AMERICAN HEALTH CONSULTANTS® A Medical Economics Company

The Practical Journal for Primary Care Physicians

Primary Care Reports™

Volume 5, Number 25 **December 13, 1999**

Editor's Note—*Accurate assessment of acute back pain is essential for preventing negative patient outcomes. Although back pain is frequently the result of simple, mechanical factors producing musculoskeletal strain (or, in the elderly, a consequence of osteoarthritis and osteophyte formation), there are a number of serious, life-threatening conditions that require prompt diagnosis and immediate intervention. These so-called "cannot miss" diagnoses include abdominal aortic aneurysm (AAA), vertebral osteomyelitis, epidural abscess, spinal malignancy, and epidural hematoma.*

These problems are common, especially in elderly patients, but this subgroup may suffer from spinal stenosis, and back pain may also be a manifestation of osteoarthritis. Historical features and radiographic examination will help identify patients who can be treated with pain management alone, including traditional NSAIDs or cyclooxygenase-2 (COX-2) inhibitors, when the etiology is osteoarthritis.

With these issues in mind, this continuing review of acute back pain discusses high-risk conditions, with a special emphasis on diagnostic procedures and clinical findings that will direct the clinician toward life- and/or limb-threatening conditions. A detailed section on back pain in the elderly outlines a clinically useful pathway for differential diagnosis and analyzes pharmacotherapeutic strategies directed at pain management.

The Challenge of Acute Back Pain: A Practical, Evidence-Based Strategy for Optimizing Clinical Outcomes

Part II: High-Risk Conditions, Osteoarthritis, and Definitive Management

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"Cannot Miss" Conditions

Nonspinal Causes. A comprehensive discussion of the many nonspinal causes of low back pain is beyond the scope of this article. Nevertheless, it is mandatory that the primary care physician consider these conditions as part of the differential diagnosis, since they will be encountered in primary care. Perhaps the most most important condition, from a morbidity and mortality standpoint, that must be considered in patients with back pain is aortic dissection and expansion or rupture of an abdominal aortic aneurysm (AAA). These vascular causes of back pain occasionally can present in a less-than-dramatic manner, and their subtle findings frequently are inappropriately

ascribed to musculoskeletal or benign causes of back pain. Moreover, pain referred to the back can be precipitated by abdominal disease, including that localized to the biliary tract, pancreas, gastrointestinal tract, and gynecological structures.

While all the aforementioned entities are considered "cannot miss" diagnoses, the remainder of this review will focus on those conditions that can lead to permanent neurologic disability if not promptly diagnosed and treated. Most of these conditions are relatively uncommon disorders; therefore, each is considered separately. Musculoskeletal causes, including central herniated disk and ankylosing spondylitis, are addressed first. Spinal stenosis will be discussed separately in the section on back pain in the elderly, although it is worth noting that in one study of 145 patients, one-third of individuals with spinal stenosis presented before age 50.[1]

Disk Herniation. The vast majority of herniated disks rupture posterolaterally and impinge on the spinal nerve as it exits the foramen. Fewer than 1% of patients with herniated disks that require surgery will displace directly posteriorly (or centrally).[2] In this scenario, disk fragments impinge on the cauda equina, causing dysfunction to the spinal nerves not as they exit, but as they traverse the spinal canal. Back and bilateral leg pain, as well as numbness and sphincter dysfunction, mark the cauda equina syndrome. Urinary retention and anal sphincter dysfunction occur in 90% and about 70% of patients, respectively.[2] Anesthesia of the perineum (saddle anesthesia) and of the posteromedial thigh (innervated by S-3 and 4) is found in 75% of patients.[3]

The clinical findings do not pinpoint the etiology, which can be metastatic disease, idiopathic, or infectious. Patients who rapidly develop neurologic dysfunction must be decompressed surgically if permanent dysfunction is to be prevented. Thus, prompt recognition and treatment are essential.

Ankylosing spondylitis is another important, though uncommon disease that presents with back pain. This inflammatory process usually affects young males and presents with slowly progressive back ache and stiffness that is worse in the morning and improves over the course of the day. Gradually, these patients develop diminished range of motion of the back. This is one of the HLA-B27-related inflammatory arthropathies that include psoriatic, Reiter's, and inflammatory bowel disease-related syndromes. Physical examination reveals diminished excursion of the lumbar spine and chest. This is one situation in which plain films and the erythrocyte sedimentation rate (ESR) are helpful.

Abdominal Aortic Aneurysm

Overview. Abdominal aortic aneurysm (AAA) must always be considered in older, hypertensive patients who present to the primary care physician (PCP) with back pain, high blood pressure, and a pulsatile abdominal mass. It is clear that clinical strategies for improving the often dismal outcome of these patients should be explored in earnest. Complicating the diagnosis of patients with this disorder is the fact that clinical features in patients with ruptured or expanding aneurysms can be extremely subtle. For example, most patients with a ruptured AAA have no prior manifestations, and a significant percentage of these patients are unaware that they are harboring an aneurysm.[4,5] On the other hand, when abdominal or flank pain, shock, and a pulsatile abdominal mass are present, the diagnosis of ruptured AAA is relatively straightforward.

Unfortunately, this triad of features is present only in 24-42% of all patients with this condition.[6] Because these "textbook" features are frequently absent, misdiagnosis is a common problem, occurring in nearly one-third of cases.[6-8] Accordingly, PCPs should be aware that ruptured AAA may present with atypical signs and symptoms, many of which will mimic other disorders such as osteoarthritic back pain, renal colic (acute flank pain with hematuria), acute diverticulitis (left lower quadrant pain), and GI bleeding.[9]

Physical Examination. The abdominal examination is highly unreliable for diagnosing an AAA. Nevertheless, several clues on physical examination should heighten the clinical suspicion for AAA in patients who present to the PCP with back pain. First, the presence of an abdominal bruit is an important finding. An AAA generally can be palpated above the umbilicus and to the right of the midline. If it does not cross the midline, it may be a tortuous aorta.[10] Although there is a widely held premise that repetitive palpation of the abdominal aorta may result in rupture of an AAA, there are no studies confirming this fear. When palpating the aorta, the physician should note the position of the pulse wave, which, in the normal aorta, will expand in an anterior direction. When palpation of the aorta reveals lateral displacement of the pulse wave, AAA should be suspected.[10] Other clues include dimin-

Primary Care Reports™, ISSN 1040-2497, is published bi-weekly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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GST Registration Number: R128870672.

POSTMASTER: Send address changes to ***Primary Care Reports™,*** P.O. Box 740059, Atlanta, GA 30374.

Periodical rate postage paid at Atlanta, GA.

Back issues: $23. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

Subscriber Information

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World-Wide Web: http://www.ahcpub.com

Subscription Prices

United States
$299 per year (Student/Resident rate: $150).

Multiple Copies
1-9 additional copies: $269 each; 10 or more copies: $239 each.

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This program has been reviewed and is acceptable for up to 50 prescribed hours by the American Academy of Family Physicians. Term of approval is for one year from beginning distribution date of January 1, 1999, with option to request yearly renewal.

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ished lower extremity pulses and evidence of peripheral emboli or arterial occlusive disease (e.g., cool skin, poor hair growth, poor capillary refill).[5]

Misdiagnosis of AAA. Unfortunately, the vast majority (> 80%) of patients who present with ruptured aneurysms have never been diagnosed as having an AAA.[4,5] Abdominal, flank, or back pain are the most common symptoms in patients with a rapidly expanding or ruptured AAA.[4,5] In addition, some patients may become syncopal due to sudden hemorrhage. Complicating the diagnosis of AAA is the fact that physical findings in patients with AAA can be subtle. Consequently, physicians may attribute such symptoms as back pain, abdominal pain, flank pain, lower extremity ischemic symptoms, or hypotension to other, more common disorders seen in the elderly.

In fact, 24-42% of patients with ruptured AAAs are misdiagnosed when they first seek medical care.[6-8,11] These patients have almost double the mortality rate of those who are diagnosed correctly at the time of their initial complaints.[12] Common misdiagnoses include renal colic, diverticulitis, GI bleeding, myocardial infarction, and musculoskeletal or osteoarthritic back pain.

The misdiagnosis rate is not surprising, considering that each of these disorders occurs more frequently than AAA in the elderly population and features of each overlap with signs and symptoms (i.e., abdominal, back, and flank pain, as well as hypotension) seen in AAA.[13,14] Nevertheless, clinical features in misdiagnosed patients differ in several important ways from those who are correctly diagnosed at the time of initial presentation. For example, only 9% of patients in one series of misdiagnosed patients presented with the triad of abdominal or back pain, shock, and a pulsatile mass.[6] A pulsatile abdominal mass was present in only 26% of misdiagnosed patients compared to greater than 70% who were correctly diagnosed, while back pain was present in only 12% of misdiagnosed patients.[6,11]

Musculoskeletal complaints also can be seen in patients with ruptured AAAs. In particular, back and leg pain from an AAA may be due to sudden expansion, intrinsic vessel wall pathology, pressure on adjacent neurosensory structures, or vertebral body erosion.[15] Because the diagnosis of AAA can be elusive, mimicking many common diseases seen in the elderly, physicians should consider this disorder in every elderly patient with hemodynamic instability or abdominal, back, GI, or lower extremity musculoskeletal symptoms.

Diagnostic Modalities. Ultrasonography (US) is essentially 100% sensitive in detecting an AAA.[16] In addition, it has the advantage of being a noninvasive, relatively inexpensive, and accurate test within 3-4 mm with respect to assessing the diameter of the aorta.[10] Moreover, in the unstable patient ultrasonography can distinguish free intraperitoneal blood as well as the presence of an AAA—findings that confirm that diagnosis.

Unfortunately, US is not particularly helpful for assessment of aneurysmal rupture, nor is it ideal for evaluating complications such as visceral or renal artery involvement.[16] Furthermore, US is not useful for imaging the thoracic or suprarenal aorta because of interference from overlying lung.[17] It should be stressed that aneurysmal involvement of these aortic segments can also present with back pain and should be considered in the differential diagnosis. Obesity, intestinal gas, adjacent lymph nodes, and barium within the bowel also interfere with US imaging.[17] Because of these limitations, US is primarily used to screen patients at risk for AAA and to follow AAA growth over time. If patients are unstable and cannot be safely moved, portable bedside US may provide an immediate answer to the question of whether an aneurysm is present.[17,18]

Computerized tomography (CT) has the advantage of being able to measure the size, as well as the full anatomic involvement of an abdominal or thoracic aneurysm. Because CT can generate two-dimensional, cross-sectional images of the aorta and other intra-abdominal structures, it is more accurate than US at detecting rupture and visceral involvement. Modern CT scanners are able to identify the entire aorta, including the suprarenal and thoracic aorta, in addition to the celiac, superior mesenteric, renal, and iliac arteries and adjacent organs.[19,20] Intravenous contrast enhancement allows for evaluation of the aortic lumen size, the presence of mural thrombus, hematoma (from rupture), dissection, and retroperitoneal structures.[19]

Spiral CT provides a rapid, three-dimensional reconstruction of intra-abdominal organs, a feature that further increases the ability of CT to identify complications of aortic aneurysms, including adjacent organ and branch vessel involvement.[20] The major drawbacks of CT include expense, time requirements, and the need for patient stability.[19,20] However, the high resolution of CT makes it superior to US in the assessment of stable patients with aneurysmal disease.

Management. Patients in whom AAA is strongly suspected must be managed in a rapid, directed manner. Measures to stabilize and monitor the patient's hemodynamic status, as surgical and radiologic consultants are being mobilized, must be instituted promptly. It should be stressed that for patients who are clinically unstable and who present with features highly suspicious for a ruptured abdominal aneurysm, radiological evaluation can waste valuable time, as the patient undergoes clinical deterioration. Consequently, unstable patients should be taken directly to the operating room. On the other hand, those patients who have less urgent symptoms are appropriate candidates for expedient diagnostic evaluation.

Infections of the Spine and Spinal Canal

The two most important spinal infections that must be considered in patients with back pain are vertebral osteomyelitis and epidural abscess. Another rare infection is intramedullary abscess.[21] In all of these conditions, the cord, cauda equina, and nerve roots are at risk, and once the diagnosis is made or strongly suspected, immediate consultation with a neurologist or neurosurgeon should be initiated. All of these patients will be hospitalized, some may require biopsy to obtain the causative organism, and surgical treatment is the rule rather than the exception. Early diagnosis and definitive therapy lead to improved outcomes.

Vertebral Osteomyelitis. Various types of infections can invade the spinal column and canal. The pathophysiology of vertebral osteomyelitis has special clinical importance. The vertebral bodies have a rich, but sluggish blood supply. In the embryo, one artery supplies two vertebrae (the lower portion of the superior body and the upper part of the inferior vertebral body) along with the intervening disk.[22] Therefore, vertebral osteomyelitis of the spine typically involves two adjacent verte-

bral bodies, whereas tumor infiltration may involve only a single vertebral body; this may be an important differential point. Vertebral osteomyelitis can develop from hematogenous or contiguous spread of infection. In some cases, no obvious source is identified.

Back pain is the symptomatic hallmark of patients with vertebral osteomyelitis. Other symptoms include fever and radicular pain, including hip pain.[22] The pain often had been present for weeks to months. Depending on the location, other symptoms referable to the GI tract (dysphagia) or pleural spaces (effusions) may develop. Fever is only present in about one-half of cases.[22,23]

The physical exam may demonstrate spinal tenderness, diminished ROM, and positive straight leg raising (SLR) test. Neurologic deficits related to the cord, cauda equina, or individual nerve roots may also be found. Because this process usually involves the anterior vertebral body, the back pain can precede onset of neurologic findings by some time. The progression from back pain to root, cord, or cauda equina compression can be gradual or abrupt. Pyogenic vertebral osteomyelitis of the posterior elements has been reported but is far less common.[24]

Staphylococcus aureus is the most common offending organism, followed by gram-negative enteric species. Salmonella has classically been associated with sickle cell disease or infected vascular tissue but is otherwise uncommon. In some areas of the world, tuberculosis and brucellosis must be considered.[22] The lumbar, thoracic, and cervical spine are involved in 50%, 35%, and 15% of cases, respectively, for bacterial cases, while the thoracic spine is much more common in tuberculous cases.[22]

An elevated white blood cell count is found in less than one-half of cases and the ESR, while usually elevated, lacks specificity.[22] Plain films are abnormal in as many as 95% of cases of vertebral osteomyelitis although in intravenous drug abusers (IVDA), this figure drops to 80%. Magnetic resonance scanning, while more expensive than plain films, is nevertheless very sensitive and adds more information about the state of the cord and nerve roots as well as other diagnostic information.

Epidural Abscess. Epidural abscess is another rare, but important, infection that can create serious morbidity and mortality. Epidural abscess can result from vertebral osteomyelitis and genitourinary and soft-tissue infections, or it can follow epidural anesthesia, back surgery, and trauma.[22,25-27] Diabetes, IVDA, and alcoholism are frequent comorbid conditions that accompany epidural abscess.[25-26,28] However, about 20% of patients have no predisposing factors identified.[25,28] Back pain is the presenting symptom in the majority of cases,[25,28-29] while no other symptoms were present in more than 50% of cases in the largest recent series.[25] Other symptoms include radicular pain; motor, sensory, or sphincter symptoms; and back (or neck) stiffness. Fever is present in about 75% of cases.[25,29] Spinal tenderness is often present, but the neurological examination is normal in approximately one-half of patients on the day of presentation.[28] When abnormal, the exam may show root, cord, or cauda equina signs.

In one large series, the white blood cell count was greater than 11,000 in less than 70% of cases; neither fever nor leukocytosis was present in 7%.[25] The ESR is usually elevated but depends upon the cut-off level used. *Staphylococcus aureus* is by far the most common organism implicated, followed by various streptococcal and gram-negative enteric organisms. Blood cultures were positive in as many as 95% of cases in one series[25] but in only about 60% in most other series.[26,28]

The location of epidural abscess in the spine has been divided equally between posterior and anterior in most series,[8,44] although one study found a preponderance of abscesses posteriorly.[29] Cervical location is not uncommon.[25,26] The abscess usually extends over multiple vertebral segments (over four segments, on average).[25] Plain x-rays are positive in 44-65% of cases[25,28] and do not predict CT or magnetic resonance (MR) findings.[25] MR imaging (MRI) has emerged as the diagnostic modality of choice[29] and has largely replaced bone scanning, CT, and conventional myelography. In cases where MR is not available, the latter two methods are still useful.

The mainstay of treatment is intravenous antibiotics and surgical decompression. Early neurosurgical consultation is important, as neurologically intact patients can deteriorate abruptly, usually as a result of vascular factors rather than mechanical cord compression.[25,28] Deterioration on intravenous antibiotics while awaiting surgery can occur,[28] although some patients have done well when treated with antibiotics alone.[25] Appropriate antibiotics would cover *S. aureus* and gram-negative enteric organisms. The choice of which antibiotics to use depends on hospital and regional resistance patterns.

Patient outcomes are largely a function of the neurologic condition at time of presentation and the duration of neurological deficits prior to examination. Patients who are diagnosed while still ambulatory generally remain so; the mortality rate ranges from 5% to 23%.[25,28-29]

Spinal Cancer

The incidence of spinal malignancy is low in unselected populations of outpatients with back pain; however, metastatic disease in the spine is a common diagnosis in patients with known cancer. In one series of 851 cancer patients seen for neurological symptoms, 18.2% had back pain.[30] Of the 133 patients in this series with back pain, 30% of the cases were due to bony metastases, 33% were due to epidural metastases, and in 20% other metastases (meninges, paravertebral soft tissues, and to the nerve plexuses) were found.

Lung, breast, and prostate were the most common primary sites of cancers associated with back pain. Other frequent primary malignancies included lymphoma, renal cell carcinoma, melanoma, sarcoma, and multiple myeloma.[31] Thyroid cancer frequently spreads to bone; it may be the cause of epidural metastasis.[32] Epidural tumor is the first manifestation of cancer in about 10% of patients with spinal metastases; accordingly, all patients with spinal metastases will not have a history of cancer.[33]

Spread of cancer to bone is second only to lung cancer in frequency. Among cases of metastatic bone involvement, the spine is the most commonly involved site.[33] The vertebral body is usually involved first; therefore, spinal metastatic disease is most commonly found anteriorly.[31,33] Experimentally, cancer cells invade the spinal canal via the foramina of vertebral veins rather than by bony destruction; therefore, radiographic evidence of vertebral metastatic disease can be a late event.[34]

The pathogenesis of metastatic spine disease in humans results from direct epidural extension from a vertebral lesion in 85% of cases. Other possibilities include extradural extension from paravertebral tumor (especially common in lymphoma),

or impingement of bony fragments, or angulation of the cord from pathologic vertebral fracture.[31,33] The degree to which vascular factors play a role is incompletely understood.

Location. A thoracic location is most common (about 60-70% of all cases), followed by lumbar involvement.[2,33] Prostate and colon cancer tend to spread to the lumbar area, whereas lung cancer preferentially affects the thoracic spine. Breast and prostate cancer tend to spread to multiple (although they are not always symptomatic) areas, while lung cancer often produces a single lesion.[33] As with most causes of spinal cord compression, the rate of development of compression is an important factor in the prognosis; the more rapid the development, the worse the outcome.

Diagnosis. Pain is the most common symptom of spinal cancer.[31,33] There is often a progression of symptoms from back pain (vertebral metastases) to radicular pain (caused by nerve root compression) to neurological signs resulting from cord or cauda equina compression.[33] The pain produced by spinal metastatic disease is similar to that described in patients with a herniated disk: both increase with activities that produce a Valsalva maneuver (coughing, sneezing, etc.).[31,33] The SLR test will be positive in both herniated disk and cord compression.[2,33]

Other symptoms help distinguish the two processes. Pain from cancer tends to be unaffected or worse with rest or at night, whereas pain from sciatica or degenerative disease behaves in the opposite manner. Cancer pain can occur at any area in the spine, whereas benign disease tends to cluster in the lower neck and lower back. Weakness, sensory, and sphincter symptoms tend to follow isolated pain.[31] The high frequency in which neurological symptoms are found at presentation in many series may be a reflection of delayed diagnosis.[33]

As previously outlined, there is evidence to suggest that ordering an ESR in this setting can be helpful.[35] The important question is, if the ESR is not elevated, should one proceed further? In one study, the combination of plain films and ESR along with careful history identified all patients with cancer.[35] There were some patients in that study who were proven to have cancer but who did not have either or both studies done. Therefore, the question is who should be imaged, when, and with what study?

One investigation divided cancer patients with back pain into three groups. It is important to note that this study was published in 1987, prior to widespread use of MR and prior to the current economic conditions.[36] In Group 1 (patients with new signs of symptoms of cord or cauda equina disease), plain films were recommended while waiting for myelography. For Group 2 (patients with evidence of "stable or mild" spinal cord compression or those with radiculopathy or plexopathy), they recommended CT scan followed by plain films and myelography for patients with suspected coexistent radiculopathy. For those without suspected radiculopathy, the algorithm called for CT along with plain films or radionuclide scan and myelography for any positive finding. In Group 3 patients (those with back pain alone), the algorithm calls for sequential plain films, followed by radionuclide scanning, and then a CT scan. A positive on any test would lead to myelography.

MRI Scanning. Since 1987, the MRI scan has become the imaging method of choice in hospitals where it is available.[31,33] For patients with neurological findings, MR scanning is clearly indicated, the only issue being how urgently. For patients with no neurological signs or symptoms, should one directly proceed to MRI scan or should plain films be obtained as an initial screen? If plain films are positive, MRI scan is still indicated, in part, to plan for radiotherapy fields. The question becomes, in cancer patients with back pain and normal plain films, how likely is there to be a spinal metastasis?

In one autopsy study of 832 consecutive patients with a "terminal" diagnosis of cancer, the spines were examined grossly, radiographically, and histologically.[32] The investigators found that 26% of metastatic deposits were not seen on plain films and conversely, 22% of cases of vertebral collapse were not due to the malignancy. In the former group, it is not known if the occult metastatic lesions were clinically relevant.

Knowledge of the primary tumor may assist in decision-making; 94% of patients with breast cancer have abnormal plain films, as do 74% of those with lung cancer. In patients with lymphoma and pediatric neoplasms, on the other hand, only one-third demonstrated abnormal plain films.[31] Two authorities conclude that while the risk of metastases may be low, in cancer patients with back pain, even those with no neurological signs or symptoms and normal plain films, MRI scanning may be useful.[31,33] The issue and approaches to the work-up of cancer patients with back pain are still a matter of debate and must be considered controversial.

The authors' opinion, based on the existing evidence, is that the rapid advances in technology and the decrease in real costs justify proceeding to MRI scanning directly as the best policy. If such patients are not imaged with MRI, they must be followed extremely closely. Remember that this controversy applies only to patients with no signs or symptoms of neurological disease. Cancer patients with neurological signs or symptoms clearly should have an MRI scan immediately. Twenty-five percent of cancer patients whose symptoms or signs suggest radiculopathy, and who have normal plain films, have metastatic epidural cord compression.[31]

In cases where MRI scanning is unavailable or if it is contraindicated (claustrophobia or metallic clips or pacemakers), conventional CT scan or myelography should be performed. Rarely, in a patient with a high suspicion for a lesion and a non-diagnostic MRI scan, conventional myelography may show the lesion.[31,33] Needle biopsy may also be indicated in patients whose primary tumor is unknown.

Regarding timing of the study, patients with signs of cord or cauda equina lesions should be imaged within hours; those with root or plexus lesions and with isolated back pain can be imaged urgently, preferably within 24 hours.

Consultation with the patient's oncologist, as well as with a radiation oncologist and neurosurgeon, should be initiated early. Steroids and radiation therapy are the mainstays of therapy, although decompressive surgery is undertaken in selected patients.[33] For patients with severe compression or rapid progression, 100 mg of intravenous dexamethasone is recommended; pain relief often occurs over hours. Lower doses may be just as effective and are used for patients with less dramatic presentations.[31,33]

Spinal Hematomas

Spontaneous spinal epidural hematoma is another rare but serious disease that can lead to poor outcomes if not promptly

diagnosed and treated. While there is a peak incidence of this entity between 50 and 80 years of age, cases were found in all age groups at a frequency not much lower than the peak.[37] Almost all are posterolateral in location and are thought to be due to rupture of veins in the spinal epidural plexus.[37] Anticoagulation of any type, recent spinal surgery, or spinal anesthesia are important risk factors, especially in combination. Moreover, spontaneous spinal epidural hematoma is a rare complication of lumbar puncture.[38]

Magnetic resonance scanning permits prompt diagnosis.[39,40] Surgical therapy is indicated in most cases, although conservative therapy has worked in selected cases.[40,41]

Back Pain in the Elderly

Patients older than the age of 50 years have a higher incidence of "cannot miss" diagnoses. This is in part because many of these conditions are more common in older patients and because herniated disk is less common, owing to age-related fibrosis of the nucleus pulposis. The Agency for Health Care Policy and Research (AHCPR) Guidelines does list age older than 70 as a risk factor for spinal fracture.[42] Patients older than the age of 50 with new or different back pain must be approached with a high degree of suspicion for serious disease.

Other than the "cannot miss" diagnoses, another important condition causing back pain in the elderly is spinal stenosis, a narrowing of the spinal canal or exit foramina of the spinal nerves. The stenosis can be of the central canal (diameter of less than 11 mm) or the lateral recesses (depth less than 3 mm).[1] While this stenosis can be congenital, it is the acquired type that results from hypertrophic soft tissue and bony degenerative changes that is most commonly seen.

The classic symptom suggesting spinal stenosis is neurogenic claudication. This typically consists of pain in the legs, with or without other neurologic symptoms (especially paresthesias), that occurs with walking, exercise in the erect posture, and even standing.[1,2] The pain can be sharp, aching, or cramping. Extension of the back increases the pain and impotence and cauda equina symptoms can be seen as sequelae.[1] The sensitivity of neurogenic claudication as an indicator of spinal stenosis has ranged from 60% to 100%.[1,2]

As compared to vascular claudication, the neurogenic variety is more commonly seen with standing alone, it may be increased by Valsalva (cough and sneeze), and it is associated with normal arterial pulses.[2] The increase in pain with extension also distinguishes the pain from herniated disk, which usually is exacerbated by flexion.[2]

Precise diagnostic criteria and therapeutic options are not clear at the present time. Measurements of the size of the spinal canal by CT scan were used in one study, which also concluded that conservative treatment with physical modalities and salmon calcitonin led to improvement in many patients.[1] Indications for surgery are unclear, but patients who have increasing symptoms or incapacitation should be referred for consultation with a skilled spine surgeon.

Osteoarthritis

Although many of the aforementioned conditions (from spinal abscess to epidural malignancy) can cause back pain in the geriatric patient, the clinician must always consider osteoarthritis in the differential diagnosis of elderly patients presenting to the primary care setting. Overall, osteoarthritis is the most commonly diagnosed joint disorder in the elderly population. If radiographic criteria are used exclusively (including joint space narrowing, bony sclerosis, cyst formation, and osteophyte formation), the prevalence of osteoarthritis by age 70 approaches almost 100%.[43] However, the number of people in this age group with functional loss or symptomatic osteoarthritis at any given time is less than 50%.[43,44]

Disease Categorization. Osteoarthritis can be divided into a) primary osteoarthritis, in which a precipitating cause of the arthritis is unknown; and b) secondary osteoarthritis, in which an initiating set of factors can be discerned. In general, osteoarthritis can be thought of as a "final common pathway" rather than as a discrete clinical entity with a consistent set of clinicopathologic correlations. Most patients, it should be stressed, have primary osteoarthritis, which is a disease of aging and is more prevalent symptomatically in females than males. Moreover, it is a disease of all races, and while various risk factors, such as obesity, have been proposed, none is conclusively established as a cause of this condition.

Secondary osteoarthritis can be precipitated by numerous underlying etiologies, most of which can be identified from a detailed history. Causes of secondary osteoarthritis can be broken down into three major categories: mechanical, congenital or developmental disorders, and systemic diseases. Trauma, including vertebral fractures, is one of the leading mechanical factors for the development of secondary osteoarthritis. This mechanical factor includes fractures that enter the joint space with disruption of the joint surface, post-operative degeneration, and major injury to the supportive structures of a joint.

Diagnosis. Ascribing acute or chronic low back pain to osteoarthritis requires historical support and radiographic confirmation of osteophytes as well as other changes and symptoms consistent with established osteoarthritis. The usual presenting complaint of osteoarthritis is joint pain, which is often characterized by pain with use and relief with rest. The pain is usually aching, and will progress to chronic pain, including nocturnal joint pain, with exacerbation from activity. The etiology of recurrent, chronic, and/or intermittent back pain is thought to be a combination of periosteal elevation and damage by osteophyte formation, and possibly even microfractures in areas of weakened cystic bone. Morning joint stiffness that is relieved rapidly with use is the cardinal symptom of osteoarthritis.

The disease is insidious and usually takes months to years to develop. There are no systemic symptoms associated with osteoarthritis unless the condition has been caused by an underlying secondary disorder. In its early presentation, osteoarthritis is usually monoarticular, but with advancing disease the cervical and lumbar spine, hips, knees, and the interphalangeal joints of the hand become involved. Involvement of the wrist, shoulder, or elbow is uncommon in osteoarthritis.

Osteoarthritic involvement of the spine, at least by radiographic criteria, is present in almost 100% of adults 70 years of age or older. This should be contrasted with rheumatoid arthritis, which usually has a more rapid polyarticular onset, and in which lumbar pain is much less common. The presenting symptoms of vertebral involvement include the insidious onset of pain, usually most prominent in the morning and with devel-

opment of stiffness.

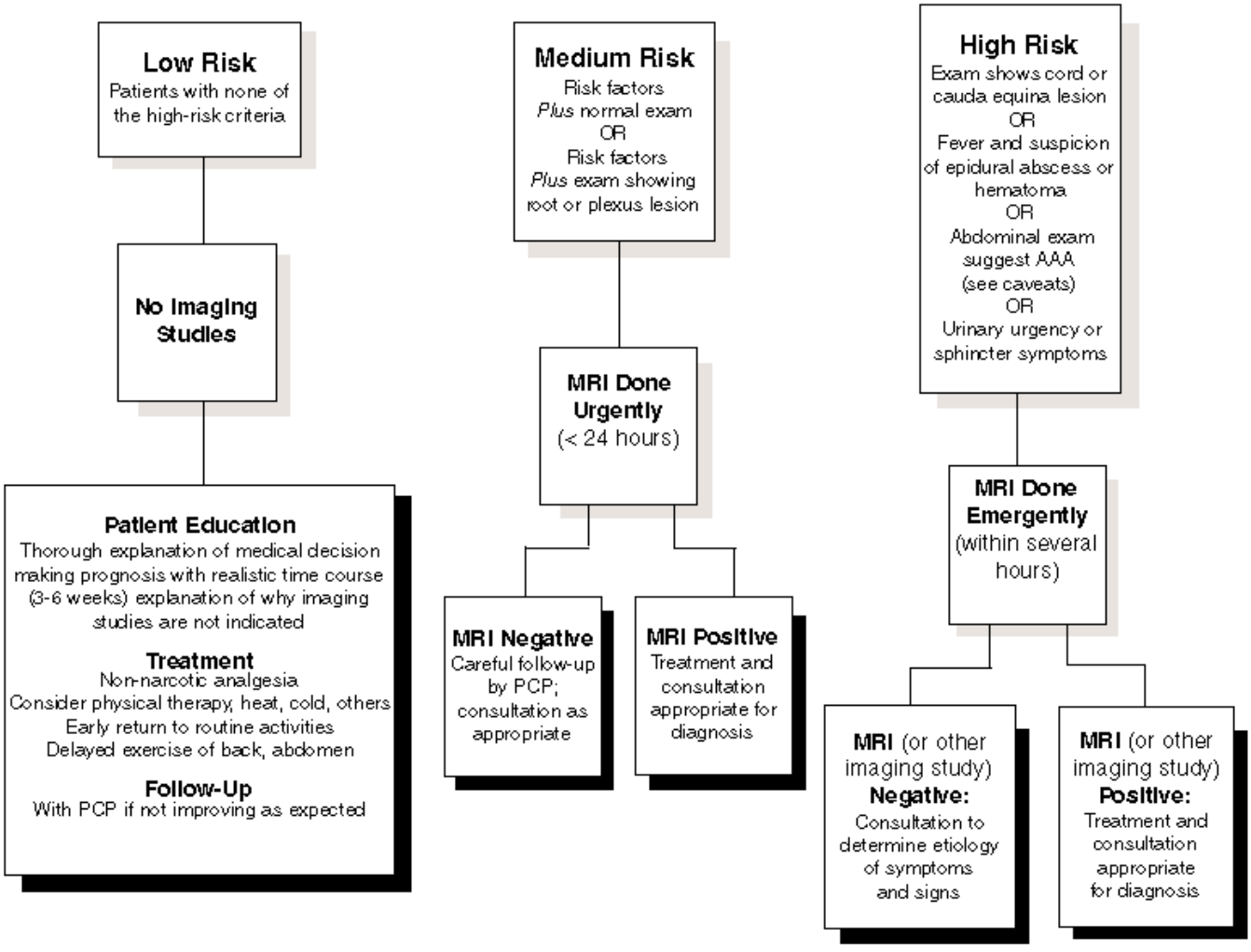
Treatment. Once the clinician has determined that the cause of back pain is osteoarthritis, pain management and functional improvement are principal goals of therapy. Acetaminophen has been used in mild cases, but the mainstay of therapy has been nonsteroidal anti-inflammatory drugs (NSAIDs), among them ibuprofen, naproxen, and a number of other agents, including once-daily preparations.

Unfortunately, NSAIDs, especially the cyclooxygenase-1 (COX-1) isoenzyme inhibitors, have been an important cause of drug-related morbidity and mortality in the elderly population. This is because, until recently, the available NSAIDs generally inhibited both COX-1 and cyclooxygenase-2 (COX-2) pathways. Inhibition of COX-2 is believed to provide the therapeutic anti-inflammatory and analgesic benefit of traditional NSAIDs, while inhibition of COX-1 may contribute to upper gastrointestinal adverse effects, such as ulcers, and also mediates the antiplatelet aggregation effects of NSAIDs.

NSAIDs are among the most commonly prescribed drugs and many are also available over the counter (OTC). Gastrointestinal toxicities are among the most serious side effects of the drugs, including ulceration, hemorrhage, or perforation. The mechanism of action of NSAIDs has been explained largely on their ability to inhibit the enzyme cyclooxygenase (COX). COX-1 is believed to have a gastroprotective effect, while COX-2 is responsible for the production of proinflammatory mediators.[45,46] Older NSAIDs are generally better inhibitors of COX-1 than COX-2, whereas newer NSAIDs, such as nabumetone and etodolac, have more balanced inhibition.[45]

The treatment landscape for pain associated with osteoarthri-

Figure. Neuro-imaging of Back Pain Patients



Reproduced with permission from Jonathan A. Edlow, MD, Boston, MA. This algorithm is based on the author's interpretation of evidence-based literature.

tis is now changing. When managing back pain that is clinically linked to osteoarthritis, practitioners have the option of using COX-2 inhibitors, which, on the basis of comparative endoscopic data evaluating gastric erosion and ulcer formation, appear to reduce the possible risk of gastrointestinal hemorrhage. The two COX-2 agents currently available for osteoarthritis include celecoxib (Celebrex) and rofecoxib (Vioxx).

Celecoxib. Celecoxib is a NSAID but, unlike most other NSAIDs previously used to manage osteoarthritis, it is a selective inhibitor of COX-2. At therapeutic concentrations, celecoxib does not inhibit COX-1. Celecoxib is indicated for the relief of the signs and symptoms of osteoarthritis and rheumatoid arthritis in adults. For the relief of the signs and symptoms of osteoarthritis, the recommended dose is 200 mg daily administered as a single dose or as 100 mg twice daily.[47] For the relief of the signs and symptoms of rheumatoid arthritis, the recommended dose is 100-200 mg twice daily.

In elderly patients (> 65 years of age), consideration should be given to starting celecoxib at a lower dose.[47] Celecoxib can be taken without regard to meals. However, a high-fat meal delays the absorption by about 1-2 hours, with an increase in total absorption of 10-20%. Coadministration with an aluminum- and magnesium-containing antacid reduces the peak plasma level by 37% and total absorption by 10%. Celecoxib is supplied as 100-mg and 200-mg capsules. Celecoxib should not be taken by patients who have demonstrated allergic-type reactions to sulfonamides.

In comparative trials between celecoxib and ibuprofen or naproxen, celecoxib was associated with a statistically significantly lower incidence of endoscopic ulcers evaluated at 12 weeks.[47] The incidences were 9.9-17.6% with naproxen (500 mg bid) and 9.6% for ibuprofen (800 mg tid), compared to 1.5-4% and 1.5-5.9% for celecoxib at 100 mg bid and 200 mg bid, respectively.[47] Moreover, among 5285 patients studied who received celecoxib over a 1-6 month period, only two patients (0.04%) experienced significant upper GI bleeding, one at 14 and another at 22 days after initiation of therapy. The discontinuation rate for celecoxib (7.1%) was similar to that for placebo (6.1%). Higher than recommended doses of celecoxib (600 mg bid for 7 days) had no effect on platelet aggregation and bleeding time. A single dose of 800 mg of celecoxib did not inhibit platelet COX-1 dependent aggregation.[48] Celecoxib does not appear to affect the anticoagulant effect of warfarin, although caution should be exercised if coadministration is considered.

It should be noted that the effect of celecoxib on the anticoagulant effect of warfarin was studied in a group of healthy subjects. In these subjects, celecoxib did not alter the anticoagulant effect of warfarin as determined by prothrombin time. However, there have been infrequent reports of increases in prothrombin time, sometimes associated with bleeding events, predominantly in the elderly. Therefore, anticoagulant activity should be monitored when therapy with celecoxib is initiated or changed in patients taking warfarin, particularly in the first few days. Celecoxib, by itself, has no effect on platelet aggregation or bleeding time at therapeutic doses and may be an appropriate treatment option in patients taking warfarin, when anti-inflammatory therapy is indicated.

The occurrence rate of dyspepsia and abdominal pain with celecoxib appears to be numerically lower than that of naproxen, ibuprofen, and diclofenac but slightly higher than placebo. The occurrence rates were 8.8% for dyspepsia and 4.1% for abdominal pain compared to 6.2% and 2.8%, 12.2% and 7.7%, 10.9% and 9%, 12.8% and 9% for placebo, naproxen, ibuprofen, and diclofenac, respectively.[47] Dyspepsia and abdominal pain were the most common side effects of celecoxib that led to discontinuation in clinical trials (0.8% and 0.7% for celecoxib compared to placebo, 0.6% and 0.6% for each symptom, respectively). Borderline elevation of one or more liver tests may occur in up to 15% of patients. Significant elevation (> 3 times the upper limits of normal) has been reported in only 1% of patients in clinical trials.[47]

Celecoxib is metabolized by cytochrome P450 2C9, and fluconazole, an inhibitor of this isoenzyme, causes a two-fold increase in plasma level. In vitro studies suggest that celecoxib is an inhibitor of P450 2D6 and there are potential interactions with substrates of this isoenzyme. Celecoxib increases the plasma level of lithium, and monitoring is recommended with coadministration.[47] Celecoxib does not appear to be renal sparing, as the renal effects are similar to other NSAIDs.

The potential superiority of celecoxib over other NSAIDs in terms of serious upper GI side effects has not been clearly established. In the celecoxib trials, endoscopic ulcers were used as surrogate markers. The correlation between endoscopic findings or symptoms and serious GI side effects has not been established. Although this method has been widely used in clinical studies, endoscopically observed ulcers may not be reliable predictors of severe GI events.[49-51] Endoscopic ulcers tend to be smaller, superficial, and predominantly gastric while serious events tend to be both gastric and duodenal.[49,50]

Despite the present lack of conclusive, prospective post-marketing studies confirming the gastrointestinal-sparing effects and safety advantages of COX-2 inhibitors such as celecoxib over other NSAIDs, the available endoscopic data showing reduction in ulcers, as well as the reduction in dyspepsia and abdominal pain, are sufficiently compelling to recommend COX-2 inhibitors such as celecoxib as initial therapy for pain management in patients with osteoarthritis. Celecoxib is priced similar to branded NSAIDs. The average wholesale price is $2.42 for the 200-mg capsules and $1.43 for the 100-mg capsules. These are similar to nabumetone (1000 mg/d) and oxaprozin (1200 mg/d).

Rofecoxib. Another COX-2 inhibitor, rofecoxib is approved for the relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults, and for the treatment of dysmenorrhea. Rofecoxib is available as 12.5-mg or 25-mg tablets and as an oral suspension containing 12.5 mg or 25 mg per 5 mL. The recommended initial dose for osteoarthritis is 12.5 mg once daily. Some patients may achieve added benefit at a dose of 25 mg once daily, which is considered the maximal dose for this indication. It may be taken without regard to meals. Rofecoxib should not be taken by patients who have experienced allergic-type reactions to aspirin or other NSAIDs.

Rofecoxib, 25 mg or 50 mg daily, has been reported to produce a lower percentage of endoscopic gastroduodenal ulcers than ibuprofen 2400 mg daily. The difference was statistically significant at 12- and 24-week assessments.[52] Rofecoxib also appears to be well tolerated in terms of GI adverse events. In a

clinical trial, the percent of patients experiencing diarrhea was 6.8% vs. 6.5% for placebo, 3.5% vs. 2.7% for dyspepsia, 3.8% vs. 2.8% for epigastric discomfort, and 4.2% vs. 3.6% for heartburn.[52] The metabolism of rofecoxib does not involve the cytochrome P450 enzymes, thus minimizing potential drug interactions. A general enzyme inducer, rifampin, has been reported to produce a 50% decrease in the plasma concentration of rofecoxib.[52] Rofecoxib has no effect on platelet function. Dosages of up to 375 mg given daily for up to 12 days did not affect bleeding time relative to placebo.[52]

Rofecoxib is approved for osteoarthritis but not for rheumatoid arthritis. The renal effects of rofecoxib are similar to those of other NSAIDs. The use of rofecoxib for the relief of pain at the 50-mg dose is not recommended beyond five days.[52] Coadministration of rofecoxib and warfarin have resulted in an increase of 8-11% in INR. Therefore, monitoring of INR is recommended with coadministration.[52]

In osteoarthritis, rofecoxib (12.5-25 mg) has been reported to be similar in effectiveness to ibuprofen 800 mg tid over six weeks or diclofenac 50 mg tid over six months.[52-54]

Although rofecoxib does carry an indication for management of acute pain, practitioners should note the following possible parameters, findings, and/or limitations regarding its use for this population. The recommended initial dose for acute pain is 50 mg once daily, and subsequent doses should also be 50 mg once daily as needed. Moreover, use of refecoxib for more than five days for management of pain has not been studied. Finally, in clinical osteoarthritis trials of up to six months, the general safety profile of the rofecoxib 50 mg qd dose was similar to the recommended 12.5 and 25 mg qd dose, although there was a higher incidence of dose-related gastrointestinal symptoms (abdominal pain, epigastric pain, heartburn, nausea, and vomiting), lower extremity edema (6.3%), and hypertension (8.2%). The additional cost of the 50-mg dose for acute pain is also a deterrent to routine use.

Summary and Diagnostic Algorithm

The algorithm proposed in the Figure is based on the authors' interpretation of evidence-based literature. It would be expected to identify the vast majority of back pain patients with serious disease, while simultaneously avoiding unnecessary imaging studies in patients whose clinical management plan would be unchanged. However, this algorithm has not been prospectively validated, and therefore its accuracy remains conjectural.

Whatever algorithm is chosen, the PCP must remain alert for patients whose back pain falls into the "cannot miss" group. Since back pain is such a common symptom, the history and physical examination, coupled with a detailed knowledge of the differential diagnosis and risk factors for serious causes will assist the PCP in arriving at the correct diagnosis.

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Physician CME Questions

69. What percentage of patients who present with ruptured aneurysms have never been diagnosed as having an AAA?
    a. 80%
    b. 70%
    c. 60%
    d. 50%
    e. None of the above

70. What percentage of patients with ruptured AAA are misdiagnosed when they first seek medical care?
    a. 84-90%
    b. 64-70%
    c. 34-42%
    d. 14-32%
    e. None of the above

71. Vertebral osteomyelitis typically involves:
    a. one vertebral body.
    b. two adjacent vertebral bodies.
    c. three nonadjacent vertebral bodies.
    d. None of the above

72. The most common organism causing vertebral osteomyelitis is:
    a. *Streptococcus osteoformans.*
    b. *Staphylococcus viridans.*
    c. *Staphylococcus aureus.*
    d. Salmonella.
    e. None of the above

73. The most common presenting symptom of epidural abscess is:
    a. neck pain.
    b. chills.
    c. back pain.
    d. neurological deficit.
    e. None of the above

In Future Issues:

Atrial Fibrillation—
Santosh Menon, MD,
Patrick Donovan MD, and Gery Tomassoni, MD