbosacral spine with and without contrast (performed in 2005) is shown in **FIGURE 1**. Degenerative disk changes are noted at multiple lumbar levels, which are similar to those seen on a magnetic resonance imaging study obtained several years earlier.

MR S: HIS VIEW

About 30 years ago, I developed pain in my leg, which I thought was a groin pull. I was athletic at the time. I limped

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Author Affiliation: Dr Rathmell is Director of the Center for Pain Medicine, Department of Anesthesia and Critical Care, Massachusetts General Hospital, and Associate Professor, Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts.

Corresponding Author: James P. Rathmell, MD, Center for Pain Medicine, Massachusetts General Hospital, 15 Parkman St, WACC 333, Boston, MA 02114 (jrathmell@partners.org).

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for a year and a half before somebody suggested I see a back doctor. That's how I found out that I had a herniated disk. I was in the hospital the next day for a myelogram, and the following day I had surgery.

I still had leg pain and went for another consult. And the doctor's famous words were, "If it didn't work the first time, we can try it again." And I said, "No, thank you," and went on to adopt a better lifestyle.

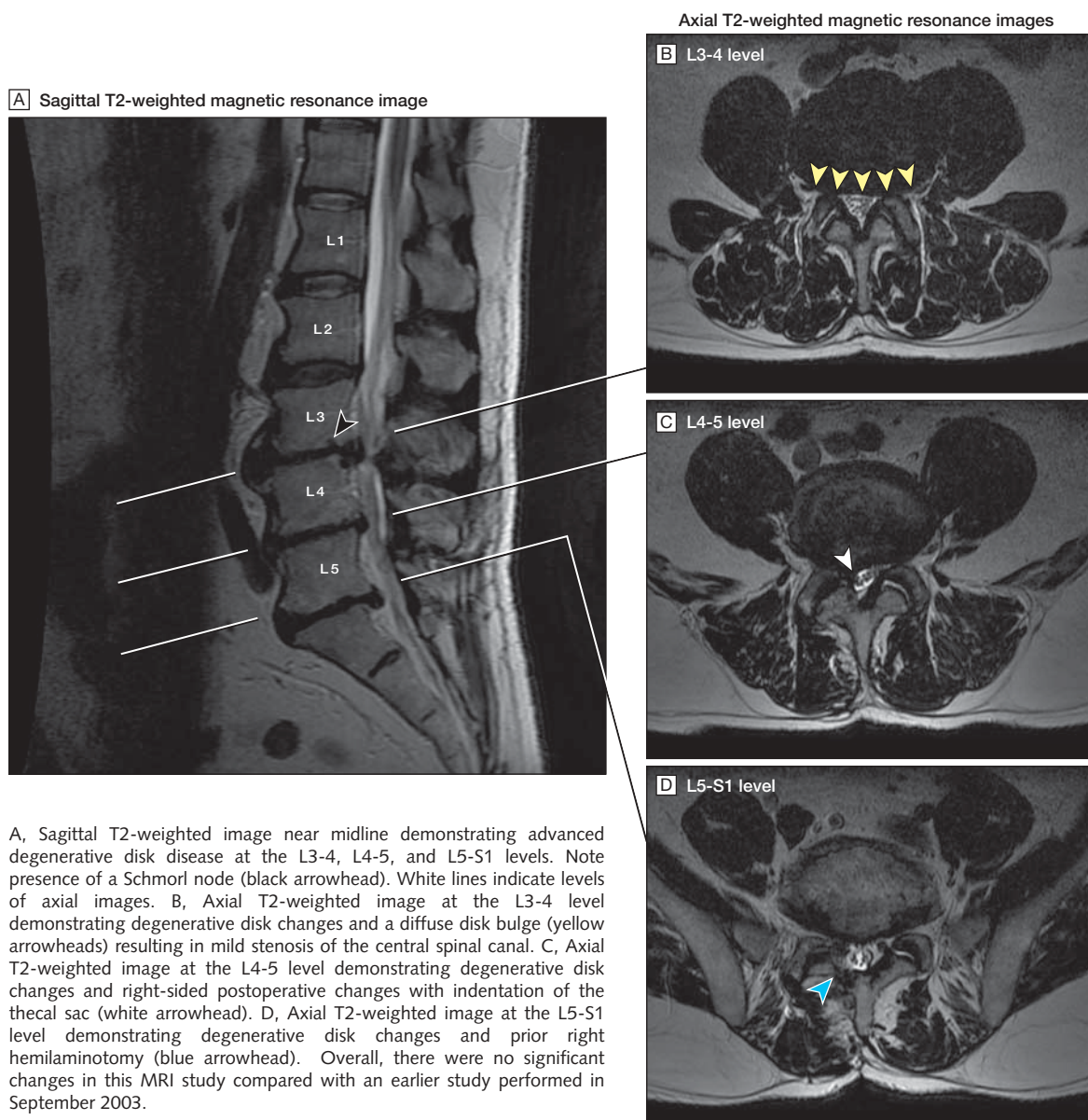
I took it upon myself to do a physical therapy regimen to develop some way to control the pain. I tried to build up my legs, back, and stomach muscles. I lived with the pain. Ten years later, the pain got worse, and it started to

go down to the other side of my left leg. In 1994, I fell out of my bathtub, which set off the pain in both legs and my back.

Time-release medications and long-acting medications, like Oxycontin or a patch, are helpful. But at times the pain is so acute that I need a short, quick-acting narcotic—to block it for an hour or two.

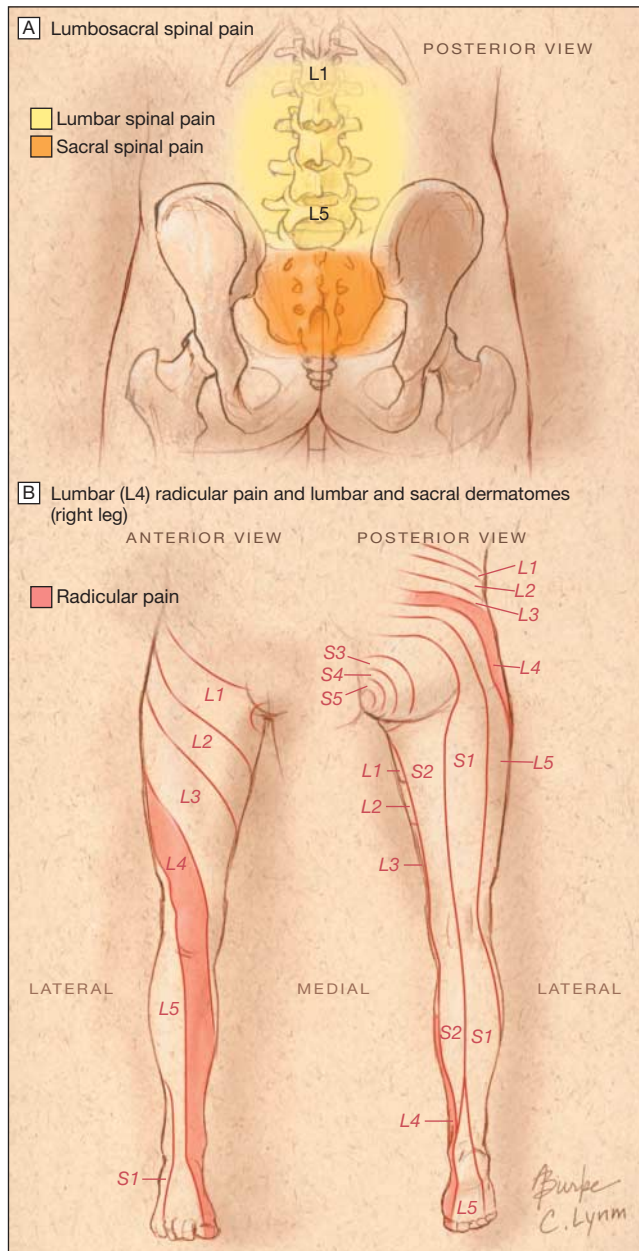
Physical therapy has come far. They know more about how the muscles and bones are interacting. If I had the money, I would have a massage twice a day. Acupuncture, because it looks at your whole body and not just the back, gives you an overall boost of energy.

Figure 1. Most Recent Magnetic Resonance Imaging (MRI) Study of Mr S's Lumbosacral Spine (April 2005)



Dealing with doctors at any level, you have to tread very lightly. If you say, “I need pain medication,” it seems like a bell goes off. They think, “This person just wants pain medication, nothing else.”

Figure 2. Distribution of Lumbosacral and Radicular Pain



A, “Low back pain” is more precisely termed *lumbosacral spinal pain*, which encompasses both *lumbar spinal pain* (L) and *sacral spinal pain* (S). Lumbosacral spinal pain is pain in either or both regions and constitutes “low back pain.” B, Radicular pain is caused by stimulation of a spinal nerve and describes pain that is referred to the lower extremity along the corresponding dermatome.

**AT THE CROSSROADS:
 QUESTIONS FOR DR RATHMELL**

What is known about the epidemiology and pathogenesis of chronic low back pain? What about facet and epidural injections, physical therapy, acupuncture, and other alternative care approaches? Would cognitive, behavioral, and psychological therapies help? In patients for whom surgery is not indicated, how should treatment be approached? What is the role of neuropathic pain medications and short- and long-acting opioid medications? What about newer treatments such as spinal cord stimulation and intrathecal drug delivery? What does the future hold in this field?

DR RATHMELL: Mr S is a middle-aged man disabled by chronic low back pain. He has had extensive evaluation and treatment, including spinal surgery and injections to reduce his pain. However, he is left with significant pain. It is difficult to recommend what more can be done to help him. However, understanding of low back pain has advanced and has made treatments available that reduce or eliminate pain associated with specific spine disorders.

Definitions

Low back pain, a nonspecific term, refers to pain centered over the lumbosacral junction. To be precise in the approach to diagnosis and treatment, pain primarily over the axis of the spinal column is differentiated from that which refers primarily to the leg (FIGURE 2). *Lumbar spinal pain* is pain inferior to the tip of the twelfth thoracic spinous process and superior to the tip of the first sacral spinous process.¹ *Sacral spinal pain* is inferior to the first sacral spinous process and superior to the sacrococcygeal joint.¹ *Lumbosacral spinal pain* is pain in either or both regions and constitutes “low back pain.” Other patients present with sciatica, or pain predominantly localized in the leg. The proper term is *radicular pain* because stimulation of the nerve roots or the dorsal root ganglion of a spinal nerve evokes the pain.

Pain is a normal physiologic process and serves as a signal of actual or impending tissue injury. Pain from tissue injury is usually well localized and associated with sensitivity in the region. Pain signals are carried toward the central nervous system via the sensory nerves. This type of pain is termed *nociceptive pain*¹ or *physiological pain*.² In contrast, persistent pain following injury to the nervous system, *neuropathic pain*,^{1,2} has unique characteristics: spontaneous pain (pain without any stimulus), hyperalgesia (more pain than expected from a painful stimulus), and allodynia (pain following a nonpainful stimulus).³

Mr S describes a deep ache in his low back with intermittent radiation of pain to his legs; thus, he has both lumbosacral pain and radicular pain, likely with mixed etiology (ie, both nociceptive and neuropathic).

Epidemiology

Low back pain, ranked fifth among the most common problems that lead patients to seek medical attention, accounted for nearly 15 million physician visits in a 1990 US survey.³ Most episodes of acute low back pain, with or without radicular pain, resolve without treatment. Overall, 60% to 70% of those affected recover by 6 weeks and 80% to 90% by 12 weeks.⁴ However, recovery after 12 weeks is slow and uncertain; fewer than half of patients disabled for longer than 6 months return to work. The return-to-work rate for those absent for 2 years is near zero.⁵ Back pain is the most common reason for limitation of activity in younger adults and is the most frequent cause of absences from work.⁶ Low back pain is frequently recurrent; most patients experience more than 1 episode.⁴ Risk factors for developing chronic low back pain include older age, female sex, low socioeconomic status and lower education level, higher body mass index, tobacco use, lower perceived general health status, physical activity (eg, bending, lifting, twisting), repetitive tasks, job dissatisfaction, depression, spinal anatomic variations, and imaging abnormalities.⁶

Pathophysiology

The basic unit of the spine is the *functional spinal unit* and comprises 2 adjacent vertebral bodies with 2 posterior facet joints, an intervertebral disk, and the surrounding ligamentous structures (FIGURE 3). The intervertebral disk absorbs energy and distributes weight evenly from one spinal segment to the next while allowing movement of the protective bony elements.⁷ Lifting, bending, twisting, or whole body vibration can damage elements of the spine. With injury and aging, progressive degenerative changes appear in each element of the functional spinal unit, along with the onset of characteristic symptoms (FIGURE 4). The earliest change in the lumbar facet joints is synovitis, which progresses to degradation of the articular surfaces, capsular laxity and subluxation, and, finally, enlargement of the articular processes (facet hypertrophy). Progressive degeneration also occurs within the intervertebral disks, starting with loss of hydration of the nucleus pulposus, followed by appearance of tears within the annulus fibrosus (internal disk disruption).

Lumbosacral pain can arise from the facet joints or the annulus fibrosus.⁸ With internal disruption of the annulus, some of the gelatinous central nucleus pulposus can extend beyond the disk margin as a disk herniation (herniated nucleus pulposus [HNP]). When HNP extends to the region adjacent to the spinal nerve, it incites an intense inflammatory reaction.⁹ Patients with HNP typically present with acute radicular pain. Hypertrophy of the facet joints and calcification of the ligamentous structures can reduce the size of the intervertebral foramina and/or central spinal canal (spinal stenosis), with onset of radicular pain and/or neurogenic claudication (intermittent, unilateral or bilateral pain in the buttock, thigh, or leg that is brought on by walking or prolonged standing).

Initial Evaluation and Treatment

In first evaluating a patient with low back pain, several features in the history—"red flag" conditions—require prompt investigation, including new-onset or worsening back pain after trauma, infection, or previous cancer. Patients with progressive neurologic deficits (typically worsening numbness or weakness) or bowel or bladder dysfunction also warrant immediate radiologic imaging to rule out a compressive lesion.¹⁰

If no red flag condition is apparent, diagnosis and treatment rely on location and duration of symptoms and determining if the pain is acute or chronic and primarily radicular or lumbosacral in nature. There is no clear point in time when acute back pain becomes chronic, but one well-accepted definition is *acute* low back pain is present for less than 3 months, while *chronic* low back pain is present for a longer time.¹

Acute Radicular Pain. Herniated nucleus pulposus typically causes acute radicular pain, with or without radiculopathy (radiculopathy would be indicated by numbness, weakness, or loss of deep tendon reflexes referable to a specific spinal nerve). In elderly patients and those with extensive lumbar spondylosis, acute radicular symptoms caused by narrowing of 1 or more intervertebral foramina can occur.¹¹ Initial treatment is symptomatic, and following HNP, symptoms resolve without specific treatment in about 90% of patients.¹² Trials comparing advice to stay active vs stay in bed show no difference in pain or functional outcomes.¹³ For those with persistent pain after HNP, lumbar discectomy may be indicated. A controlled trial of surgical vs nonoperative treatment showed significant improvement in both groups over 2 years but remained inconclusive about the superiority of either approach.¹⁴

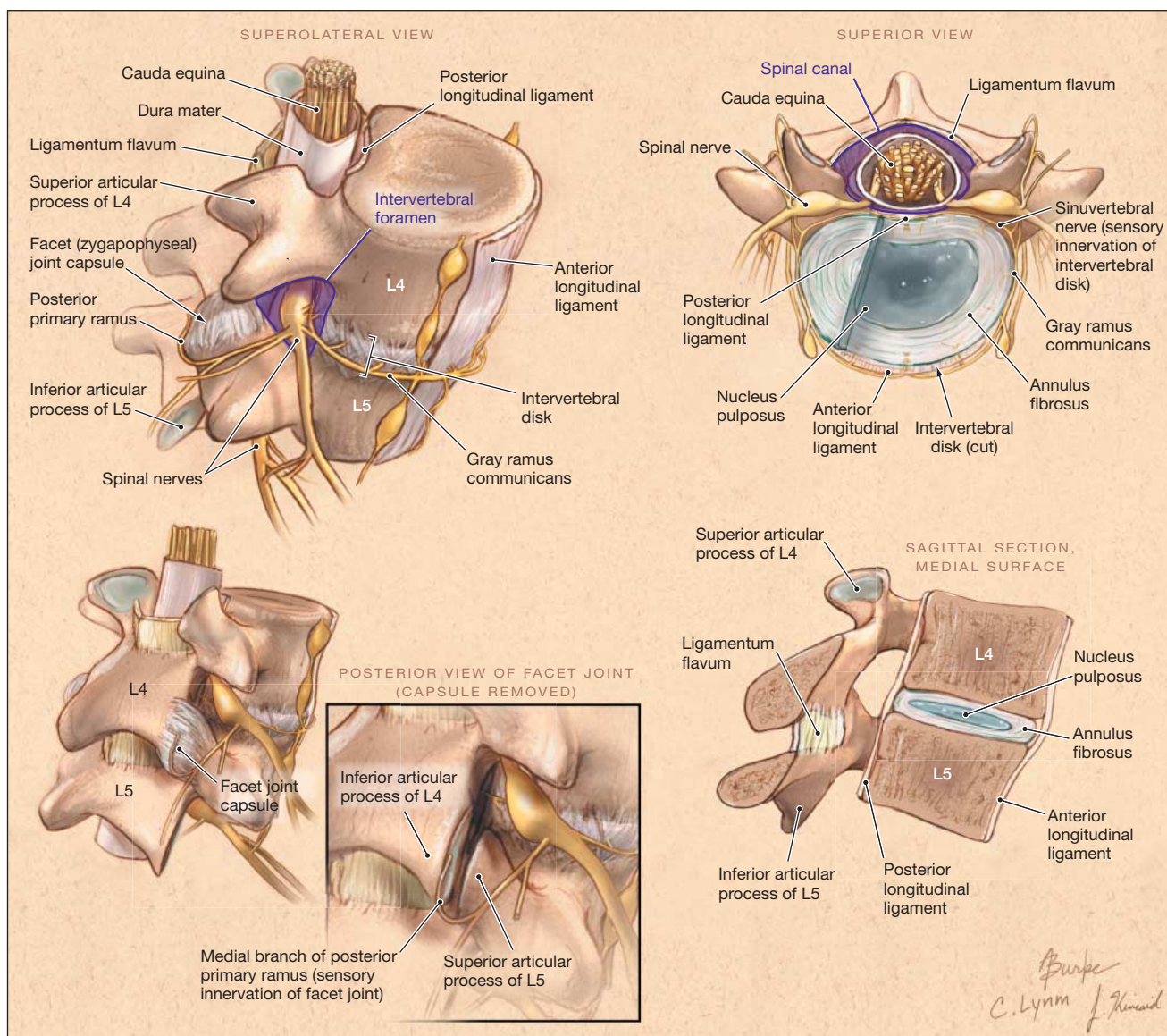
Chronic Radicular Pain. Persistent leg pain in the distribution of a spinal nerve may occur in patients with disk herniation with or without subsequent surgery. In those with persistent pain, a search for a reversible cause of spinal nerve compression is warranted. In some individuals, after surgery, scarring around the nerve root at the operative site can be seen on magnetic resonance imaging,¹⁵ and electrodiagnostic studies show a pattern suggesting chronic radiculopathy.¹⁶ This patient group has characteristics similar to those with other nerve injuries, and initial management should consist of pharmacologic treatment for neuropathic pain.¹⁷

Acute Lumbosacral Pain. Most patients presenting with acute onset of lumbosacral pain without radicular symptoms have no obvious abnormal findings¹⁸ and radiologic imaging is unlikely to be helpful.¹⁹ Traumatic sprain of the muscles and ligaments of the lumbar spine or the zygapophyseal joints and early internal disk disruption are significant causes of acute lumbosacral pain. Similar to acute radicular pain, this type of pain is best managed symptomatically. Advice for patients to stay active results in improved functional status and pain reduction at 3 to 4 weeks relative to advice to stay in bed.¹³

Chronic Lumbosacral Pain. There are many causes of chronic lumbosacral pain, and identification of the anatomic cause cannot be made with certainty in up to 90% of cases.¹⁰ The structures most commonly implicated include the sacroiliac joint, lumbar facets, and lumbar intervertebral disks.²⁰ In chronic low back pain, the incidence of internal disk disruption has been estimated to be 39% (range, 29%-49%); facet joint pain, 15% (range, 10%-20%); and sacroiliac joint pain, 15% (range, 7%-23%).²⁰ The gold standard for diagnosing sacroiliac and facet joint pain is injection of local anesthetic at the site.²¹ However, the use of

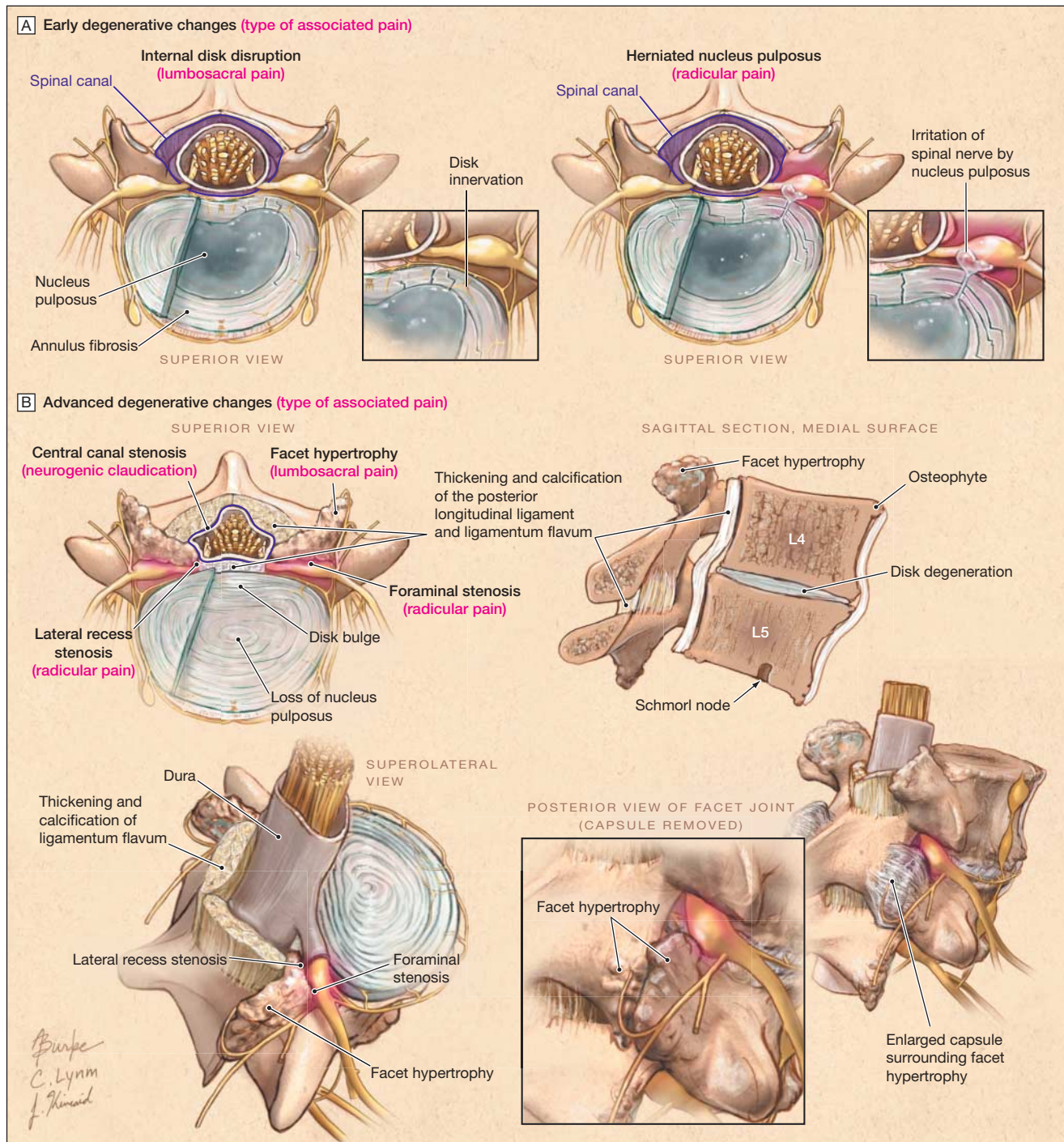
uncontrolled local anesthetic blocks for diagnostic purposes is plagued by placebo response.²² For patients achieving significant short-term pain relief with diagnostic blocks, randomized controlled trials (RCTs) suggest that radiofrequency treatment can provide pain reduction for 3 to 6 months in those with facet-related pain. Pain from degenerating intervertebral disks is also a source of chronic axial back pain.²⁰ Diagnostic diskography may identify symptomatic disks prior to management with therapies such as intradiskal electrothermal therapy (IDET) or surgical fusion. Overall, the evidence regarding treatment of chronic lum-

Figure 3. Normal Anatomy of the Functional Spinal Unit (L4-5) and Associated Neural Structures



The basic unit of the spine, the functional spinal unit, is composed of 2 adjacent vertebral bodies with 2 posterior facet joints, an intervertebral disk, and surrounding ligamentous structures. See online interactive supplement at <http://jama.ama-assn.org/cgi/content/full/299/17/2066/DC1>.

Figure 4. Progressive Degenerative Changes of the Functional Spinal Unit (L4-5) Associated With Repetitive Mechanical Stress and Aging



Patterns of pain associated with specific degenerative changes are shown in red. A, Early degenerative changes of the functional spinal unit include loss of hydration of the nucleus pulposus accompanied by mild loss of height of the intervertebral disk. Internal disk disruption (left) begins with radial and/or concentric fissures that extend from the periphery of the nucleus pulposus into the annulus fibrosus. Extension of these fissures or of material from the nucleus pulposus to the peripheral portion of the annulus fibrosus can produce lumbosacral pain mediated by the sinuvertebral nerve. Extension of material from the nucleus pulposus posterolaterally outside the annulus fibrosus (herniated nucleus pulposus, right) can produce an intense inflammatory reaction surrounding the spinal nerve leading to radicular pain. B, Advanced degenerative changes include complete loss of hydration of the nucleus pulposus, marked loss of height of the intervertebral disk, osteophyte formation, and thickening of ligaments. Central canal stenosis results from the combined effects of facet hypertrophy and thickening of the ligamentum flavum and posterior longitudinal ligaments. These degenerative changes can produce neurogenic claudication. Progressive degeneration of the disk or facets can produce chronic lumbosacral pain. Facet hypertrophy can produce stenosis of the lateral recess of the spinal canal and the intervertebral foramen, which may result in radicular pain.

bosacral pain is conflicting, precluding strong conclusions from being drawn.

Patients with prior lumbar surgery and either recurrent or persistent low back pain, often termed *failed back surgery syndrome*, need mention.²³ Knowing the type of surgery performed, the indications for and results of the surgery, and the time course and characteristics of any changes in the pattern and severity of postoperative pain is essential. Recurrent pain or progressive symptoms signal the need for further diagnostic evaluation. Mr S's back pain began as acute radicular pain from a disk herniation, but his pain persisted, worsening after discectomy. Now the pattern and severity of his pain are stable, suggesting that further diagnostic evaluation is of questionable benefit.

Medical Therapies

Numerous pharmacologic agents and minimally invasive treatments are beneficial in treating specific types of pain. There is no consensus on the order in which these therapies should be initiated for persistent low back pain; the general approach to each therapy is shown in the TABLE.

Neuropathic Pain Medications. Treatments of neuropathic pain such as chronic lumbar radicular pain are extrapolated from RCTs examining common forms of neuro-

pathic pain: diabetic neuropathy, and postherpetic neuralgia.^{42,43} Tricyclic antidepressants (eg, nortriptyline, desipramine) and newer selective norepinephrine reuptake inhibitors (eg, venlafaxine, duloxetine) are effective in the treatment of neuropathic pain.^{42,43} Antiepileptic drugs (eg, gabapentin, pregabalin) also treat neuropathic pain.^{42,43} Decisions regarding pharmacologic treatment of neuropathic pain may be based on an analysis of the number needed to treat derived from treatment of diabetic neuropathy and postherpetic neuralgia. Across various neuropathic pain conditions, the numbers needed to treat (95% confidence interval [CI]) for tricyclic antidepressants ranged from 2.1 (1.8-2.6) to 3.1 (2.2-5.5); for selective norepinephrine reuptake inhibitors, 5.1 (3.9-7.4); for gabapentin, 3.8 (3.1-5.1); and for pregabalin, 3.7 (3.2-4.4).⁴³ If Mr S has not already received a trial of neuropathic pain medications, a trial to reduce his chronic radicular pain would be worthwhile.

Long-term Opioid Therapy. Long-term opioid therapy in the management of non-cancer-related pain remains controversial.⁴⁴⁻⁴⁶ Advocates point to long-term efficacy and improvement in function in patients with chronic painful conditions, including low back pain. Opponents cite difficulties in prescribing these drugs long-term.²⁶ While aberrant drug-related behavior (eg, losing prescriptions, escalating drug

Table. Rational Sequence for Application of Medical Therapies in Treating Low Back Pain and Level of Evidence Supporting Each Treatment^a

| Type of Pain | Initial Therapy | Therapy for Persistent Pain | Treatment Costs and Insurance Coverage ^b |
|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Acute radicular pain | Seven- to 10-day course of an oral analgesic (NSAID or acetaminophen with or without opioid analgesic) with a muscle relaxant for those with superimposed muscle spasm (level 1). ²⁴ | Two to 6 weeks after onset of acute radicular pain, consider lumbar epidural steroid injection to speed resolution of radicular symptoms (level 2). ²⁵ | Oxycodone-acetaminophen + muscle relaxant × 7-10 days: \$; variable coverage Lumbar epidural steroid injection: \$\$; covered by most insurers |
| Chronic radicular pain | Chronic radicular pain may respond to treatment with chronic opioids, but neuropathic pain is less responsive to opioids than nociceptive pain (level 2). ^{26,27} | Consider evaluation for a trial of spinal cord stimulation (level 2). ²⁸⁻³³ | Medication (see text): \$; variable coverage Spinal cord stimulation: \$\$\$\$; covered by most insurers |
| Acute lumbosacral pain | Seven- to 10-day course of an oral analgesic (NSAID or acetaminophen with or without opioid analgesic) with a muscle relaxant for those with superimposed muscle spasm (level 1). ²⁴ | Two to 6 weeks after onset of chronic radicular pain, consider referral for physical therapy for stretching, strengthening, and aerobic exercise in conjunction with patient education (level 1). ^{24,34} | Physical therapy (2-3×/wk for 3-4 wk): \$; single course covered by most insurers |
| Chronic lumbosacral pain | Consider diagnostic medial branch blocks of the nerves to the facet joints. If >50% pain relief with the diagnostic blocks, consider radiofrequency treatment (level 2). ^{35,36} | Consider a formal multidisciplinary pain program that incorporates medical management, behavioral therapy, and physical therapy (level 1). ³⁷ Consider cognitive-behavioral therapy (level 1). ³⁸ If no response to diagnostic facet blocks and MRI evidence of early degenerative disk disease affecting a single intervertebral disk, consider diagnostic provocative diskography (level 3). ³⁹ If diskography is concordant (pain is reproduced at anatomically abnormal level[s] and no pain at an adjacent anatomically normal level), consider treatment with IDET at symptomatic level(s) (level 2). ⁴⁰ | Radiofrequency treatment: \$\$; covered by most insurers Multidisciplinary pain program: \$\$\$; variable coverage but many exclude chronic pain programs Cognitive-behavioral therapy: \$\$; variable coverage IDET: \$\$\$\$; variable coverage |

Abbreviations: IDET, intradiskal electrothermal therapy; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug.

^aLevels of evidence are defined by the Oxford Centre for Evidence-Based Medicine⁴¹: level 1, high-quality randomized controlled trials (RCTs) or systematic reviews of RCTs; level 2, low-quality RCTs, cohort studies, or systematic reviews of cohort studies; level 3, case-control studies or systematic reviews of case-control studies; level 4, case series; level 5, expert opinion.

^bRelative costs represent the average US cost for a single course of treatment for 1 patient with low back pain: \$, <\$500; \$\$, \$500-\$2000; \$\$\$, \$2000-\$10 000; and \$\$\$\$\$, >\$10 000.

use) is relatively common in patients receiving opioids for chronic pain,⁴⁷ overt addiction is unusual.⁴⁸ However, treating acute pain in opioid-tolerant patients is difficult,^{49,50} and it is becoming evident that chronic opioid use can worsen pain by inducing hyperalgesia.⁵¹ Few high-quality RCTs are available to guide the use of opioids in treating chronic low back pain. A Cochrane review identified only 3 trials deemed methodologically sufficient; all compared tramadol with placebo over a 30- to 90-day period.²⁷ Pooled results showed that tramadol was more effective than placebo for pain relief, with a standardized mean difference (SMD) of 0.71 (95% CI, 0.39-1.02), and for improving function, with an SMD of 0.17 (95% CI, 0.04-0.30).

When treating a patient with long-term opioids, many drugs are available. The traditional paradigm for opioid treatment is based on cancer pain management.⁵² In this approach, patients with significant chronic pain are given a long-acting opioid for continuous analgesia and a short-acting opioid for intermittent pain that “breaks through” the control provided by the long-acting drug alone.

Nearly every available opioid has been used successfully in treating chronic low back pain, including short-acting agents (eg, hydrocodone, oxycodone) alone or in combination with ibuprofen or acetaminophen, and long-acting agents (eg, methadone, transdermal fentanyl, controlled-release oxycodone). A new type of “ultra-fast-onset” opioid (eg, oral transmucosal fentanyl citrate, fentanyl buccal tablet) has emerged for rapid treatment of breakthrough pain.⁵³ As with the patient selection process, choosing the opioid drug and appropriate dose remains empirical. The decision to use short- or long-acting agents alone or in combination should be tailored to the individual patient’s pattern of pain. Mr S receives methadone, a potent, long-acting oral opioid, and oxycodone-acetaminophen, a short-acting combination analgesic, for breakthrough pain.

Physical Therapy

Physical therapy, generally consisting of stretching, strengthening, and aerobic exercise, is widely used and improves both pain and physical function in those with low back pain persisting beyond 6 weeks.³⁴ In the first weeks following acute lumbar strain with or without radicular pain, exercise therapy is no more effective than other conservative treatments or no treatment at all.⁵⁴

Even brief patient education through one-on-one, group, or video instruction can lead to significantly less disability and worry about reinjury.⁵⁵ Modalities such as heat, ultrasound, and transcutaneous electrical stimulation are often used by physical therapists; these may provide short-term symptomatic relief, but there is no evidence that they alter the long-term course of acute or chronic low back pain.^{54,56}

Behavioral Therapy

Persistent pain is a problem that often has physical, psychological, and social/occupational components.⁵⁷ Two types

of behavioral therapy, operant conditioning and cognitive therapy, are used for back pain. Operant conditioning aims to eliminate maladaptive pain behaviors. Cognitive therapy addresses how patients cope with their pain: what they do as a result of their pain and how their thoughts and feelings influence their behavior. Cognitive-behavioral therapy is superior to a wait-list control for reducing short-term pain intensity (SMD, 0.59; 95% CI, 0.10-1.09) but not for improving functional status (SMD, 0.31; 95% CI, -0.20 to 0.82).³⁸ Behavioral outcomes (eg, pain behavior, cognitive errors, perceived or observed levels of tension, anxiety, depression) were also superior to no treatment.³⁸

Multidisciplinary Pain Treatment Programs

A typical multidisciplinary treatment program includes a medical manager, usually a physician, overseeing all aspects of care and working with other health care professionals who deliver physical and behavioral therapies. However, declining reimbursement has forced many inpatient programs to transition to the outpatient setting.⁵⁸ In a systematic review of 10 high-quality RCTs, intensive (>100 hours of therapy) multidisciplinary biopsychosocial rehabilitation significantly reduced pain and improved function over the long term (as long as 60 months after program completion) vs inpatient or outpatient nonmultidisciplinary approaches or usual care.³⁷ Multidisciplinary pain treatment programs are an important option for patients with chronic pain whose function is significantly impaired.

Interventional Pain Therapy

Interventional pain therapy refers to a group of targeted treatments used for specific spine disorders, ranging from epidural injection of steroids to percutaneous intradiskal techniques. Some have been rigorously tested in RCTs, while others are in widespread use without critical evaluation. When these treatment techniques are used for the disorders they are most likely to benefit (Table), they can be highly effective; however, when used haphazardly, they are unlikely to be helpful and, indeed, may cause harm.

Epidural Injection of Steroids. Numerous RCTs have examined the efficacy of epidural corticosteroid injection for acute radicular pain. Such injections into the epidural space are thought to combat the inflammatory response after acute disk herniation.⁵⁹ In acute radicular pain with HNP, evidence⁵⁹⁻⁶¹ shows that epidural steroids reduce the severity and duration of leg pain if given between 3 and 6 weeks after onset. Adverse effects, such as injection site pain and transient worsening of radicular pain, occur in less than 1% of those treated.⁵⁹ Beyond 3 months after treatment, there appear to be no long-term reductions in pain or improvements in function.^{59,62} This therapy has never proven helpful for lumbosacral pain without radicular symptoms. Soon after the onset of Mr S’s radicular pain, use of epidural injection of steroids would have been reasonable. Epidural ste-

roid injections should be considered for future exacerbations of his radicular pain.

Facet Blocks and Radiofrequency Treatment. Pain from the lumbar facet joints affects up to 15% of patients with chronic low back pain.⁶³ These patients typically have referred pain, with maximal pain located directly over the facet joints and pain on palpation over the facets; radiographic findings are variable, but some degree of facet arthropathy is typically present.⁶⁴ Case series and studies lacking adequate comparator groups or blinding suggest that the intra-articular injection of anesthetics and corticosteroids leads to intermediate-term pain relief (1-3 months) in patients with an active inflammatory process.⁶³ Radiofrequency denervation delivers energy through an insulated, small-diameter needle positioned adjacent to the sensory nerve to the facet joint, creating a small area of tissue coagulation that denervates the facet joint. Two systematic reviews concluded that there is moderate evidence that radiofrequency denervation provides better pain relief than sham intervention.^{35,36} The quality of the 6 available RCTs was deemed adequate, but they were conducted in a technically heterogeneous manner (eg, varying inclusion criteria, differing treatment protocols); thus, their findings could not be easily combined. Approximately half of patients treated reported at least 50% pain reduction. Pain typically returned 6 and 12 months after treatment, and denervation could be repeated.⁶⁵ Adverse events were uncommon; in 1% of treated patients, pain at the treatment site lasted 2 weeks or less.⁶⁶ Mr S has received facet injections but had no pain relief; this lack of response and the reproduction of his pain during subsequent diskography suggests that his ongoing lumbosacral pain arises from his intervertebral disks.

Intradiskal Electrothermal Therapy. Intervertebral disks are estimated to be involved in 39% of chronic low back pain cases.²⁰ Provocative diskography is a controversial diagnostic test in which needles are placed into the intervertebral disks; radiographic contrast is then introduced to try to reproduce the patient's typical pain and determine the offending disk. This test has been used to select patients for surgical fusion, but its ability to predict outcome is questionable.³⁹ Mr S had diskography some years ago, presumably in preparation for lumbar fusion surgery. However, numerous disks produced his pain, and no specific levels could be identified to target the fusion.

Diskography has also been used to select patients for IDET, which is used to treat chronic diskogenic lumbosacral pain. A steerable thermal resistance wire is placed along the posterior anulus fibrosus and thermal energy is applied to destroy penetrating nociceptive fibers and to change the cross-linking of glycosaminoglycans, thereby stiffening the intervertebral disk.⁶⁷ Clinical study results are mixed; one high-quality RCT showed that 40% of patients achieved greater than 50% pain relief while 50% of patients had no appreciable benefit (number needed to treat to achieve 75% relief of pain=5),⁶⁸ while a second high-quality RCT showed

no effect.⁶⁹ A meta-analysis of 17 studies showed a 50% reduction in pain and improvement in sitting and standing tolerance in 40% to 50% of patients receiving IDET at a single level with concordant diskography and well-preserved disk height.⁴⁰ For Mr S, the numerous disks involved and his advanced disk degeneration suggest that IDET is unlikely to benefit him.

Spinal Cord Stimulation. Based on the theory that non-noxious sensory input interferes with the perception of pain, direct activation of the dorsal columns of the spinal cord is used to treat chronic back pain. A pacemaker-like implanted pulse generator is connected to a small electrode array positioned within the dorsal epidural space. This system is implanted in a simple, brief surgical procedure.²⁸ Observational trials²⁹⁻³¹ and a recent RCT²⁸ support that spinal cord stimulation is effective in patients with chronic radicular pain following prior lumbar surgery. Trials are of low quality but suggest that half of patients report at least 50% ongoing pain relief 5 years after device implantation.³¹ Use of spinal cord stimulation for chronic lumbosacral pain has been less satisfactory, but results have improved, with new dual-lead systems and electrode arrays providing a broad area of stimulation.^{28,29} Spinal cord stimulation is less expensive and more effective than reoperation in the management of persistent postoperative radicular pain; at a mean 3.1-year follow-up, 13 of 21 patients (62%) crossed over from reoperation vs 5 of 19 patients (26%) who crossed over from spinal cord stimulation to reoperation ($P < .025$).³³ In the most recent RCT, 32% of patients had at least 1 complication, with lead displacement requiring reoperation in 10% and infection or wound breakdown in 8%.²⁸ Observational studies²⁹⁻³¹ and 2 recent high-quality RCTs^{28,33} suggest that spinal cord stimulation has the most favorable outcomes in unilateral radicular pain. Based on these data,²⁸ Mr S is a candidate for spinal cord stimulation for his persistent lumbosacral pain.

Intrathecal Drug Delivery. Direct application of morphine to the spinal cord produces spinally mediated analgesia, and small, programmable pumps are now available that can be implanted in the abdominal wall to deliver precise, continuous drug infusions to patients with chronic non-cancer-related pain.⁷⁰ Intrathecal drug delivery is usually reserved for patients with severe pain that does not respond to conservative management. In cancer-related pain, pain relief was similar and opioid-related adverse effects were fewer than with orally administered opioids.⁷¹ While morphine is currently the only opioid that is approved for intrathecal use by the US Food and Drug Administration, other drugs are also used, singly and in combination. An RCT of intrathecally delivered ziconotide for severe chronic pain demonstrated a mean pain reduction of 50% vs a 20% reduction in those receiving placebo ($P < .001$). However, adverse effects were common, with 97% of treated patients experiencing 1 or more adverse effect vs 73% of those receiving placebo, with the most common being central nervous system adverse effects.⁷² Intrathecal drug delivery in noncan-

cer pain has not been subject to controlled trials and remains controversial, but observational studies suggest it relieves pain in some patients whose chronic low back pain fails to respond to more conservative management.^{70,73}

Other Therapeutic Approaches

Acupuncture. A meta-analysis of 33 RCTs comparing acupuncture with sham interventions in treating back pain found that for short-term pain relief, acupuncture was significantly more effective than sham treatment (SMD, 0.54; 95% CI, 0.35-0.73 in 7 trials). Acupuncture was also more effective than no treatment (SMD, 0.69; 95% CI, 0.40-0.98 in 8 trials). For acute low back pain, data were “sparse and inconclusive.”⁷⁴ The effectiveness of acupuncture in comparison with other treatments has not been studied, nor has the frequency and duration of acupuncture required to produce durable pain reduction.⁷⁵

Spinal Manipulation. Generally, spinal manipulation involves the hands being applied to the patient to deliver a forceful load to specific body tissues to reduce pain and/or improve range of movement.⁷⁶ Mechanisms include increase of joint movement, changes in joint kinematics, increase of pain threshold and muscle strength, and release of endogenous analgesic peptides.⁷⁷ Available data are conflicting and the methodologic quality is low, with lack of blinding and/or meaningful comparator groups. However, spinal manipulation generally results in more rapid recovery if applied within 3 weeks of onset of acute low back pain.⁷⁸ The outcomes for treatment of chronic low back pain are less clear, and the conclusions of systematic reviews are inconsistent. One systematic review concluded that spinal manipulation for chronic low back pain provides benefits similar to a prescription nonsteroidal anti-inflammatory drug; it is more effective in the short-term than placebo and general practitioner care and in the long term vs physical therapy.⁷⁸ However, in a review of 16 systematic reviews, spinal manipulation was ineffective in treating any condition, including low back pain.⁷⁶ Nonetheless, the authors underscored the low quality of the available evidence and the need for additional clinical trials.⁷⁶

Experimental Treatment Options

Tumor necrosis factor α is an important mediator of sciatica in animal models of disk herniation,⁷⁹ but while early uncontrolled trials of the anti-tumor necrosis factor α agents infliximab⁸⁰ and etanercept⁸¹ showed faster pain reduction, a subsequent RCT showed no benefit of infliximab over placebo.⁸² Trials examining periradicular application are currently under way.⁸³

The progressive loss of proteoglycan within the nucleus pulposus, a characteristic finding in degenerative disk disease, has suggested a possible role for growth factors. Although some growth factors (human transforming growth factor β 1, tissue inhibitor of matrix metalloproteinase 1) may up-regulate the anabolism or inhibit the catabolism of

proteoglycans within isolated intervertebral disk cells,^{84,85} their short elimination half-lives preclude direct delivery. Adenoviral-mediated delivery of growth factors increases proteoglycan synthesis.^{86,87} Intradiskal injection of the genes (in rabbits) that encode growth factors could be used to regenerate or slow degeneration of disks. Clinical trials have not yet begun.

RECOMMENDATIONS FOR MR S

Mr S's chronic low back pain is associated with degenerative disk disease; diskography points to several lumbar intervertebral disks. He underwent treatments for facet-related pain with little or no success. He continues to take chronic opioid therapy and reports reasonable pain relief with moderate doses of methadone (a long-acting opioid) in combination with oxycodone-acetaminophen, a short-acting combination analgesic.

Additional treatment depends entirely on Mr S's lifestyle and goals; there is no clear path to certain pain reduction or improvement in his functional status. If his overall level of function is poor or declining, enrollment in a multidisciplinary program offers the best hope of long-term improvement; weight reduction may also improve his level of function and his back pain. Given the duration of his chronic pain, he is unlikely to have dramatically improved analgesia or functional status. Treatment with spinal cord stimulation or intrathecal drug delivery are reasonable approaches, with stronger evidence supporting the use of spinal cord stimulation, but selecting patients for these therapies is difficult. It is essential that Mr S understand that he should not ignore exacerbations of pain; changing patterns often signal the need for further diagnostic evaluation. These can often be successfully managed, even in the context of long-standing pain.

QUESTIONS AND DISCUSSION

QUESTION: Would a personal trainer be of benefit for Mr S?

DR RATHMELL: Why not use a personal trainer? Well, who's going to pay for a personal trainer? Mr S mentions the benefits he got from massage. He says, “I used to get massages, but I couldn't afford it.” So, even when treatments prove useful, who will pay for it in our health care reimbursement system? Evidence from trials and meta-analyses shows the efficacy of multidisciplinary pain treatment programs.³⁷ But these programs are becoming less available because of the expense and the difficulty in gathering all of the needed practitioners in one place to coordinate their patients' care.

QUESTION: How are we training medical students or residents to be more empathetic to patients with chronic pain? One of Mr S's biggest complaints about physicians is that the first thing we think is that this man wants drugs.

DR RATHMELL: When adopting a reasonable approach to chronic opioid therapy for chronic noncancer pain, there are no easy answers. It is hard to decide who should and should not receive opioids; there is no objective measure of pain. I think that young physicians see such widely vary-

ing approaches during their education that they do not know what is right.

As pain specialists, what we do now is rely more on primary care physicians to help us make decisions about the use of chronic opioid therapy. Because of the long-term relationships they develop with their patients, primary care physicians are best equipped to observe their patients' behaviors over time.

To train young physicians to be empathic, I think the only approach is to show them how to discuss their own philosophy—*why* they do what they do—with each patient they care for.

QUESTION: What are your thoughts on epidural steroids as a maintenance therapy for patients—getting them every couple of months?

DR RATHMELL: Epidural steroids speed resolution of pain in patients with acute radicular pain—sciatica—associated with lumbar intervertebral disk herniations.⁵⁹ They do not otherwise appear to change the long-term outcome of this group of patients.

Epidural steroids have never shown benefit in treating chronic lumbosacral pain or chronic, stable radicular pain. In patients with intermittent, acute exacerbations of radicular pain, epidural steroid injection is reasonable, for instance, in patients with chronic back pain who present with new radicular pain, and in spinal stenosis patients, particularly those with lateral recess stenosis and periodic exacerbation of radicular pain. Whenever radicular symptoms flair, one suspects inflammation of 1 or more spinal nerves. Under these circumstances, the use of repeated epidural steroid injections makes sense. I would use this treatment only after the radicular symptoms recurred and had persisted for at least 2 weeks, because most improve without treatment.

QUESTION: Lifestyle changes remain a big issue; people need to take some ownership of their own disease process. When they receive opioids in the pain clinic, aren't we just conditioning them to return, get an injection, and get their medication without taking responsibility for their illness?

DR RATHMELL: Mr S also could do much to help himself. Counseling him on how to improve his own overall health will not worsen his back pain. The pain may not improve, but it's unlikely to get worse, and he may find himself more involved in life. The best programs address all of a patient's medical conditions. Mr S's cholesterol is high; an exercise program, dietary changes, and medication might be useful. Exercise programs don't reduce chronic low back pain, but they help improve function. Mr S also has fear avoidance behavior; he fears going out with friends because activity increases his pain. Behavioral management strategies are a helpful part of many exercise programs.

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