A surgical revisitation of Pott distemper of the spine

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Abstract

Background context: Pott disease and tuberculosis have been with humans for countless millennia. Before the mid-twentieth century, the treatment of tuberculous spondylitis was primarily supportive and typically resulted in dismal neurological, functional and cosmetic outcomes. The contemporary development of effective antituberculous medications, imaging modalities, anesthesia, operative techniques and spinal instrumentation resulted in quantum improvements in the diagnosis, management and outcome of spinal tuberculosis. With the successful treatment of tuberculosis worldwide, interest in Pott disease has faded from the surgical forefront over the last 20 years. With the recent unchecked global pandemic of human immunodeficiency virus, the number of tuberculosis and secondary spondylitis cases is again increasing at an alarming rate. A surgical revisitation of Pott disease is thus essential to prepare spinal surgeons for this impending resurgence of tuberculosis.

Purpose: To revisit the numerous treatment modalities for Pott disease and their outcomes. From this information, a critical reappraisal of surgical nuances with regard to decision making, timing, operative approach, graft types and the use of instrumentation were conducted.

Study design: A concise review of the diagnosis, management and surgical treatment of Pott disease.

Methods: A broad review of the literature was conducted with a particular focus on the different surgical treatment modalities for Pott disease and their outcomes regarding neurological deficit, kyphosis and spinal stability.

Results: Whereas a variety of management schemes have been used for the debridement and reconstruction of tuberculous spondylitis, there has also been a spectrum of outcomes regarding neurological function and deformity. Medical treatment alone remains the cornerstone of therapy for the majority of Pott disease cases. Surgical intervention should be limited primarily to cases of severe or progressive deformity and/or neurological deficit. Based on the available evidence, radical ventral debridement and grafting appears to provide reproducibly good long-term neurological outcomes. Furthermore, recurrence of infection is lowest with such techniques. Posterior operative techniques are most effective in the reduction and prevention of spinal deformity.

Conclusions: Unlike historical times, effective medical and surgical management of tuberculous spondylitis is now possible. Proper selection of drug therapy and operative modalities, however, is needed to optimize functional outcomes for each individual case of Pott disease. © 2003 Elsevier Science Inc. All rights reserved.

Keywords: Pott disease; Tuberculosis; Spondylitis

Introduction

Tuberculosis has and continues to be the world’s most prevalent and lethal infectious disease with over 3.5 million deaths yearly [1–6]. More individuals died from tuberculosis in 1996 than in any previous year in history [7]. There are presently over 40 million active cases of tuberculosis globally with 8 to 10 million new cases expected each year [8]. Based on a 1% to 2% incidence of skeletal involvement, World Health Organization figures estimate that there are over 800,000 active cases of tuberculous spondylitis [8,9]. Within the United States itself, the prevalence of tuberculosis increased from 1986 to 1992. Increasing populations of elderly nursing home patients, the homeless, Southeast Asian and Central American immigrants and patients infected with the human immunodeficiency virus (HIV) have
all contributed to this increasing prevalence [10–14]. Despite improved screening and treatment programs, tuberculosis persists as a significant health problem in the United States [6,8]. In African nations, the reported rate of cases has increased by over 200% in the last 5 years because of the region’s unchecked HIV pandemic [3,15]. In sub-Saharan Africa alone, conservative estimates show that there are approximately 25 million cases of active HIV with up to 50 million cases worldwide [16]. Of HIV cases in developing nations, approximately 10% to 15% will develop active tuberculosis. Up to 60% of these HIV-positive tuberculosis patients will have skeletal involvement, a figure that is far greater than the usual 1% to 2% incidence seen in HIV-negative patients [17,18]. From these epidemiological data, it is clear that a global resurgence of Pott disease is upon us.

Historical perspectives

“To attend to a distemper from its beginning through a long and painful course, to its last fatal period, without even a hope of being able to do anything which shall be really serviceable, is of all tasks the most unpleasant” (Sir Percival Pott, 1779) [19]. Although Dr. Pott is credited with this early grim description of spondylitis, tuberculosis as a disease has afflicted humans since the dawn of time [19]. From the Arene Candide cave in Liguria, Italy, the remains of a 15-year old male buried in the first half of the fourth millennium BC were found to have tubercular lesions of the vertebral column [20]. Similarly, evidence of tuberculous spondylitis has been found in the mummified remains of both Egyptian kings and slaves alike from as early as 3400 BC [21]. In the Sanskrit writings of ancient India, numerous references to tuberculosis under the eponym “Yakshma” are replete in the Rig, Atharva Vedas (3500 to 1800 BC) and Susruta Samhitas (1000 to 600 BC) [21,22]. It is humbling to note that the Vedic physicians’ prescription of high altitude, fresh air, rest, immobilization and constitutional supplementation was the same as that used by “modern” Western doctors until the 1940s [23].

One millennium later, Hippocrates in his work, On Articulations, vividly described both the deforming kyphus and draining fistulae in patients afflicted by “Pott’s Distemper.” Galen subsequently recognized the relationship between these tubercular changes and spinal deformity and published his observations in the second century AD [24]. As such, both Hippocratic and Galenic physicians used a novel “extension” bench to control spinal deformities through manual reduction techniques (Fig. 1). In their respective sixteenth- and seventeenth-century publications, Diechamp in France and Severino in Italy both postulated that the progressive spinal deformity was responsible for the paraplegia observed in these patients [8]. With the advent of germ theory, Robert Koch correctly identified M. tuberculosis in 1892 as the microbial culprit responsible for this wake of human suffering [23]. In 1944, the introduction by Schatz and Waksman of streptomycin emancipated thousands from the sanitoriums and also made surgical intervention feasible by lowering the mortality rate [25–29]. In an effort to assess the efficacy of these new medical and surgical treatments, the Medical Research Council (MRC) was founded in 1963 to direct prospective research on the epidemiology, diagnosis and treatment of tuberculosis [26,30–37].

Pathophysiology

Tuberculosis is a chronic, insidious and recurrent bacterial infection caused by M. tuberculosis, Mycobacterium bovis or Mycobacterium africanum. M tuberculosis is the most common cause of tuberculosis and appears as an “acid-fast bacillus” with appropriate staining on microscopic examination. The lungs are most commonly infected because M tuberculosis is a strict aerobe and strongly de-
Miliary spread of the bacilli with tuberculoma formation can, however, occur in virtually any organ [1,2,38–40]. The gross pathologic finding in tuberculous spondylitis is one of granuloma formation consisting of exudative granulation tissue and interspersed abscesses. As the abscesses coalesce, regions of caseating necrosis result and appear as a yellow, opaque, “cheesy” substance. Microscopic examination of the granuloma reveals a nodular pattern with central necrosis. Langerhans giant cells with peripheral nuclei are common, although not pathognomonic [41]. Special staining of adequate pathologic samples may expediently reveal a causative acid-fast bacilli in the case of *M. tuberculosis* or other fungus [17].

Tuberculosis infections of the spine are usually the result of seeding from an extraspinal source (eg, pulmonary infection) and commonly manifest as paradiscal, anterior or central lesions [17]. In adults, there are four primary patterns of involvement: 1) paradiscal, 2) anterior granuloma, 3) central lesions and 4) appendiceal type lesions [8,9,42]. Of these, the paradiscal lesion is the most common and represents approximately half of all cases [41]. In the paradiscal lesion, the primary focus of infection is in the vertebral metaphysis. The enlarging granuloma subsequently erodes through the cartilaginous end plate and then begins to narrow the disc space (Fig. 2). Anterior granulomas develop beneath the anterior longitudinal ligament and can span several vertebral segments. Although anterior granulomas typically demonstrate less bony destruction and deformity than paradiscal or central lesions, elevation of the periosteum can result in bone devascularization with subsequent development of an abscess, necrosis and deformity. In central lesions, the entire vertebral body is involved, thereby causing significant deformity as the body loses structural integrity causing one or more pathologic fractures. Patients with central lesions will commonly have two or three affected vertebrae. Infections of the atlas, axis and isolated neural arches are less frequent but more likely to cause neurological deficits [43,44]. Skip lesions in different stages of development occur in approximately 10% of patients [41]. Lastly, the appendiceal type of lesion propagates in the laminae, pedicles, articular facets and spinous processes, causing initial expansion followed by subsequent rupture and failure [8].

Abscesses, commonly found in spinal tuberculosis, follow tissue planes but may extend into the spinal canal at any level. The periphery of the abscess can form thin or dense adhesions with visceral and vascular structures. Further, these lesions may cause symptoms resulting from neurovascular compression (eg, pain), hemorrhage and direct mass effect [4,20,21,26,30–37,39,45–48]. In the neck, abscesses are more common in children than adults. Such lesions are often symptomatic because of compression of the trachea and esophagus [49]. In the thorax, the abscess may invade the lung and create pleural and/or diaphragmatic adhesions with the lung. Invasion of the femoral trigone occurs when the abscess travels down the psoas sheath from the lumbar region. Abscesses in the sacral region can also invade the perineum or the gluteal region through the greater sciatic foramen. A rupture of an abscess through the skin may create a draining sinus, thereby increasing the risk of superinfection.
Neurological deficits are a consequence of 1) direct neural compression by granulomas, abscesses, sequestra of vertebral bodies and discs (extra- and intradural extramedullary tuberculomas), 2) direct invasion of the neural parenchyma (intramedullary intradural tuberculosis), 3) tuberculous meningitis, 4) pathological dislocation and subluxation of bony elements, 5) vascular compromise (thrombosis, direct pressure) [8,17,24,38,50–52]. The granulomas can create neurological compromise by transdural compression of neural elements or by invading the dura. The majority of such compressive lesions are secondary to an admixture of purulent material and osseous elements [53]. However, pure granulomatous or abscess-only compression of neural elements without an associated bony lesion has also been reported [54,55].

Intramedullary tuberculomas, first described in 1830 by Sere, are much rarer than their intracranial counterparts but have the same histological appearance of central caseation surrounded by an often intense pachymeningitic arachnoiditis [8,51]. Because of the predominance of anterior spinal element involvement, ventral neural compression is most common, but isolated or concomitant posterior compression may occur. Also, abscesses or the sequestra of vertebral body or disc in the epidural space may directly press on neural elements resulting in neurological deficits. Tuberculous spinal meningitis may present in three main forms: 1) tuberculoma arising in the pachymeninges, 2) secondary extension of intracranial basal meningitis and 3) secondary extension from tuberculous meningitis [52]. Thick exudates are typically seen surrounding the meninges, cord and nerve roots with intermingled fibrous bands of granulation tissue. At times, cystic formation with pockets of cerebrospinal fluid can occur as a result of these changes [56]. Vascular ischemia, infarction, delayed myelomalacia, gliosis and syringomyelia may also result [57]. Isolated pathologic dislocation or subluxation of the bony elements is an infrequent cause of neurological compromise [58–61]. In the setting of apparent disease quiescence, late paraplegia may occur because of such vertebral body failure. Paraplegia is far more common in tuberculosis than in other forms of pyogenic spondylitis because of the increased frequency of neural arch involvement and of pathological fracture with neural compression [62,63].

Spinal lesions comprise 50% of cases of articuloskeletal tuberculosis, which comprise 3% of tuberculosis cases in HIV-negative and 60% of HIV-positive cases [8,9,17,18]. Of spinal tuberculomas, 5% are in the cervical spine, 75% in the thoracic spine and 20% in the lumbar and sacral spine. Kyphotic deformity results from the collapse of anterior vertebral elements and is most commonly seen in thoracic lesions. The loss of one vertebral body may produce as much as 32 degrees of kyphosis, but often multiple levels are affected [39,49,64–66]. Kyphotic deformity progresses until the collapsing vertebral bodies meet anteriorly or the granulating and caseating tissue mature into bone. By the first 18 months after medical treatment, most of the vertebral collapse has occurred, and the ultimate degree of kyphotic deformity is proportional to the initial loss of the vertebral bodies as opposed to the initial degree of radiographic kyphosis [17]. With circumferential erosion of both the posterior arch and anterior body, translational instability can occur with resultant anterior, lateral, rotatory subluxation and a significantly increased risk of neurological compromise [3,62].

Clinical presentation

The clinical presentation of a particular patient will vary depending on the age and health status of the patient, the location of the infection, the stage of the disease and the absence or presence of abscesses, sinus tracts and neurological compromise. Systemic symptoms of weight loss, fever and malaise usually precede spinal involvement for several months. When the spine is involved, the most common presenting complaint is one of pain with an insidious onset as opposed to complaints of acute pain with pyogenic infections [60]. Cervical involvement may present with complaints of torticollis, neck pain and stiffness, stridor and dysphagia. Neurological compromise reported in 10% to 61% of patients with spinal tuberculosis may be manifested as somatosensory changes, weakness and changes in bowel and bladder function [60]. In underdeveloped countries, paraplegia, kyphosis, deformity and draining sinuses are common presenting complaints because of poor health-care access and patient neglect [32,67]. Even in industrialized nations, the diagnosis of tuberculosis can be delayed for up to 2 years after the onset of symptoms [58]. A complete physical and ophthalmological examination may yield systemic signs of mycosis, spinal alignment deformity, subcutaneous flank masses and evidence of cutaneous fungal infections and/or sinuses. The neurological examination should assess the function of cranial nerves, somatosensory and motor systems and the rectal sphincter, and determine the presence of myelopathy (ie, hyperreflexia, sustained clonus and pathological reflexes, such as Babinski and Hoffman signs). Classical physical findings include local tenderness, muscle spasm, restricted spinal motion, deformity and neurological deficit [3,4,26,30–37,46–48,62,68–72]. Pain is an excellent localizing sign with the most common locations being the thoracic spine followed by the lumbar, cervical and sacral regions [67,73]. Paraplegia is most often from thoracic and cervical spondylitic destruction [49,73]. Abscesses and fistulae are found in the groin and buttocks and can be mistaken for other types of anorectal fistulae [38].

Clinical subgroups

In younger children, far more extensive disease with military spread is often found at the time of diagnosis. Although larger abscesses are more frequently encountered, there is a relatively low incidence of paraparesis (15% to 20%) and paralysis in pediatric cases. This is in direct contrast to the adult subgroup that has far more localized disease but a much higher incidence of paraplegia (over 80%)
In the United States, Europe and Middle East, where disease prevalence is relatively low, older adults are more commonly infected than children. However, in areas of higher prevalence (e.g., Asia and Central America) children are more commonly infected than adults [3,4,26,30–37,46–48,62,68–72]. In western countries, spinal involvement is typically less severe with fewer neurological symptoms and a milder degree of deformity [6,75,77]. Also spondylitis without disc involvement has been increasingly reported in industrialized nations in contrast to the classic spondylodiscitis typically seen elsewhere [6], presumably because of better access to care and early diagnosis.

In immunocompromised patients with advanced HIV disease, the clinical presentation can be masked by numerous other HIV-associated changes in the central and peripheral nervous system, including vacular myelopathy of the spinal cord, demyelinating neuropathy, dementia and coexistent infection with other organisms (cytomegalovirus, herpes, varicella, Jacob-crunzfeld, treponema, Candida, Cryptococcus, Mucorncysis, Toxoplasma) [18]. Instead of classic paraplegia, deformity and pain, these individuals may present with progressive ataxia, dementia, spastic paraparesis, myelopathy and sphincter disturbances [8,78,79]. Lastly, a distinct syndrome of tuberculous spondylitis has been reported in intravenous drug addicts, many of whom are HIV positive as well. In these patients, acute fever, intense back pain, weight loss, night sweats and rapidly evolving deficits with diffuse milillary spread was observed [24,80].

Evaluation and diagnosis
Laboratory investigations

In the laboratory evaluation the white blood cell count is typically normal and the erythrocyte sedimentation rate (ESR) is elevated above 20 mm/hour in 80% to 100% of patients with spinal osteomyelitis [81]. However, 5% to 10% of children have an ESR greater than 20 mm/hour [82], and healthy elderly patients and pregnant women have mildly elevated ESRS [83]. The Mantoux test (tuberculin skin test) is typically positive, but anergic individuals will produce false-negative results. Serological testing using enzyme-linked immunosorbent assay and agglutination titers can provide additional information about tuberculous and fungal infections. The definitive diagnosis is made with open or percutaneous trephine needle biopsy of the bone and disc using computed tomography (CT) or fluoroscopic guidance [84,85]. Cultures and special stains of the biopsied specimens will identify the causative pathogen. However, such isolation of the bacterium from clinical specimens can often take several weeks with sensitivities as low as 50% [86]. Recent advances in polymerase chain reaction (PCR) techniques have opened exciting new avenues of diagnosis and treatment. By amplifying species-specific DNA sequences in even formalin-fixed paraffin-embedded samples, PCR is able to rapidly detect and diagnose several strains of Mycobacterium without the need for prolonged culture and special histological staining techniques [87]. Furthermore, PCR techniques have been used to identify discrete genetic mutations in DNA sequences associated with drug resistance [88]. Rifampin resistance has been mapped to a small region of an RNA polymerase (rPOB) gene, and ciprofloxacin and streptomycin resistance has been localized to gyrase A (Gyr A) and ribosomal protein SR (rPSL) genes [3]. As such, PCR techniques can now be used to specifically select drug therapy based on the organism’s genetic makeup for each case [89].

Radiographic evaluation

The classic case of tuberculous spondylitis is described as beginning anteriorly and advancing superiorly and inferiorty to the disc space. However, hematogeneous seeding to the end-plate subchondral metaphyseal bone is more likely because of its rich vasculature [90]. As the disease progresses, paravertebral abscesses develop, the disc space is destroyed and adjacent bodies become rarefied, resulting in kyphotic deformity as the vertebral body collapses. Imaging studies are used to visualize this process and include spine and chest plain films, radionuclide scanning, CT and magnetic resonance imaging (MRI). The basic imaging analysis includes spine and chest plain films to visualize advanced rarefaction, bony deformity, disc space narrowing, anterior vertebral collapse, vertebral plana, kyphosis and abscesses. Rarefaction, vertebral edge lucency and loss of cortical margins can be seen 2 to 4 weeks after spinal infection and may involve multiple segments. Paravertebral shadows indicating paravertebral swelling usually over two to three segments is often seen as the illness progresses. Abscesses may appear as widened paravertebral shadows with soft tissue calcifications and loss of the psoas muscle shadow. Involvement of the disc space resulting in disc space narrowing on radiographs is commonly seen before vertebral body collapse (Fig. 2, A to C). With plain radiographs, the extent of the disease is often underestimated, requiring radionuclide scanning, CT and MRI with contrast enhancement to fully demonstrate the extent of the tuberculosis and abscesses (Fig. 2, D and E). The differential diagnosis of granulomatous disorders of the spine includes sarcoidosis, Candida, Torulopsis, Aspergillus, Coccidiodes immitis, Blastomyces, Actinomyces [91], Nocardia [91–93], atypical Mycobacterium [21,93–96], Brucella [97,98], nonvenereal Treponema (yaws) [99] and Echinococcus (hydatid disease) [100].

Technetium 99m pyrophosphate is the most common scintigraphic study, because it is the most sensitive. However, it is not specific [101]. Gallium scintigraphy can be performed in early stages of disease and is useful for whole body screening. CT is excellent for defining the anatomy of bony destruction, extension into the spinal canal, posterior element involvement and formation of paravertebral abscess. As a single modality, however, MRI is the modality of choice, because it provides superior anatomic detail of
the thecal sac, neural structures and paravertebral areas [40]. CT myelography can show similar details, but scintigraphy cannot. Myelography also allows for collection of cerebrospinal fluid for analysis to evaluate neurological involvement. With gadolinium, MRI can discriminate between abscesses and granulation tissue and can define a soft tissue mass and the extent of bony destruction. Noncontrasted CT scans provide useful and complementing rendering of bone detail, especially for surgical planning.

Medical management

In general, chemotherapy and adequate rest and nutrition are the cornerstones of therapy for spondylitis caused by typical and atypical Mycobacterium, fungi, actinomycoses, nocardia, brucella, echinococcus and nonvenereal treponema organisms. The overall goals of medical treatment include 1) recovery and/or maintenance of neurological function, 2) recovery and/or maintenance of mechanical spine stability, 3) diagnosis and elimination of the causative pathogen and 4) functional return to activities of daily living as soon as possible. Medical and conservative management alone for cases without significant paraplegia, deformity or instability has yielded good results in countless patients. In Tuli’s classic series of over 200 cases without neurological deficit, resolution of disease with good outcomes was obtained in 94% of patients with antibiotic treatment alone [9]. This “middle-path” of reserving surgery only for medical failures is further substantiated by findings of the MRC, who found 93% favorable outcomes in patients treated with only a 6- or 9-month regimen of antibiotics [46,47]. However, the true meaning of “favorable” must be interpreted in light of the health-care resources available and the functional expectations of the patient and physician.

Antimicrobial regimens

The modern era of antituberculous therapy began in 1943 with Waksman’s discovery of streptomycin [28]. Within 5 years after its introduction, mortality rates in conservatively managed patients decreased by nearly 70% across the globe [102]. Isoniazid (INH) and p-aminosalicylic acid (PAS) were subsequently introduced in 1952 with excellent clinical efficacy in eliminating the risk of disease dissemination and preventing chronic abscess and sinus formation [103]. These drugs were also successfully used without surgery when patients were kept immobilized in orthoses at bed rest for long periods [104].

A second major evolution in tuberculosis treatment came about in Nigeria when a shortage of beds forced physicians to use INH and PAS on an ambulatory basis. Although cosmetic deformity was problematic, over 96% of their patients were cured with this regimen [105]. The MRC subsequently conducted controlled prospective studies on the effect of the length of bed rest, plaster of Paris jacket orthoses and the addition of streptomycin to standardized INH and PAS regimens. The 5- and 10-year results confirmed the effectiveness of the ambulatory regimen and could demonstrate no benefit of the other adjunctive measures [34,36]. With the addition of rifampin, the MRC altered their recommendations to the following front-line agents: INH, rifampin, pyrazinamide, streptomycin and ethambutol. Second-line agents include ethionamide, cycloserine, kanamycin, capreomycinc and PAS. The latest MRC studies have demonstrated that isoniazid and rifampin given for 6 to 9 months was as effective as isoniazid and paraaminosalicylic acid or ethambutol given for 18 months [31,33]. However, significant controversy continues to surround the optimal length of therapy. In particular, several authors have criticized the large degree of bone resorption and kyphosis seen with only short-course 6- and 9-month regimens [106–108]. To prevent recurrence, prevent delayed kyphosis and to eradicate a paucibacillary disease with slow-growing bacilli, triple-drug therapy (INH, rifampin, ethambutol) for 18 months or four-drug therapy (add pyrazinamide) has been advocated by these groups. For the cases typically seen in Western industrialized nations, a 6-month, three-drug regimen with INH, rifampin and pyrazinamide should be used for most patients with drug-sensitive infection [109].

Isoniazid is administered at a typical dose of 5 mg/kg/day up to 300 mg/day and should be supplemented with pyridoxine to prevent peripheral neuropathy. Rifampin 10 mg/kg/day up to 600 mg/day is concurrently given with isoniazid. Pyrazinamide should also be prescribed at a dose of 15 to 30 mg/kg/day up to 2.0 g/day for up to 2 months only to prevent hepatotoxicity [4,26,30–37,46–48]. Because pain, inflammation and bone resorption are of particular concern during the initial phase of therapy, several groups have advocated the use of nonsteroidal anti-inflammatory agents. The antiprostaglandin effect of these agents is thought to decrease nonspecific synovial inflammation and bone resorption as well [62,69,110]. Baseline laboratory values for hepatic enzymes, bilirubin, serum creatinine, Blood Urea Nitrogen (BUN), Complete Blood Count (CBC), and platelets should be obtained initially, and these values may be monitored at 1 or 3 months or more frequently depending on particular clinical situations. Directly observed therapy is an important component of medical management, because patient nonadherence to a prescribed treatment is a major cause of therapeutic failure and of the emergence of resistant organisms. In this multi–drug resistant era, drug susceptibility should be tested before starting treatment and again 3 months later. When technically feasible, PCR should be performed early on to allow for rapid identification of resistant strains and timely adjustment of the drug regimen. If the organisms are resistant to isoniazid, then ethambutol 15 to 25 mg/kg/day up to 2.5 g/day should be added to the chemotherapy.

Operative indications and timing

With the indisputable efficacy of medical treatment alone, the proper role of surgery in the treatment of tubercu-
lous spondylitis is a subject of ongoing controversy [40]. On the one hand, Hodgson and Stock [111] advocated surgical debridement of tuberculous spinal lesions as soon as possible after the diagnosis has been made. From their experience, they observed that earlier surgical extirpation was technically easier, prevented delayed deformity, shortened the patient’s length of hospitalization and reduced the incidence of relapse. On the other hand, the prospective trials comparing the outcomes of surgical intervention with that of medical treatment alone have not substantiated such a philosophy. Indeed, present MRC recommendations are that surgery be reserved only for diagnostic biopsy, spinal instability, severe deformity, myelopathy, severe sepsis, significant abscesses and open draining sinuses [4,26,30–37,46–48]. As a useful heuristic, the surgical surgeon should consider three main questions for every case of tuberculous spondylitis. First, what is the rationale for the operation (eg, to treat infection, neurological deficit, deformity pain or functional restriction)? Second, when should the operation be performed (ie, early, during medical treatment or after)? Finally, what is the best operation or combination of procedures to accomplish these goals?

Treatment of neurological deficits

For cases of mild neurological deficit (eg, paraparesis) or even early paraplegia, several studies have demonstrated the effectiveness of medical therapy without surgery [112,113]. Lin et al. found that the majority of patients with only mild neurological symptoms would improve without surgical decompression [114]. Of 89 consecutive patients with clear paraplegia who were treated with antibiotics and bedrest alone, Pattison [63] demonstrated that 85% returned to a normal life with full activity. Similarly, Moon et al. [69] conservatively treated 75 such patients with favorable outcomes seen in 95% of them. However, more recent prospective data would suggest that the prognosis of patients with moderate to severe neurological impairment is significantly improved by early surgical decompression and reconstruction. When Lin et al. considered all patients with neurological deficit, they found that there was an improvement rate of 94% with early surgery versus only 79% with nonsurgical management [114]. Patients with deficits that were managed according to the “middle-path” regimen who subsequently had surgery obtained a similar overall success rate of 78.5% as well [9,61,115]. From a review of the literature, patients with less severe neurological deficit and those undergoing earlier surgical intervention fare better than patients with severe deficits and later surgery [9,38,67,116–119]. Ultimately, numerous studies have emphasized that neurological outcome is directly correlated with rigid bony fusion regardless of whether it is spontaneous or surgically induced [38,120,121].

As such, some authors have advocated only a fusion procedure for patients with mild deficits and reserved aggressive decompression for cases of severe paraplegia [45,49].

The overall prognosis for neurological recovery after timely surgical intervention is generally good but can often be slow and prolonged [67]. Patients with active caseating disease and nonosseous abscesses typically recover faster than those with a chronic hard, bony kyphus and long-standing neural compression [45]. Hodgson and Stock [111] underscored this finding in their study that demonstrated a direct correlation between the duration of neurological symptoms before surgery and the time to recovery postoperatively. Other poor prognosticators for neurological improvement include direct infiltration of the pachymeninges and radiographic evidence of spinal cord atrophy [67,118]. Surgical morbidity and complications also increase for delayed procedures, because late fibrosis makes operative debride ment more difficult as well [24].

Treatment of kyphosis

The residual kyphosis that is seen after ambulant chemotherapy has always been a source of concern. In Konstam’s original study of ambulant chemotherapy, only 75% developed a clear radiographic bony fusion with 49% having 0 to 10 degrees of residual kyphosis and 18% having more than 30 degrees of kyphosis [105]. Data from other MRC studies have also echoed these findings with nonsurgical regimens yielding a solid fusion in 65% to 79% of cases [31,36]. From a review of their experience, Moon et al. found that the kyphotic progression in these patients was typically arrested within the first 6 months of drug treatment and was not influenced by the overall length of therapy beyond that [3,62,68–70]. A controlled study by the Medical Research Council of England compared the results of inpatient versus outpatient medical treatment and found a slightly greater mean total vertebral loss and angulation in patients treated on an ambulant basis [36]. Further, use of orthoses and plaster casts did not seem to affect the ultimate kyphotic angulation in either group. When compared with adult cases as a whole, more advanced cases of tuberculous spondylitis and children with posterior element involvement are more likely to be complicated by significant residual kyphosis after ambulant chemotherapy [30,31,69,122,123]. Rajasekaran and Shanmugasundaram [124] prospectively analyzed the kyphotic angulations after medical treatment in over 90 patients for 6 years. From the controlled nonsurgical arm of the study, these authors were able to extrapolate a unique formula to predict the final gibbus angle after treatment within a 90% degree of accuracy [125]. From the formula \( Y = 5.5 + 30.5X \) \((Y = \text{final angle of the deformity}, X = \text{initial loss of vertebral body height})\), patients with an excessive predicted \( Y \) value were surgically reconstructed. Cases with multiple levels of vertebral involvement, thoracic lesions, active growth and skeletal immaturity were also predictive of an increased amount of posttreatment kyphosis [8,115].

Based on these considerations, an attempt should be made to estimate the amount of kyphosis expected after medical treatment alone. When this figure is excessively high or there is evidence of significant progression during medical treatment, surgical intervention to correct and pre-
vent deformity is reasonable. Absolute criteria of the degree of acceptable deformity will vary tremendously from case to case. Whereas a 20-degree deformity may be considered acceptable to patients in developing nations with limited medical resources, few patients in Western countries would be willing to accept such a severe long-term cosmetic deformity. However, operative correction of severe kyphosis is extremely technically demanding and carries a high risk of neurological injury [116,126]. Reduction of significant chronic fixed deformities for cosmetic reasons should be performed sparingly and with great caution [3]. In such cases, it is best to operate earlier on while the kyphosis is still mobile and not excessive.

Surgical techniques

From the late 1800s until the early 1900s, thousands of posterior laminectomies were performed worldwide for tuberculosis. The outcomes of these operations were, however, uniformly disappointing [64,74,116,127–129]. Seddon [130], in his 1934 review on the topic, openly condemned laminectomy for its dismal results, its inability to provide adequate access for safe debridement and its failure to arrest progression of the deformity. Founded on the orthopedic principle that ankylosis of peripheral joints often led to re- mission of destructive synovitides, Hibbs [64] introduced the concept of in situ posterior arthrodesis with autogenous bone grafting in 1911. Because of the lack of spinal instrumentation at the time, such unsupported fusions proved ineffective in preventing delayed kyphosis and subsequent paraplegia and were thus largely abandoned as a surgical solution [131].

To address these surgical shortcomings, Capener [132] and Menard [76,133] used a lateral rachiotomy (eg, costotransversectomy) approach to obtain an improved postero-lateral corridor for the debridement of ventral tuberculomas in the late 1920s (Fig. 3). Like laminectomy, however, postero-lateral approaches also contributed to the instability of the spinal column. Transperitoneal and transthoracic surgical exposures of the anterior spine were subsequently developed in the 1930s to treat both tuberculosis and spondylitis [134,135]. On the other side of the globe, Ito et al. [129] concurrently reported his series of tuberculosis patients who were successfully treated by anterior debridement and grafting. Many surgeons, however, openly opposed such aggressive surgical debridement in light of the extremely high mortality (30% to 70%) that resulted from secondary infections [66,127,128]. The morbidity of open surgery before antituberculous therapy was so high that Calot [136] remarked in 1930, “The surgeon who, so far as tuberculosis is concerned, swears to remove the evil from the very root, will find only one result awaiting him—the death of his patient.” Despite these grim outcomes, the knowledge gained from these early pioneering efforts would serve as the bedrock on which modern spinal surgery would be built [66,76,133,137,138]. After the introduction of streptomycin and INH in the 1950s, the surgical mortality rate plummeted from 70% to 0% to 2.1%, thereby causing a renaissance of surgical treatment for Pott disease [139].

Abscess drainage and excision

In his original manuscript, Sir Percival Pott described successful drainage of a tuberculoma: “The remedy for this most dreadful disease consists merely in procuring a large discharge of matter... and in maintaining such discharge until the patient shall have perfectly recovered the use of his legs” [19]. For the majority of cases of tuberculous spondylitis, such open drainage was generally ineffective and often lethal. With the efficacy of modern antituberculous therapy, many patients now experience early resolution of their sepsis but still demonstrate persistent large tuberculomas known as “cold abscesses” [3,56,75,80,112]. Percutaneous aspiration or open drainage of these lesions was originally thought to speed patient recovery, to prevent abscess extension and to minimize subsequent bony destruction and deformity. After decades of experience, this technique has been shown to be ineffective with an increased risk of morbidity and no benefit over chemotherapy alone for treatment of tuberculous infection [3,62,69,70]. As such, simple aspiration or drainage of large abscesses is not indicated except for purposes of obtaining a tissue diagnosis. CT-directed biopsies using a fine needle have proven quite effective in confirming the causative organism, thereby obviating the need for open spinal biopsy [140]. For rare cases where aggressive debridement is not possible because of either extensive disease or poor medical condition of the patient, ab-

Fig. 3. Numerous corridors of access have been used in the surgical treatment of tuberculous spondylitis. The specific choice of approach should be tailored to the location of the bulk of the abscess and tuberculoma. For most cases of Pott’s disease, the pathology lies ventrally thereby necessitating an anterior approach for adequate debridement and reconstruction. These approaches are shown in italics.
scess drainage can be accomplished by means of a limited transpedicular, costotransverse or retroperitoneal approach [132,141].

More aggressive drainage and excision of infected foci without fusion was commonly performed worldwide for similar reasons [32,139]. By removing all bony and soft tissue sequestra and opening new vascular channels, excisional therapy was shown to reduce general toxemia and total time to disease remission in the preantibiotic era [8,115]. Somerville and Wilkinson [142] retrospectively studied 130 patients treated with excisional therapy without fusion and compared these results with 105 patients treated only with antituberculous therapy; they could demonstrate no difference in outcome. In response to these findings, Tuli et al. [9,61,115] suggested that only cases with progressive bony destruction, increasing size of abscess, new neurological deficit, disease recrudescence and failure to respond to drug therapy should undergo excisional therapy. Subsequent prospective MRC data have, however, shown no long-term benefit of focal debridement and abscess evacuation over that of ambulant chemotherapy alone [30,31]. Other authors such as Neville [143] actually reported poorer outcomes for patients undergoing excisional therapy. As excisional therapy without fusion generally leaves a significant anterior column bony deficit, several studies have found an increased rate of nonunion, progressive kyphosis, persistent draining sinuses and delayed neurological deficits in this group of patients [3,65,89,124,143] Based on these considerations, it would seem that excisional surgery without fusion should be performed only in rare circumstances.

Anterior surgical techniques

Based on present MRC guidelines, radical ventral debridement, fusion and reconstruction of the vertebral column remains the gold standard of surgical treatment for tuberculous spondylitis [4,26,30–37,46–48]. Although anterolateral decompression of the lumbar spine had previously been reported by other surgeons [8], it was Hodgson and coworkers’ [67,111,144] experience that led to popularization of radical anterior debridement or what is now known as the “Hong Kong” procedure. Although numerous variants of the Hong Kong operation have been described, the hallmarks of the procedure are aggressive extirpation of all infected foci, thorough neural decompression and solid arthrodesis by means of bone grafting. Infected bone, caseous pus and sequestra must be aggressively extirpated back to the level of healthy, bleeding bone. Leaving behind infected sequestra can lead to disease recurrence and delayed deformity with neurological deterioration [131]. Decompression for cases with neurological deficit should be carried to the level of dura, thereby increasing the chance of recovery [3,68]. In cases where only debridement is required, the posterior longitudinal ligament can be left intact [24,38].

The success of radical anterior operation and concurrent chemotherapy has been well substantiated both retrospectively and prospectively in the literature. Better outcomes for deformity, disease recurrence, neurological deficit and disease elimination have been demonstrated [67,106,108,111,144–148]. The results of the MRC’s controlled long-term trial comparing the Hong Kong operation, simple debridement and medical treatment alone, demonstrated that 1) anterior bony fusion occurs earlier and in a higher percentage of patients undergoing the more radical operation (70% vs. 20% and 26%, respectively, at 5-year follow-up), 2) kyphotic angulation was less common at 5 years, and 3) at 10 years, kyphotic angulation increased in the simple debridement group but stabilized and decreased in the radical debridement plus fusion group [26]. In their series of 412 consecutive patients treated with this procedure, Hodgson et al. [144] had a mortality rate of 2.9% with no cases of delayed paraplegia.

Surgical approaches

Tuberculomas of the anterior craniovertebral junction and atlantoaxial region can be debrided through either transoral or extreme lateral approaches. These cases typically require concurrent occipitocervical fusion to prevent collapse, instability and delayed deformity in this biomechanically tenuous area of the spine [38]. Mid-cervical lesions are typically treated by means of standard anterior cervical approaches with excellent results (eg, Cloward and Southwick-Robinson) [49] or combined anterior and posterior reconstruction. Some authors have advocated approaches through the posterior cervical triangle, because abscess cavities in this region seem to have a propensity for dorsal extension [145]. For lesions of the cervicothoracic junction, transsternal, transmanubrial, or lateral extracavitary approaches have been employed with varying degrees of success [8,149–151]. In the thoracic spine, radical debridement and reconstruction can be accomplished through either a transthoracic, extrapleural anterolateral or extended posterolateral approach (eg, costotransversectomy, lateral extracavitary approach; Fig. 3) [26,38,152]. Extrapleural techniques afford the theoretical benefit of avoiding tuberculous empyema, although there have been no data to substantiate its superiority over standard thoracotomy [153]. Because of the limited access afforded by posterolateral approaches, there may be increased risks of blind neurovascular and visceral injury, residual foci of abscesses and infected sequestra and a decreased rate of fusion because of a smaller graft area available for arthrodesis. Compared with transthoracic approaches, costotransversectomy (lateral rachitomy) yielded a lower rate of solid fusion (78% vs. 95%) and a higher mortality rate (8% vs. 3%) [154]. However, more recent literature would suggest that wider posterolateral exposures by means of lateral extracavitary approaches might yield outcomes equivalent to that of transthoracic approaches [152]. In such regions as the high thoracic spine, which are poorly accessed by means of thoracotomy, a lateral extracavitary procedure provides an ef-
fective alternate approach. Larger degrees of kyphosis tend to allow better access through such posterolateral approaches, with better visualization of the dura. For the lumbar spine, the debridement and reconstruction is typically performed through a lateral retroperitoneal approach to afford maximal extensile exposure of the vertebral column and psoas musculature [67,111,144]. Anterior transperitoneal or retroperitoneal approaches used for lumbar interbody fusion operations typically are too restrictive in their exposure of the mid and upper lumbar spine to allow for safe debridement and reconstruction [155]. On the other hand, these approaches are well suited for access to the low lumbar and lumbosacral regions [124,125,156]. Supplemental posterior sequential instrumentation and fusion is often necessary.

Fig. 3 summarizes the operative corridors provided by these various approaches.

Tuberculosis patients undergoing surgery frequently have a compromised immune system, depleted nutritional reserve and an overall poor potential for wound healing. As such, wound closure in such cases should be performed in multiple layers with interrupted nonabsorbable monofilament sutures to prevent chronic draining sinuses [38]. As infected exudates typically persist at the operative site for some time after surgery, it is desirable to have well-vascularized surfaces nearby to allow for effective antibiotic concentrations and maximal reabsorption of fluids. Many surgeons thus preferentially debride tuberculomas anteriorly to allow for drainage of the operative site to either the pleural or peritoneal surfaces [17,67,106,129].

Grafting considerations

After debridement, grafting should be performed to reconstruct the anterior support column of the spine, promote solid bony arthrodesis and ensure a successful fusion. In an MRC prospective study of 119 patients, 58 underwent radical anterior debridement with autologous grafting, whereas the other 61 had debridement alone. Fusion rates, nonunion rates and mean kyphotic angles were lower in the grafted group both at 5- and 10-year follow-up [30]. Traditionally, iliac crest, rib or fibular autologous grafts have been employed with reliable results [30,58,67,146,149,154,157–159]. More recently, metallic cage or mesh type devices containing nonstructural autograft have also been successfully used [152]. The ideal graft must provide strong support while bony arthrodesis occurs. Fibular grafts provide excellent structural integrity but also contain a large area of cortical bone that is slowly remodeled, often requiring several years to fully incorporate [160]. During this time, the poorly vascularized necrotic matrix of the cortical bone may shelter microbes from antibiotics in the bloodstream, thereby increasing the risk of persistent disease. For these reasons, Bradford and Daher [161] and Louw [162] have used vascularized rib grafts for stabilization in children and demonstrated significantly earlier incorporation (mean, 8.5 weeks) and higher fusion rates. The ease of use and ready availability of rib graft during thoracotomy made their use popular in adults as well (Fig. 4). Clinical results have, however, been mixed in this population. In adults, Kemp et al. [149] demonstrated a high incidence of delayed rib fracture (32%), partial collapse and pistoning of the struts into the adjacent end plates. When compared with full-thickness iliac crest grafts, rib segments yielded a markedly lower long-term fusion rate (62% vs. 94.5%) and a higher mean increase in kyphosis as well (20 degrees). Similarly, Hodgson et al. [144], who exclusively used iliac crest grafts in Hong Kong, reported a far lower amount of delayed kyphosis and pseudoarthrosis. For these reasons, most experienced authors have advocated the use of full-thickness iliac crest for reconstruction of large defects with significant kyphosis [111,125,149]. The use of anterior compressive spinal instrumentation as an adjunct to debridement and grafting has been successfully described [163,164]. Others have cited poor bone stock, potential for progressive bone erosion from local disease progression and fear of persistent hardware infection as reasons to avoid the use of anterior instrumentation [24,38].
**Posterior surgical techniques**

Although many patients often improve initially after decompressive laminectomy, neurological compromise typically recurs without fusion as instability progresses. Bosworth et al. [120] studied this phenomena in 14 patients decompressed with laminectomy with all unfused patients dying. Laminectomy for tuberculous spondylitis should thus be reserved only for rare cases of isolated posterior neural arch disease with posterior epidural compression [43,112,130]. For these cases, 60% to 90% can expect a good to fair result with those with lesser deficits, subacute disease and young age faring the best [43,165]. Even for such cases, several experienced authors recommend a subsequent instrumented fusion to prevent delayed kyphotic progression and neurological deterioration [8,24,166]. For Pott disease, posterior spinal operations thus continue to play a pivotal role in the treatment of kyphosis for both prevention and correction of the deformity.

There is evidence that young children are at particular risk of progressive kyphosis after successful anterior reconstruction because of persistence of growth in the posterior spine despite anterior arrest. Posterior in situ arthrodesis either prophylactically or as a salvage procedure has been advocated by several authors to treat this skeletal growth imbalance. Schulitz et al. [167] followed 117 children operated for Pott disease with either anterior or posterior noninstrumented fusions. At 10 years, the anterior fusion group had a mean kyphotic increase of 12 degrees, whereas the combined anterior-posterior fusion group actually experienced an improved correction of 7 degrees. On the other hand, such authors as Bailey et al. [58], Fountain et al. [168], and Upadhyay et al. [148,169] have reported a much lower incidence of late kyphotic progression in children after successful anterior debridement and fusion. Of note, however, is that these authors typically included children who were older than the cohort of Schulitz et al. Nevertheless, it is prudent to follow children closely after anterior reconstruction so that posterior fusion can be performed when needed to arrest progressive kyphosis [24,170].

In adults, posterior instrumented techniques have also been used to prevent delayed deformity as well as to promote fusion and prevent kyphotic progression after anterior reconstruction. Several authors have expressed dissatisfaction with the ability of anterior grafting alone to correct preoperative kyphosis and to prevent delayed deformity [3,62,69,70,124]. A significant loss of gibbus correction has often been observed within the first 6 to 24 months after radical anterior debridement and fusion [171]. This has been particularly true for cases involving larger defects more than two disc spaces in size where over 25% of patients may have late kyphotic angles over 20 degrees [124]. Thoracic lesions, marked preoperative kyphosis and the use of rib grafting have also been associated with more severe late deformity after anterior surgery [38]. For such cases, some surgeons have advocated use of a two-staged approach with an instrumented posterior fusion either preceded or followed by an anterior debridement and grafting [62,68,172]. Moon et al. [71] reported on the use of posterior Harrington rod instrumentation as a first-stage procedure in 39 adults with multisegmental spondylitis and obtained excellent postoperative reduction of the deformity with minor long-term loss of correction (less than 3 degrees).

Güven et al [173] have used single-stage pedicle-screw type posterior instrumentation for cases of limited monosegmental spondylitis without paraplegia or extensive destruction and obtained good control of delayed kyphotic progression as well (less than 3.4 degrees). Compared with prior hook-type or sublaminar wire-type constructs, transpedicular fixation has been shown to be biomechanically far superior with regard to rigidity, stiffness, torsional strength and its ability to maintain the correction of deformity [65,71,72,106,152,173]. However, large postdebridement defects should still be grafted after transpedicular fixation to ensure adequate ventral column support. In such instances, posterior instrumented correction without anterior grafting can lead to corporal collapse, failed union, pseudarthroses, hardware breakage and progressive kyphosis [3,71,72]. Use of distraction maneuvers without anterior support further increases the possibility of these complications. Hooks and sublaminar wire fixation should be used where transpedicular fixation is not possible. Examples of this include thoracic vertebrae with very small pedicles, severely osteoprotic bone and incompetent pedicles from either erosion or prior fracture. Long-segment constructs can often exert excessive lever-arm moments at the ends of the implants, thereby also increasing the risk of screw pullout. Use of hooks or sublaminar wires at the termini of the construct can help to prevent this (Fig. 4).

Surgical correction of a severe kyphotic deformity (greater than 30 degrees) will often require posterior techniques that are more complex and technically demanding. Smith-Peterson et al. [174] first described a posterior closed wedge osteotomy in 1945 with V-shaped resection of a portion of the posterior arch and a subsequent closure in extension. With this technique, Simmons [175] was able to achieve an average of 56 degrees of correction in kyphotic lumbar deformities. However, use of this type of closing osteotomies necessitates anterior grafting, because a large defect is created ventrally after extension. In the classic Galveston one-stage posterior closing wedge osteotomy, a modified bilateral costotransversectomy approach to the spine is performed to allow for wedge-shaped resections of the vertebral arch, intervertebral disc and a portion of the body centrum. Once this wedge of bone has been removed, the posterior and middle columns of the spine are preferentially shortened, thereby allowing for angular corrections of 30 to 50 degrees [116]. Because there is bone-on-bone contact ventrally, the need for anterior reconstruction is obviated unless there is a need for either debridement or decompression. The decancellation or corporal eggshell technique
of Thiranont and Netrawichien [89] can also be used to achieve excellent correction of kyphosis as well. As the procedure involves transpedicular curettage and evacuation of the vertebral body’s cancellous bone in addition to excision of the posterior elements, this operation carries additional surgical risks [173,176]. Surgical morbidity and mortality can be significant for these technically demanding procedures, with an 8% to 10% incidence of postcorrection neurological complication [3,173–175]. For these reasons, Puschel and Zielke [177] and Roy-Camille et al. [178] have advocated multiple-wedge osteotomies at several levels as a safer method of reducing severe rigid deformities by dissipating reduction forces over several levels.

For all such posterior closing-wedge osteotomies, most authors universally advocate concurrent internal fixation. For most cases, compressive posterior instrumentation with either screws or hooks should be applied to maintain the correction and compress the anterior arthrodesis site [179]. In the past, there have been concerns raised regarding the use of metallic instrumentation in Pott disease for fear of a persistent focus of infection [180–182]. Whereas other bacteria adhere readily to biologically inert surfaces, such as titanium, Mycobacterium typically is less adhesive and produces less extra polysaccharide biofilm than other bacteria [182]. Many surgeons have reviewed their instrumented Pott cases and have not reported problems related to infection persistence or reactivation [162,183–186].

**Conclusion**

As cases of HIV-related tuberculosis demonstrate exceptionally high rates of spinal involvement, the prevalence of Pott disease will continue to increase rapidly across the globe over the next decade. It is with a sense of irony that spinal surgeons must now revisit our own history to apply refined operative techniques to treat this new but also very old disease. With the advances made in antituberculous drugs over the last century, medical therapy remains the cornerstone of treatment for tuberculosis and tuberculous spondylitis. The effectiveness of ambulant chemotherapy has been proven time and time again in numerous retrospective and prospective studies. With the gains in laboratory and radiological diagnosis made, tuberculosis and Pott disease can now be treated in a more timely, effective and selective fashion. In contrast to the early twentieth century, spinal surgery as a discipline has also made major strides in visualization, hemostasis, corrective ability, anesthesia and antisepsis. Anterior debridement and reconstruction can be performed safely and with low morbidity for patients with kyphosis and neurological deficit. The ability to stabilize and correct the spine with rigid instrumentation has opened whole new avenues of deformity management as well. As a result of these innovations, operating on Pott disease is far less daunting than it was to our predecessors. Despite these revolutionary improvements, surgery should still be used sparingly as a second-line of defense. For cases of spondylitis uncomplicated by significant kyphosis, unresponsive sepsis, questionable diagnosis or neural deficit, early detection and medical treatment should always be the mainstay of management. Only when progressive deformity, neurological deficit or incapacitating pain/dysfunction ensue should the spine surgeon be prepared to intervene.

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Four Hundred Sixty Years Ago in Spine . . .

At the age of 29, Andreas Vesalius published what is generally called The Fabrica. This encyclopedic work was the most thorough text ever published on human anatomy. It not only added to but also corrected the errors of established works, such as those of Galen. His insistence that cadaver dissection be an essential part of the education of physicians fueled a controversy that lasted for centuries. The extraordinary beauty of the illustrations not only served to establish the authority of the science but also became treasures of art. Who should be credited with the original illustrations is an unresolved topic of scholarly debate.

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