

Tuberculous pleural effusion

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INTRODUCTION

Tuberculous pleural effusion is the second most common form of extrapulmonary tuberculosis (TB) (after lymphatic involvement) and is the most common cause of pleural effusion in areas where TB is endemic [1-5]. Tuberculous pleural effusion is synonymous with the term tuberculous pleurisy.

Issues related to the evaluation and management of tuberculous pleural effusions will be reviewed here. Issues related to pulmonary TB are discussed separately. (See "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults without HIV infection" and "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults with HIV infection: Initiation of therapy".)

TERMINOLOGY

Tuberculosis terminology is inconsistent in the literature [6]. Relevant terms are defined in the table (table 1).

PATHOGENESIS

Tuberculous pleural effusions can occur in association with reactivation disease or primary tuberculosis [4,7-10]. In adults, most often they occur due to reactivation disease [8,9]; in children, most often they occur in the setting of primary disease [10].

Development of tuberculous pleural effusion may occur as a result of delayed hypersensitivity reaction to mycobacteria or mycobacterial antigens in the pleural space in sensitized individuals [11] or by rupture of a subpleural focus of pulmonary disease into the pleural space [12].

In patients without apparent parenchymal involvement, pleural disease may develop via hematogenous spread following primary infection.

Tuberculous empyema can develop via extension of infection from thoracic lymph nodes or a subdiaphragmatic focus, via hematogenous spread, or in the setting of pneumothorax.

CLINICAL MANIFESTATIONS

Signs and symptoms

— Patients with tuberculous pleural effusion usually have an acute febrile illness with nonproductive cough (94 percent) and pleuritic chest pain (78 percent) [13]. Night sweats, chills, weakness, dyspnea, and weight loss can also occur. The peripheral white blood cell count is typically normal [13].

Tuberculous pleural effusion can progress to tuberculous empyema, characterized by purulent fluid containing numerous organisms. Tuberculous empyema is often associated with a thickened, scarred, and calcified pleura (image 1) [14,15].

Patients with human immunodeficiency virus (HIV) infection are at increased risk for progression from tuberculosis (TB) infection to active TB disease, and pleural involvement is common in the presence of HIV coinfection [16-18]. Clinical manifestations of tuberculous pleural effusion in the setting of HIV infection include fever (85 percent), cough (77 percent), chest pain (36 percent), dyspnea (23 percent), and weight loss >2 kg (74 percent) [19-21]. Additional signs and symptoms such as night sweats, diarrhea, hepatosplenomegaly, and lymphadenopathy are also more common in patients with HIV infection.

Radiographic findings

— Tuberculous pleural effusions are usually unilateral, small to moderate in size, and self-limited [7]. In patients without HIV infection, tuberculous pleural effusions occur slightly more frequently on the right side than the left (55 versus 45 percent) [16,22] and occupy less than two-thirds of the hemithorax in 82 percent of cases [22]. In patients with HIV infection, tuberculous pleural effusions are equally distributed on the left and right; a miliary pattern is observed in 7 to 10 percent of cases. Adenopathy occurs in 5 to 18 percent of cases [23].

- **Chest radiography** – Chest radiography demonstrates parenchymal disease in association with pleural effusion in up to 50 percent of patients without HIV infection [4] and 73 percent of patients with HIV infection [20,21]. Among patients without HIV infection, the upper lobe is involved in approximately 75 percent of cases (suggestive of reactivation TB), and the lower lobe is involved in approximately 25 percent of cases (suggesting primary disease). Among patients with HIV infection, in contrast, parenchymal disease occurs most often in the lower lobe (75 percent) [23]. The pleural effusion virtually always occurs on the same side as the parenchymal infiltrate [13].
- **Computed tomography (CT)** – CT is more sensitive than chest radiography; it demonstrates parenchymal disease in over 80 percent of cases, supporting the theory of spread to the pleura from a subpleural focus (image 2) [24]. (See 'Pathogenesis' above.)
- **Ultrasonography** – Thoracic ultrasound is primarily a procedural tool for thoracentesis guidance [25]. The sonographic appearance of tuberculous pleural effusion ranges from anechoic free-flowing fluid with thin mobile fibrin strands to loculated pockets [26,27]. A complex, septated pattern has been described in approximately 47 percent of tuberculous effusions across multiple studies [28-30]. Pleural thickening (<1 cm) is present in up to 90 percent of cases, and pleural nodules are visible in approximately 20 percent [26].

Complications

Tuberculosis empyema

— TB empyema (pus in the pleural space) can develop as a complication of tuberculous pleuritis or pulmonary TB [15]. TB empyema is characterized by chronic mycobacterial infection of the pleural space [15]. In patients with long-standing TB empyema, the pleura is thickened and may calcify. In patients with TB empyema, the pleural effusion is neutrophilic predominant with high mycobacterial burden [15]. The diagnostic yield of acid-fast bacilli smear and culture is higher for TB empyema than for tuberculous pleural effusion without empyema [25]. Invasive surgery is often required to remove the focus of infection and prevention of fibrothorax [31,32].

Chylothorax and pseudochylothorax

— Tuberculous pleural effusion can cause chylothorax via lymphatic obstruction by enlarged lymph nodes [33]. In addition, tuberculous pleural effusion is the most common cause of pseudochylothorax (cholesterol effusion) worldwide. (See "Clinical presentation, diagnosis, and management of cholesterol pleural effusions".)

Residual pleural thickening

— Residual pleural thickening can occur in up to 50 percent of patients [21,34-38]. In one study, including 56 patients without HIV infection with tuberculous pleural effusion, residual pleural thickening following completion of medical therapy was more likely among those with initial pleural fluid analysis notable for relatively low pH, low glucose concentration, high lysozyme concentration, and high tumor necrosis factor-alpha concentration [39].

DIAGNOSIS

Clinical approach

— Diagnostic evaluation of suspected tuberculous pleural effusion requires a thorough assessment of clinical, radiographic, and pleural fluid characteristics.

- **Clinical suspicion** – The diagnosis of tuberculous pleural effusion should be suspected in patients with pleural effusion and relevant epidemiologic risk factors for tuberculosis (TB) infection (these include current or prior history of TB infection, known or possible TB exposure, and/or past or present residence in or travel to an area where TB is endemic). (See "Epidemiology of tuberculosis".)
- **Establishing a diagnosis** – The diagnosis of tuberculous pleural effusion may be definitively established via identification of *Mycobacterium tuberculosis* in pleural fluid or tissue (via mycobacterial culture) or a pleural biopsy specimen (via demonstration of caseating granuloma with acid-fast bacilli [AFB]) (algorithm 1)[1,7].

However, establishing a definitive diagnosis is challenging; it is difficult to isolate mycobacteria in the setting of low bacillary burden.

- **Presumptive diagnosis** – It is reasonable to make a presumptive diagnosis of tuberculous pleural effusion without pathologic confirmation in the following scenarios:
 - In a patient with an established diagnosis of pulmonary TB, in the absence of signs or symptoms that raise suspicion for an alternative cause of pleural effusion (such as malignancy) (see 'Differential diagnosis' below)
 - In the setting of high clinical suspicion for TB, pleural fluid analysis with lymphocytic-to-neutrophil ratio >0.75 and adenosine deaminase (ADA) >40 units/L, or by demonstration of one or more caseating granulomas on pleural biopsy [1,2,40,41] (see 'Pleural fluid analysis' below and 'Pleural biopsy' below)

The initial evaluation of patients with suspected tuberculous pleural effusion should include diagnostic evaluation for pulmonary TB, beginning with sputum collection for smear/culture for AFB and for nucleic acid amplification (NAA) testing. (See "Diagnosis of pulmonary tuberculosis disease in adults".)

Diagnostic thoracentesis is warranted in the following circumstances (see 'Pleural fluid analysis' below):

- Suspected tuberculous pleural effusion in the absence of an established diagnosis of pulmonary TB (via sputum or other studies)
- Diagnosis of pulmonary TB established (via sputum or other studies) but additional etiology for pleural effusion (such as malignancy) suspected clinically

Pleural biopsy is warranted if the above circumstances persist and the pleural fluid ADA level is <40 units/L and/or pleural fluid evaluation is otherwise not diagnostic. Pleural biopsy also may be indicated if drug resistance is suspected, since the yield for mycobacterial culture of pleural tissue is higher than for pleural fluid alone, and

culture-based susceptibility testing is needed to inform a final treatment regimen.

Given the low microbiologic-confirmatory yield from pleural fluid alone and the length of time that may be required for growth in culture (up to eight weeks), pursuit of pleural biopsy early in the diagnostic evaluation may be warranted, especially in complex patients with broad differential diagnosis or suspected drug resistance. (See 'Pleural biopsy' below.)

Patients with tuberculous pleural effusion should undergo diagnostic testing for HIV infection. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

Pleural fluid analysis

— Indications for thoracentesis are described above. (See 'Clinical approach' above.)

- **Diagnostic evaluation** — Pleural fluid should be sent for the following studies: cell count, protein, glucose, pH, lactate dehydrogenase (LDH), AFB smear and culture, Gram stain and culture, and ADA level (if the effusion is lymphocyte predominant) [1]. NAA testing for *M. tuberculosis* in pleural fluid has not been approved by the US Food and Drug Administration (FDA) in the United States. Confirmation of the diagnosis of TB requires growth in culture, which may take up to eight weeks. (See "Diagnosis of pulmonary tuberculosis disease in adults".)
- **Characteristics of tuberculous pleural effusion** — Tuberculous pleural effusion is an exudative, lymphocyte-predominant pleural effusion, usually with the following characteristics [19,20,22,42]:
 - Color — Straw colored [43].
 - Protein concentration — >3 g/dL (30 g/L) [13,44].
 - LDH — Elevated in approximately 75 percent of cases, with levels commonly exceeding 500 international units/L [4,13,22,44].
 - pH — Less than 7.40 in most cases; pH <7.30 is observed in about 20 percent of cases.
 - Glucose — Usually between 60 and 100 mg/dL (3.3 and 5.6 mmol/L); glucose levels below 50 mg/dL (2.8 mmol/L) are observed in 7 to 20 percent of effusions, and extremely low glucose concentrations (<30 mg/dL [1.7 mmol/L]) can occur occasionally [13,44].
- **Pleural fluid cell count**
 - **Lymphocyte predominance in most cases** — The pleural fluid nucleated cell count is usually between 1000 and 6000 cells/mm³ [22]. It is lymphocyte predominant in approximately 90 percent of cases. Neutrophils typically predominate in the first few days following onset of pleural inflammation; lymphocytes predominate thereafter [43,45,46].
 - **Neutrophil predominance occurs less commonly** — Neutrophil predominance occurs in approximately 10 percent of cases [4,13,44]. This presentation is usually associated with higher levels of inflammatory markers (serum and pleural fluid), higher bacillary burden on AFB smear, and is more likely to have positive mycobacterial culture results. However, in such cases, there is a less robust granulomatous response on histology (compared with lymphocytic predominant tuberculous effusion) [47].
 - **Other cell count patterns**
 - **Eosinophils** — TB pleural effusion accounts for approximately 5 percent of eosinophilic pleural effusions [48,49].
 - **Mesothelial cells** — Rarely, the pleural fluid contains >5 percent mesothelial cells; the laboratory may report "many mesothelial cells" without providing a percentage.

There is no correlation between the CD4 cell count and pleural fluid cell count or composition [21,42].

- **Pleural fluid ADA level** — The pleural fluid ADA level may be useful to establish a diagnosis of tuberculous pleural effusion, even when AFB smear and culture are negative [1,2,5]. Elevated pleural fluid ADA levels can occur in other conditions besides TB infection, including malignancy. Some studies suggest that an ADA level >45 to 60 units/L is 100 percent sensitive and up to 97 percent specific for tuberculous pleural effusion [22,42,50-55].

The diagnostic performance of ADA level can be affected by the local prevalence of TB. In low-prevalence regions, its main advantage is in its negative predictive value. As an example, in one study from South London between 2009 to 2015, patients with lymphocytic predominant pleural effusion and pleural fluid ADA level <40 U/L were unlikely to have tuberculous pleural effusion (negative predictive value 98 percent) [56]. However, in high-prevalence regions, tuberculous pleural effusion cannot be excluded in the presence of lymphocytic predominant pleural effusion by any level of ADA in pleural fluid [57]. The diagnostic probability of tuberculous pleural effusion is very high in patients with pleural fluid ADA levels >70 U/L. However, if the ADA level is indeterminate (40 to 70 U/L), further interventions depend upon the pretest probability of TB [57]. Patients with risk factors for TB, a lymphocytic predominant pleural effusion, and a low ADA level (<40 U/L) should be considered for a pleural biopsy to assess for tubercular pleural effusion or an alternative cause.

HIV status can affect the diagnostic accuracy of pleural fluid ADA levels. Among patients with HIV infection, one study noted an ADA cutoff level of 60 units/L in patients with HIV infection and provided a sensitivity and specificity of 95 and 96 percent, respectively [42,58,59]. (See 'Differential diagnosis' below.)

Elevated pleural fluid ADA levels can occur in other conditions besides TB infection; these include bacterial empyema, mesothelioma, lung cancer, lymphoma, parapneumonic effusion, and hematologic malignancies. Most assays report only the total ADA level and do not distinguish between the two principal isoenzymes, ADA-1 and ADA-2. ADA-2 is increased in tuberculous effusions, while ADA-1 is increased in other conditions [60].

- **Pleural fluid AFB culture** – Pleural fluid AFB cultures are positive in fewer than 20 to 30 percent of patients without HIV infection [7]. Patients with HIV infection may present with a greater burden of organisms than patients without HIV infection; in patients with HIV infection with CD4 count less than 100 cells/mm³, AFB cultures are positive in approximately 50 percent of cases [61-63]. Tuberculous empyema fluid is grossly purulent and usually AFB smear and culture positive [1].
- **Role of NAA assays** – NAA assays approved by the FDA for use with sputum are not approved for use with pleural fluid in the United States. Some laboratories perform NAA testing of pleural fluid as a laboratory-validated, "off-label" application of the testing platform; in such cases, the test characteristics should be reviewed with the laboratory before a clinical sample is submitted.

NAA techniques for evaluation of tuberculous pleural effusion in patients without HIV infection appear to have high specificity but relatively low sensitivity [64,65]. In one meta-analysis including 18 studies, the sensitivity and specificity for the Xpert MTB/RIF assay (compared with culture) in pleural fluid were 46 and 99 percent, respectively [65]. In a meta-analysis including 74 studies comparing diagnostic accuracy of pleural fluid Xpert MTB/RIF and Xpert MTB/RIF Ultra assays, sensitivity was higher with Ultra than Xpert (68 versus 52 percent); specificity was high and similar (97 percent versus 99 percent, respectively) [66].

Among patients with HIV infection, it is reasonable to anticipate that the higher microbial burden in the pleural fluid is likely to be associated with a higher sensitivity of NAA assays (compared with patients without HIV infection); data are limited. (See "[Diagnosis of pulmonary tuberculosis disease in adults](#)".)

- **Other assays** – Other assays that may be useful for supporting or excluding a diagnosis of tuberculous pleural effusion include pleural fluid interferon-gamma concentration and pleural fluid lysozyme concentrations [5,52,55,67-71]. However, these tests have not been approved by the FDA for this purpose and they do not have a role in routine evaluation of suspected tuberculous pleural effusion.

Pleural biopsy

— Indications for pleural biopsy are described above. (See '[Clinical approach](#)' above.)

Pleural biopsy should be sent for AFB smear and culture as well as histopathologic evaluation. Positive culture allows organism identification and drug susceptibility testing. Histopathology may demonstrate granulomas and/or AFB. The presence of caseating (necrotizing) granulomas on histologic examination is virtually diagnostic of tuberculous pleural effusion. Noncaseating granulomas may also be observed; occasionally, these can be seen in other disorders as well. (See '[Differential diagnosis](#)' below.)

In patients without HIV infection, the diagnostic yield of pleural biopsy tissue is 60 to 95 percent [7,43,72,73]. Culture of pleural biopsy material is positive in 40 to 80 percent of cases, and histology demonstrates granulomas in 50 to 97 percent of cases [7]. In patients with HIV infection, the diagnostic yield of pleural biopsy tissue is 44 to 69 percent [20,21]. Granulomas are observed less frequently than in patients without HIV infection but may be seen [20,21,63].

Pleural tissue can be obtained via thoracoscopy, ultrasound-guided pleural biopsy, or closed percutaneous needle biopsy. In a randomized trial including 196 adults with AFB-negative exudative pleural effusion, the diagnostic yield of ultrasound-guided pleural biopsy and thoracoscopic pleural biopsy was similar (83 versus 86 percent, respectively) [74]. The sensitivities of these techniques were comparable when pleural fluid ADA and lymphocyte to neutrophil ratios were considered with the needle biopsy analysis; needle biopsy is generally preferred in areas where tuberculous pleuritis is common [75,76]. (See "[Diagnostic evaluation of the hemodynamically stable adult with a pleural effusion](#)", section on 'Pleural biopsy'.)

Additional evaluation

— In addition to pleural evaluation, routine diagnostic evaluation for pulmonary TB should also be pursued; this is discussed in detail separately. (See "[Diagnosis of pulmonary tuberculosis disease in adults](#)".)

Sputum culture is positive in 20 to 50 percent of patients without HIV infection with pleural effusion; positive sputum culture is more likely in the setting of concomitant parenchymal disease [4,12,13,44,77]. In one report of 70 patients without HIV infection with tuberculous pleural effusions, sputum culture was positive in 89 percent of patients with parenchymal changes but only 11 percent of patients without parenchymal changes [77]. The yields for induced sputum and pleural biopsy were 52 and 62 percent, respectively [77]. Among patients with HIV infection, the sputum smear or culture is positive in one-third to one-half of cases [20,21,63] and may even be positive when the chest radiograph is negative [77].

Tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) cannot distinguish between TB infection and TB disease [78]. Older series reported almost uniformly positive TST results in patients with tuberculous pleural effusions; subsequent reports have observed false-negative tests in 7 to 30 percent of patients [4,13]. Many patients without HIV infection with tuberculous pleural effusion and an initially negative TST have a positive TST if retested two months later. One possible explanation for the initial negative TST is suppression of sensitized T cells in the peripheral circulation and skin by circulating adherent mononuclear cells (chiefly monocytes, not classic CD8 suppressor cells); these monocytes are known to suppress antigen-induced lymphocyte blastogenesis and the production of interleukin 2. Among patients with HIV infection with tuberculous pleural effusion, the TST is positive in 20 to 64 percent of cases [19-21,63].

The use of IGRAs on pleural fluid for the diagnosis of tuberculous pleural effusion lacks sufficient sensitivity and specificity for diagnostic use. One meta-analysis evaluating the diagnostic performance of blood and pleural fluid–based IGRAs in tuberculous pleural effusion noted pooled sensitivity and specificity for blood assays of 77 percent (95% CI 0.71-0.83) and 71 percent (95% CI 0.65-0.76), respectively; the pooled sensitivity and specificity for the pleural fluid assays were 72 percent (95% CI 0.55-0.84) and 78 percent (95% CI 0.65-0.87), respectively [79]. A study from China showed improved diagnostic accuracy with use of a diagnostic model based on the combination of TB-specific antigen and IFN-gamma, with AUC of 0.983 in differentiating tuberculous pleural effusion from nontuberculous pleural effusion (95 percent sensitivity and specificity) [80]. (See "[Use of interferon-gamma release assays for diagnosis of tuberculosis infection \(tuberculosis screening\) in adults](#)".)

The sensitivity of the Xpert MTB/RIF Ultra assay for diagnosis of pleural TB is poor. In a cohort study including 317 patients with suspected pleural TB, the sensitivity of Xpert MTB/RIF Ultra was poor (44 percent); however, the assay performance was superior to culture (26 percent) and smear (1.4 percent) [81]. The sensitivity of the

assay was driven by individuals who were smear positive; such is clearly driven by organism burden when compared with those who were smear-negative individuals.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for tuberculous pleural effusion includes other causes of exudative pleural effusion (table 2) [82]. Many may be suspected clinically, and some can be confirmed by pleural fluid analysis or biopsy (table 3). In addition, alternative causes of pleural effusions may coexist in patients with pulmonary tuberculosis.

The following are the common causes of nontuberculous pleural effusions:

- Malignant pleural effusion – The diagnosis of malignant pleural effusion may be established via pleural fluid cytology and/or pleural biopsy. (See "Pleural fluid analysis in adults with a pleural effusion".)
- Congestive heart failure – The diagnosis of congestive heart failure may be established via echocardiography and other studies. (See "Heart failure: Clinical manifestations and diagnosis in adults".)
- Parapneumonic effusion or empyema – Parapneumonic effusion or empyema may be caused by bacterial infection; the diagnosis may be established by bacterial culture. (See "Epidemiology, clinical presentation, and diagnostic evaluation of parapneumonic effusion and empyema in adults".)
- Sarcoidosis-associated pleural effusion (SAPE) – Pleural fluid analysis in patients with SAPE can be indistinguishable from tuberculous pleural effusion. Tuberculous pleural effusion can be differentiated from SAPE by clinical features and microbiologic data [83]. (See "Clinical manifestations and diagnosis of sarcoidosis".)

The differential diagnosis of caseating (necrotizing) granulomas includes fungal infection such as histoplasmosis and cryptococcus. (See "Diagnosis and treatment of pulmonary histoplasmosis" and "*Cryptococcus neoformans*: Pulmonary and other infections outside the central nervous system".)

The differential diagnosis of noncaseating granulomas includes sarcoidosis, rheumatoid pleuritis, and berylliosis. (See "Clinical manifestations and diagnosis of sarcoidosis" and "Overview of pleuropulmonary diseases associated with rheumatoid arthritis" and "Chronic beryllium disease (berylliosis)".)

MANAGEMENT

Management of tuberculous pleural effusion consists of antituberculous therapy; pleural drainage is usually reserved for patients with severe symptoms.

Antituberculous therapy

— The approach to antituberculous therapy for treatment of tuberculous pleural effusion is the same as the approach to treatment of active pulmonary tuberculosis (TB); this is discussed in detail separately. (See "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults without HIV infection" and "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults with HIV infection: Initiation of therapy".)

In the absence of definitive diagnosis, presumptive antituberculous therapy is warranted for patients with epidemiologic risk factors for TB infection and supportive diagnostic studies in the absence of an alternative diagnosis. As an example, this includes patients with TB risk factors and/or a positive TST or interferon-gamma release assay, exudative pleural effusion with lymphocyte predominance, elevated pleural ADA level (>40 units/L), low pleural fluid glucose level, negative pleural fluid cytology, and supporting pathology on pleural biopsy. (See 'Pleural fluid analysis' above.)

In general, the expected clinical response for patients on appropriate antituberculous therapy is resolution of fever in two weeks and resolution of pleural effusion in six weeks; if these are not observed, further considerations include drug-resistant TB or alternative diagnosis.

No role for routine steroid use

— Data are insufficient to support routine adjunctive use of corticosteroids for management of tuberculous pleural effusions [2,84]. Some older studies suggest that administration of corticosteroids may shorten the duration of fever and time to fluid resorption [85,86]. However, no difference in mortality was observed in a randomized trial including more than 190 patients with HIV infection with tuberculous pleural effusion treated with or without a prednisolone taper (in conjunction with antituberculous therapy) [87]. In Cochrane analysis, the long-term impact of corticosteroid therapy in patients with tuberculous pleural effusion is uncertain [84].

Pleural drainage

— Therapeutic thoracentesis is reasonable if the effusion is causing dyspnea; otherwise, routine complete drainage of pleural fluid at the time of diagnosis does not appear to affect long-term outcomes [36]. This was demonstrated in a randomized trial including 61 patients with newly diagnosed tuberculous pleural effusion treated with antituberculous therapy with or without catheter drainage [34]. Drainage was associated with more rapid resolution of dyspnea (four versus eight days), although after the first week, there were no differences in symptoms between groups during the 24-week follow-up period. Pulmonary function and the degree of residual pleural thickening on chest radiography were the same in both groups at the conclusion of the trial.

Data are insufficient to support routine use of intrapleural fibrinolytic agents for management of loculated tuberculous effusion. Several studies have demonstrated lower incidence of residual pleural thickening [88-90] and higher lung volumes [90]; however, the role of these agents requires further study by using clinical outcomes. Issues

related to their use is discussed further separately. (See "Epidemiology, clinical presentation, and diagnostic evaluation of parapneumonic effusion and empyema in adults".)

Patients with tuberculous empyema may require decortication [91]. Issues related to management of empyema are discussed further separately. (See "Epidemiology, clinical presentation, and diagnostic evaluation of parapneumonic effusion and empyema in adults".)

FOLLOW-UP

With appropriate therapy, most patients defervesce within two weeks; in most cases, pleural fluid is resorbed within six weeks. However, some patients take up to two months to defervesce, and fluid resorption may take up to four months.

Among patients with HIV infection, a paradoxical worsening of signs and symptoms may be observed in the first months following initiation of antiretroviral therapy; this is known as the immune reconstitution inflammatory syndrome. (See "Overview of immune reconstitution inflammatory syndromes".)

SUMMARY AND RECOMMENDATIONS

- **Clinical manifestations** – Patients with tuberculous pleural effusion usually have an acute febrile illness with nonproductive cough and pleuritic chest pain. Night sweats, chills, weakness, dyspnea, and weight loss can also occur. Computed tomography is more sensitive than chest radiography; it demonstrates parenchymal disease in over 80 percent of cases. (See 'Clinical manifestations' above.)
- **Diagnosis** (see 'Clinical approach' above)

- **Clinical suspicion** – The diagnosis of tuberculous pleural effusion should be suspected in patients with pleural effusion and relevant epidemiologic risk factors for tuberculosis (TB) infection (these include prior history of TB infection, known or possible TB exposure, positive test for TB infection ([tuberculin skin test](#) or interferon-gamma release assay), and/or past or present residence in or travel to an area where TB is endemic).
- **Establishing a diagnosis** – The diagnosis of tuberculous pleural effusion may be definitively established via demonstration of *Mycobacterium tuberculosis* in pleural fluid or a pleural biopsy specimen ([algorithm 1](#)). In the setting of high clinical suspicion for TB, a presumptive diagnosis of tuberculous pleural effusion may be established in the setting of pleural fluid analysis with lymphocytic-to-neutrophil ratio >0.75 and adenosine deaminase (ADA) >40 units/L or by demonstration of one or more caseating granulomas on pleural biopsy.
- **Thoracentesis** – Indications for thoracentesis include:
 - Suspected tuberculous pleural effusion in the absence of an established diagnosis of pulmonary TB (via sputum or other studies)
 - Diagnosis of pulmonary TB established (via sputum or other studies) but additional etiology for pleural effusion (such as malignancy) suspected clinically

Pleural fluid should be sent for the following studies: cell count, protein, glucose, pH, lactate dehydrogenase, acid-fast bacilli (AFB) smear and culture, Gram stain and culture, and ADA level (if the effusion is lymphocyte predominant). Confirmation of the diagnosis of TB requires growth in culture, which may take up to eight weeks. (See 'Pleural fluid analysis' above.)

- **Indications for pleural biopsy** – Pleural biopsy is warranted if the pleural fluid ADA level is <40 units/L and/or pleural fluid evaluation is otherwise not diagnostic. Pleural biopsy also may be indicated if drug susceptibility data are needed and previous studies are not informative. Pleural biopsy should be sent for AFB smear and culture as well as histopathologic evaluation. Histopathology may demonstrate granulomas and/or AFB. The presence of caseating (necrotizing) granulomas on histologic examination is virtually diagnostic of tuberculous pleural effusion. (See 'Pleural biopsy' above.)
- **Treatment**
 - **Antituberculous therapy**
 - The approach to antituberculous therapy for treatment of tuberculous pleural effusion is the same as the approach to treatment of active pulmonary TB; this is discussed in detail separately. (See "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults without HIV infection" and "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults with HIV infection: Initiation of therapy".)
 - In the absence of definitive diagnosis, presumptive antituberculous therapy is warranted for patients with epidemiologic risk factors for TB infection and supportive diagnostic studies in the absence of an alternative diagnosis. (See 'Antituberculous therapy' above.)
 - **Pleural drainage** – Therapeutic thoracentesis is reasonable if the effusion is causing dyspnea; otherwise, routine complete drainage of pleural fluid at the time of diagnosis does not appear to affect long-term outcomes. (See 'Pleural drainage' above.)

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