# Extrapulmonary Tuberculosis

## *A Review*

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The increase in cases of tuberculosis that has occurred with the increasing number of individuals infected with the human immunodeficiency virus (HIV) has focused attention on the problems in diagnosing and treating tuberculosis. While it is primarily considered a pulmonary disease, tuberculosis has the potential to infect almost every organ system via lymphohematogenous dissemination during the initial pulmonary infection. Since 1984 the incidence of extrapulmonary tuberculosis has increased at an even faster rate than that of pulmonary tuberculosis. Extrapulmonary tuberculosis is considered a diagnostic criterion in the case definition of the acquired immunodeficiency syndrome. Immunocompromised individuals, such as patients with HIV, are at increased risk for extrapulmonary tuberculosis. The clinical manifestations are often nonspecific and insidious, and diagnosis may be delayed for years. Cases of miliary and meningeal tuberculosis are an exception, and they often constitute medical emergencies. Tuberculosis skin tests should be performed on all individuals suspected of having tuberculosis, but a negative test result does not exclude the diagnosis. Chest roentgenograms will often show signs of old or active pulmonary tuberculosis. Microscopic examination and culture of infected body fluids and/or tissue are necessary for definitive diagnosis. Treatment is with standard antituberculous medications. Short-course therapy (6 or 9 months) is probably adequate in most patients with extrapulmonary tuberculosis, but patients with human immunodeficiency viral infection need longer treatment. Extrapulmonary tuberculosis is a persistent problem in the United States and will become more prevalent as the number of patients with HIV increases. A high index of suspicion is needed to diagnose and treat extrapulmonary tuberculosis in a timely and health-preserving manner.

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During the past decade, tuberculosis (TB), once a nearly forgotten public health problem in the United States, has increased as a cause of morbidity and mortality. Much of this increase has been due to the acquired immunodeficiency syndrome. However, homelessness, increasing drug abuse, and the large wave of immigrants from TB-endemic areas have also contributed to this increase.[1]

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### OVERVIEW

Primarily considered a pulmonary disease, TB has the potential to affect almost any organ system. The number of new cases

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of extrapulmonary TB has remained stable for many years, at approximately 4000 per year. Because the diagnosis of extrapulmonary TB is often delayed for months to years,[2] an increase in extrapulmonary TB may not be noted until several years after it has occurred. From 1984 to 1989, the number of cases of extrapulmonary TB increased by 20%, compared with a 3% increase in pulmonary TB.[3] In 1989, the latest year for which complete published data are available, 18.5% of the total cases of TB were extrapulmonary (**Table 1**).[4]

Even for physicians with a great deal of experience with the disease, extrapulmonary TB may be difficult to diagnose. Many of today's primary care physicians have little experience with pulmonary TB, let alone extrapulmonary disease. Extrapulmonary TB is often found in those persons with immunocompromising diseases. Forty percent of persons infected with the human immunodeficiency virus (HIV) with TB have extrapulmonary disease,[1] and the presence of extrapulmonary TB is considered a diagnostic criterion in the case definition of acquired immunodeficiency syndrome.[5] It is becoming increasingly important for physicians to consider and look for extrapulmonary TB so that appropriate treatment can be started early.

Extrapulmonary TB has been known by many names, including Pott's disease (TB of the spine), lupus vulgaris (skin), and scrofula (lymph nodes).[6] With the advent of effective chemotherapy and improved public health measures in this century, the character of extrapulmonary TB changed. Certain common forms, such as TB enteritis, which had been mainly due to bovine TB, became rare, and other sites became more common.[7] Extrapulmonary TB evolved into a disease of older individuals. Now, however, young, HIV-positive patients are also getting this form of the disease.[8]

The majority of cases of extrapulmonary TB are due to lymphohematogenous dissemination during the primary pulmonary TB infection, as a bacillemia deposits the mycobacteria throughout the body. Most of these organisms are eliminated by the immune-mediated granulomatous inflammatory reaction. However, some mycobacteria may persist and later result in active disease. A few forms of extrapulmonary TB are not due to lymphohematogenous spread. These include pleural TB due to local spread from the lung, intestinal disease from swallowing organisms with respiratory secretions, and cutaneous infection due to direct inoculation.

The diagnosis of extrapulmonary TB depends foremost on a high index of suspicion. In addition to HIV infection, predisposing factors to TB include, in general (including extrapulmonary TB), alcoholism, diabetes mellitus, renal failure, blood dyscrasias, neoplasms, and prolonged steroid use.[9] General symptoms in extrapulmonary TB are nonspecific and protean and may include weakness, anorexia, fatigue, weight loss, cough, and fever.[9] Diagnosis is based on the clinical presentation, laboratory findings, and results of TB skin testing, and is definitively made by culture of fluids and examination of biopsy specimens.

Tuberculosis skin testing should be performed on any patients suspected of having extrapulmonary TB, although negative test results do not necessarily exclude the diagnosis. Positive TB skin test results were found in from fewer than half to more than 90% of patients with extrapulmonary TB, depending on the site of disease.[2,9,10] Some case series do not discuss how many patients had exhibited anergy or what strength of purified protein derivative was used. Patients with acquired immunodeficiency syndrome, in particular, may not have a reaction. Chest roentgenography should also be performed on all patients suspected of having extrapulmonary TB, since many patients with extrapulmonary TB also have pulmonary TB. In 1989, 26% of all reported cases of extrapulmonary TB also involved active pulmonary disease,[4] and abnormal chest roentgenograms have been reported in 18% to 83% of patients in case series.[2,9]

The clinical presentation and laboratory findings in specific forms of extrapulmonary TB in the United States are discussed below by organ system.

## Lymphadenitis

**Epidemiology.** Tuberculous lymphadenitis is the most common form of extrapulmonary TB, accounting for 25% of the reported cases in 1989.[4] The cervical nodes are most commonly involved. Tuberculous lymphadenitis is a disease of both adults and children. It usually occurs in children younger than age 4 years; when present in older children, it is likely to be due to an atypical mycobacterium.[4,11,12] Blacks and Asian/Pacific Islanders are more likely than whites to have TB lymphadenitis.[13] Lymph nodes also constitute the most common extrapulmonary site of TB in HIV-positive patients.[3]

**Clinical Presentation.** Tuberculous lymphadenitis presents as an enlarging, painless mass in a lymphatic area. Occasionally, there may be fluctuance and even formation of an abscess or sinus. Systemic complaints are infrequent.[10,14] Differential diagnoses include lymphoma, metastatic carcinoma, fungal diseases, cat-scratch disease, sarcoidosis, toxoplasmosis, and bacterial adenitis as well as reactive adenitis.[11,14]

**Diagnostic Tests.** Tuberculosis skin testing has been reported to be positive in 77% to 100% of patients.[11] Tissue examination is necessary for definitive diagnosis. Excisional biopsy is the preferred route, since fine-needle aspiration detects only 46% to 87% of granulomas and 17% to 50% of acid-fast bacilli (AFB).[15] Incision and drainage is to be avoided since permanent sinuses and prolonged drainage may result.[11]

Although some authors have contended that TB lymphadenitis is

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a local infection that can be cured with excision alone, this is most likely true only of atypical mycobacterial adenitis; TB adenitis is usually an early manifestation of the initial systemic infection.[11,14]

### Pleural

**Epidemiology.** The second most common site of extrapulmonary TB is the pleural lining.[4] Most cases of pleural TB arise within a few months after the primary TB infection, but it can occur years later with reactivation of the disease. When it does, the onset of symptoms tends to be more indolent. American Indian/Alaska natives are most likely among all racial groups to have pleural TB.[13] Pleural TB is thought to arise from the rupture of a subpleural focus in the lung into the pleural space.[16]

**Clinical Presentation.** Symptoms may include cough, fever, dyspnea, chest pain, and weight loss.[16,17] In more than half the patients the onset of symptoms is abrupt, often mimicking acute pneumonia. In those patients with a more insidious onset (often older patients), the differential diagnosis includes congestive heart failure, cancer, pneumonia, and pulmonary embolism.[16]

**Diagnostic Tests.** The TB skin test results, although occasionally initially negative, were found to be positive in all nonanergic patients with TB pleurisy in two reported case series.[16,17] The effusion in pleural TB tends to be unilateral, occurring on the right side about twice as often as on the left side. The fluid is a serous exudate, with protein concentrations rarely less than 30 g/L and frequently above 50 g/L. The white blood cell count is usually between $1\times10^9$/L and $6\times10^9$/L, with a lymphocytosis. However, early in the course of the disease, there may be a transient predominance of polymorphonuclear cells.

*The majority of cases of extrapulmonary TB are due to lymphohematogenous dissemination during the primary pulmonary TB infection*

The glucose level is usually low, often less than 1.7 mmol/L (30 mg/dL). However, in pleural effusions secondary to a reactivation of disease, the glucose level may be greater than 3.3 mmol/L (60 mg/dL).[16,17] Pleural fluid smears are rarely positive for AFB, and most case series report positive pleural fluid cultures in fewer than 40% of patients.[16,17] Pleural biopsy is usually needed for diagnosis. Granulomas on biopsy, while not pathognomonic for TB, are usually sufficient for presumptive diagnosis while the results of the culture of the biopsy specimen are awaited. Granulomas or cultures from biopsy specimens have been reported positive in TB. Care should be taken to split 50% to 88% of pleural biopsy specimens into appropriate containers for the histopathology and bacteriology laboratories.[16,17]

**Table 1. Tuberculosis Cases by Predominant Site of Disease, 1989[4]**

| Site | No. (%) of Cases |
|---|---|
| Pulmonary | 19 124 (81.5) |
| Extrapulmonary | 4350 (18.5) |
| Lymphatic | 1336 (30.7) |
| Pleural | 1082 (24.9) |
| Bone and/or joint | 427 (9.8) |
| Genitourinary | 383 (8.8) |
| Miliary | 372 (8.6) |
| Meningeal | 224 (5.1) |
| Peritoneal | 177 (4.1) |
| Other | 349 (8.0) |

### Genitourinary

**Epidemiology.** Tuberculosis of the genitourinary tract accounts for about 9% of all cases of extrapulmonary TB in the United States.[4] While some patients have only disease of the urinary tract or the genital tract, both sites are often infected together. Urinary TB is reported in all ages, although it is most commonly found in patients between the ages of 20 and 40 years, and in those older than age 65 years.[4,10,18,19] American Indian/Alaska natives are more likely to have urinary TB than other racial groups.[13] Tuberculosis of the genital tract alone is rare in the United States. While a significant cause of female infertility in countries with high rates of TB, genital TB accounts for less than 1% of the infertility cases in the United States.[20]

**Clinical Presentation.** The common presenting symptoms in urinary TB are related to bladder inflammation and include dysuria, urinary frequency, and hematuria. These symptoms are nonspecific and may be absent in 20% to 30% of patients, even in those with advanced cavitary renal TB.[10,19] Other clinical signs and symptoms include flank pain, renal colic (from passing blood clots), and, more rarely, hypertension and renal insufficiency.[18-21] The classic finding of sterile pyuria is neither sensitive nor specific for urinary TB. In one series, half the female patients with renal TB also had other pathogens cultured from the urine.[18]

In male genital TB a painless mass may be present in the epididymis or scrotum, and vague constitutional symptoms, such as fever, may be present.[10] Genital TB in women begins in the fallopian tubes and spreads to the ovaries and endometrium.[22,23] The symptoms are nonspecific and may include infertility, pelvic pain, menstrual disturbances, fatigue, and, rarely, vaginal discharge.[22]


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**Diagnostic Tests.** Diagnosis of urinary TB is made with skin test, intravenous pyelography, and culture of the urine. The skin test results have been reported to be positive in 86% to 88% of cases of renal TB.[10,19] Nonspecific abnormalities are commonly found on the intravenous pyelogram. These include calyceal dilatation and parenchymal calcifications.[10,18,19] The urinalysis commonly reveals pyuria, hematuria, and albuminuria, but the results may be normal. Early morning urine samples cultured for mycobacterium are necessary to definitively diagnose urinary TB, although the cultures are reported to be positive in only 76% to 78% of cases.[10,18] Due to the sporadic nature of urinary shedding of the bacillus, a single negative culture does not rule out the disease. Several cultures should be done. Often, cultures from other sites, such as sputum, are positive.

Definite diagnosis of genital TB is made with a tissue biopsy. Granulomas may be found in the endometrial lining, and cultures of the endometrium are often positive. When the endometrium is not involved, however, hysterosalpingography or laparoscopy may show suspicious lesions.[22,23] In advanced or resistant cases of genital TB, surgery may be needed to relieve symptoms and remove infected organs.[20]

### Bone and Joint

**Epidemiology.** The bony structures in the body are the fourth most common site for extrapulmonary TB.[4] Often a disease of elderly persons, the onset is often insidious. It is not unusual for years to pass from the onset of symptoms until the diagnosis of TB is made.[24,25] Women are slightly more likely than men to get bone and joint TB, and all races seem to be equally affected.[13]

**Clinical Presentation.** Patients frequently complain of general constitutional symptoms as well as symptoms from the bony or articular site. The spine is the most common bony site, and patients with spinal TB present mainly with back pain. Less commonly, draining sinus tracts, iliopsoas "cold" abscesses (that may present as flank or groin masses), or signs of neurologic impingement, such as weakness or paralysis, may be present.[10,25,26] In the spine the differential diagnosis includes osteoporosis, malignancy, and infection.[27] The large weight-bearing joints are the next most frequently involved sites. Involvement is usually monarticular, and patients present with insidious pain and swelling.[28] Joint TB must be distinguished from osteoarthritis, rheumatoid arthritis, and infections of the joint space.

**Diagnostic Tests.** Positive TB skin test results are found in 90% to 100% of nonanergic patients.[10,26,28] Chest roentgenograms show abnormalities in up to 50% of patients.[2] Plain roentgenograms are helpful in making the diagnosis. There may be radiolucency of vertebral bodies in the spine, with joint-space narrowing and subsequent vertebral collapse.[27,28] The lower thoracic and lumbar vertebrae are most likely to be involved.[25] In other joints, there is also joint-space narrowing, with metaphyseal and subchondral erosions and cysts.[28] Computed tomography is useful in finding adjacent soft-tissue involvement, such as psoas or paraspinous abscesses. Any incremental value of magnetic resonance imaging over computed tomography remains to be determined.[26,29]

Diagnosis is based on bone or synovial biopsy specimens, which show granulomatous changes and yield positive cultures. The AFB smears of these tissues are unlikely to be positive due to the small number of bacilli present.[25] Surgical treatment of spinal disease, once a mainstay of treatment, is now only occasionally needed to prevent neurologic complications.[25,26]

### Miliary

**Epidemiology.** Nationwide, miliary or disseminated TB is found in about 9% of cases of extrapulmonary TB,[4] but in some series it accounts for up to 20% of cases.[9] Miliary TB, while statistically more prevalent among older people, can occur in any immunocompromised individual following the initial pulmonary infection. Blacks and American Indians/Alaska natives are more likely to have miliary TB than are whites.[13] The term *miliary* refers to the presence on chest roentgenography of diffuse, fine, nodular shadows roughly the size of a millet seed. However, these classic miliary findings may be absent in half of the patients.[10]

**Clinical Presentation.** In older individuals, symptoms are vague and may persist for several months. Fever is common, and miliary TB should be considered in the differential diagnosis of a fever of unknown origin.[24] Fatigue, weight loss, headaches, abdominal pain, change in mental status, lymphadenopathy, splenomegaly, hepatomegaly, and neurologic abnormalities have all been described in disseminated TB. Meningeal involvement is common, and a lumbar puncture should be performed when miliary TB is suspected.[10] Miliary TB is more likely in patients with some underlying immunologic impairment, such as pregnancy, malignancy, alcoholism, and HIV infection.[2]

**Diagnostic Tests.** The TB skin test is less helpful in diagnosing miliary TB than with other forms of extrapulmonary TB, and the results may be negative in 20% to 45% of patients.[2,10] Often, immune function is so compromised by the disseminated disease that anergy is present. Mycobacteria may be cultured from many sites, including the sputum, gastric aspirate, cerebrospinal fluid (CSF), bone marrow, liver biopsy specimen, and urine, but cultures are not helpful in making a timely diagno-


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sis.[2,10] Liver biopsy specimens have been reported to contain granulomas in 88% of cases, and the biopsy may be the most rapid test for diagnosing disseminated TB.[10] Patients with HIV have been reported to have positive blood cultures in 26% to 42% of cases.[3] Mortality is higher than for other forms of extrapulmonary TB, with some case series reporting mortality rates of 25% to 50%.[2,10]

### Meningeal

**Epidemiology.** Tuberculosis of the meninges, while accounting for only a small percentage of the cases of extrapulmonary TB,[2,4,10] has generated a great deal of interest in trying to find a rapid diagnostic test. Early treatment offers excellent chances for full recovery, but delay of treatment is associated with high mortality and morbidity.[30,31]

Patients with HIV are at higher risk for TB meningitis, but infection with HIV does not appear to change the clinical presentation or outcome.[32] Among non-HIV–infected persons, children and the elderly are the most commonly affected age groups. Tuberculous meningitis is more commonly found in Hispanics and American Indians and Alaska natives than in other racial groups.[13]

**Clinical Presentation.** The symptoms of TB meningitis evolve over days or weeks. Early symptoms may include malaise, low-grade fever, irritability, and intermittent headaches. Later, more specific neurologic symptoms occur. Fever, headache, and altered mentation are the most common presenting symptoms. Presenting signs may include elevated temperature and meningeal signs, such as a stiff neck and altered mentation.[32-34] Cranial nerve palsies, while found in fewer than one fourth of patients, are more specific for TB meningitis than for other causes of meningitis.[2,34] Hyponatremia has also been noted in patients with TB meningitis, and is probably due to inappropriate antidiuretic hormone secretion.[9]

**Diagnostic Tests.** The TB skin test results have been reported to be negative in more than half the cases, and, therefore, the test is of limited diagnostic value.[32,34,35] On examination, the CSF is nonspecific. The protein level tends to be elevated, the glucose level is low, and the white blood cell count is elevated, with a lymphocytosis. However, the ranges of values found have been quite wide.[32-35] Adenosine deaminase, an enzyme produced by T lymphocytes, is elevated in 60% to 100% of patients with TB meningitis, and may prove to be helpful in diagnosis. Unfortunately, it has also been found to be elevated in 16% of patients with other forms of meningitis.[31]

*About 90% of the cases of drug-resistant TB have occurred in HIV-infected individuals*

Direct examination of the CSF for AFB has been disappointing. In only 10% to 40% of cases are bacilli seen on a smear of the CSF.[31,32] However, this may increase to as high as 87% if three separate specimens of CSF are examined.[31] Other rapid tests for diagnosis are under investigation and include detection of mycobacterial antigen in CSF and biochemical identification of mycobacterial products,[31] but none of these tests is in common use.[35]

The CSF cultures are positive more often than the AFB smears, but the long growth time needed makes them impractical for therapeutic decisions.[31] Computed tomographic scans are often abnormal (up to 70% of patients in case series[32,34]), but the abnormalities are nonspecific. Ventricular dilatation is the most common finding, with focal abnormalities and meningeal enhancement seen less commonly.[32,34] Mortality may be as high as 35%, and is inversely related to the rapidity with which the diagnosis is made and treatment started.[31,33] Of all forms of extrapulmonary TB, meningeal is the most rapidly fatal.

### Gastrointestinal and Peritoneal

**Epidemiology.** Abdominal TB occurs in about 4% of cases of extrapulmonary TB.[2] Peritoneal disease occurs most often, with the ileocecal region being the most common site in the gastrointestinal tract.[36,37] Peritoneal TB is found more commonly among blacks and American Indians/Alaska natives.[13]

**Clinical Presentation.** Symptoms depend somewhat on the site of disease, but fever, fatigue, weight loss, and abdominal pain are uniformly mentioned in case series.[37-41] The abdominal pain is usually vague, but because of the preponderance of disease in the ileocecal region, it is often located in the right lower quadrant and periumbilical regions.[38] Both diarrhea and constipation occur with abdominal TB.[40] Ascites is commonly found with peritoneal TB, but the examination results in gastrointestinal TB are vague. Fever and abdominal tenderness are often present, and occasionally an abdominal mass is noted.[36,37] Symptoms may be present for weeks to years before the diagnosis is made.[38,41] Abdominal TB is most common in the fourth decade of life, and the differential diagnosis includes Crohn's disease, ulcerative colitis, carcinoma, diverticulitis, lymphoma, and appendicitis.[38]

**Diagnostic Tests.** The TB skin test has wide variability in patients with abdominal TB. Positive test results have been reported in as few as 14% of patients[42] to as many as 100% of patients.[40,43] A barium enema or up-


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per gastrointestinal series may be helpful in making the diagnosis, although the abnormalities seen are nonspecific. Findings include a "pipestem colon," a persistently narrowed ileum ("string sign"), filling defects, hyperirritability, narrowing, and irregularities.[7,38] The ascitic fluid, when present, tends to be a lymphocytic exudate. It is very unusual to see AFB on smears of fluid, and cultures of fluid are positive for the mycobacterium from 0% to 83% of the time.[40,42]

Diagnosis is usually made with biopsies of the peritoneum or gastrointestinal tract. Initially performed with open laparotomy, laparoscopy and endoscopy are being used more often.[37,40] Blind peritoneal biopsies are discouraged due to the risk of complications.[37] Complications, including small-bowel obstruction, fistulas, and perforations, may require surgery.[39,41]

### Other Sites

Tuberculosis has been reported in other sites as well. Cutaneous TB, which may occur from disseminated hematogenous spread as well as from direct inoculation, presents with a variety of clinical manifestations, including chancres, "warts," ulcers, and lupus vulgaris.[44] Cardiac and pericardial TB may occur,[45,46] as well as scleritis,[47] mastoiditis,[48] thyroiditis,[49] and even TB of the tongue.[50] There are reported cases of congenital TB acquired transplacentally from an infected mother.[51] These types of TB are quite rare, even in countries with high rates of TB, and when seen in the United States are unusual, isolated occurrences.

## TREATMENT

Treatment for TB has changed dramatically during the last 20 years, since the introduction of rifampin began the era of short-course therapy. The necessity of using multiple drugs to avoid selecting for resistant organisms is well accepted.[52] There have been few evaluations of the use of short-course therapy (6 or 9 months) in extrapulmonary TB, although its use is well accepted for pulmonary TB.

**Table 2. First-Line Tuberculosis Drugs***

| Drug | Daily Dosage, mg/kg | | Maximum Daily Dose |
|---|---|---|---|
| | Children | Adults | |
| Isoniazid (by mouth or intramuscularly) | 10-20 | 5 | 300 mg |
| Rifampin (by mouth) | 10-20 | 10 | 600 mg |
| Pyrazinamide (by mouth) | 15-30 | 15-30 | 2 g |
| Streptomycin (intramuscularly) | 20-40 | 15 | 1 g |
| Ethambutol (by mouth)† | 15-25 | 15-25 | 2.5 g |

**Detailed recommendations from the Centers for Disease Control for first- and second-line drugs can be found in reference 56.*

*†Not recommended for children younger than age 13 years.*

A 9-year study of 350 patients with extrapulmonary TB treated for 9 months with isoniazid and rifampin reported a 95% success rate,[53] and a 6-month trial of the same drugs to treat pleural TB achieved a 99% success rate.[54] The consensus statement from the American College of Chest Surgeons supports the use of short-course therapy in extrapulmonary TB, although the surgeons noted that it has not been studied in large-scale, prospective, controlled trials.[55,56]

The HIV epidemic has necessitated a reexamination of the appropriate length of treatment in immunocompromised individuals. Patients with HIV and extrapulmonary TB tend to have lower CD4+ cell counts and, therefore, more immunosuppression than HIV-infected patients with pulmonary TB alone.[57]

Initial recommendations for treatment of all patients with extrapulmonary TB include a regimen of isoniazid, rifampin, and either ethambutol or pyrazinamide (**Table 2**). The last two drugs are usually given only during the first 2 months of therapy. Four drugs are usually given in the case of meningeal or miliary disease or if isoniazid resistance is suspected.[3,56,58-60] In nonimmunocompromised patients, therapy is continued for a total of 6 to 9 months,[3,53,56] while in HIV-infected patients, therapy should continue for 9 to 12 months or for 6 months after cultures are negative, whichever is longer.[3,57]

Second-line drugs may be needed when drug resistance is present. About 90% of the cases of drug-resistant TB have occurred in HIV-infected individuals.[61] In addition, in the last several years, reports have surfaced of multidrug-resistant strains of TB in the United States.[62] Second-line drugs are usually more toxic and include ethionamide (15 to 30 mg/kg up to 1 g per day by mouth), para-aminosalicylic acid (150 mg/kg up to 12 g per day by mouth), capreomycin (15 to 30 mg/kg up to 1 g per day intramuscularly), and cycloserine (10 to 20 mg/kg up to 1 g per day by mouth).[55,56] The quinolones, especially ciprofloxacin and ofloxacin, also have antimycobacterial activity, although their long-term usefulness against TB has yet to be determined.[52] If isoniazid or rifampin is not used, then therapy should continue for a minimum of 18 months, or 12 months after cultures are negative.[3] Their use should be guided by sensitivity results. The actual choice of TB therapy depends on severity of disease, other underlying health problems, and expected compliance with the drug regimen.

The use of steroids in extrapulmonary TB is controversial. A recent randomized trial of systemic steroid use in pleural TB found more rapid relief of symptoms and reso-


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lution of effusion in the prednisolone-treated group.[63] In cases of severe miliary disease, adult respiratory distress syndrome may develop and ventilatory support and steroid treatment may be needed.[9,64] While the benefit is still uncertain, steroid therapy is often used to treat meningeal TB.[32-34]

## COMMENT

Following initial declines after the advent of effective TB treatment, the number of cases of extrapulmonary TB has persisted relatively unchanged for the last 20 years. While the incidence of extrapulmonary TB has declined slightly (as the United States population has grown), the proportion of extrapulmonary TB among all cases of TB has doubled from 8% to 18%.[4,13] The predilection of HIV-infected individuals for this disease will result in younger persons contracting extrapulmonary TB as well as a probable increase in the number of cases. Because the signs and symptoms of extrapulmonary TB may be nonspecific and insidious, a high index of suspicion is necessary to consider extrapulmonary TB in the differential diagnosis.

While each site will determine the specifics of diagnosis, some generalizations can be made. If the results are positive, the TB skin test can be helpful, but if the results are negative, the test does not exclude the presence of TB, especially in immunocompromised patients. Chest roentgenography should be performed in all patients suspected of having extrapulmonary TB, since abnormalities suggestive of old or current disease are frequently present. Whenever possible, body fluids or tissue should be cultured for TB. While the diagnosis may be made from microscopic examination of tissue, a positive culture will eventually help guide treatment.

While extrapulmonary TB is often not diagnosed or treated for years, in cases of life-threatening meningitis or miliary disease, rapid initiation of treatment can be life saving. Extrapulmonary TB will remain a persistent problem in American medicine. A high index of suspicion, combined with diligence in investigation, will be needed to diagnose and treat extrapulmonary TB in a timely and health-preserving manner.

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