Tuberculosis in Children and Adolescents

Description/Etiology

Tuberculosis (TB) is a bacterial infection caused by *Mycobacterium tuberculosis* (and in rare cases by *M. bovis* or *M. africonum*), which is spread by aerosolized droplets and invades tissue. A T cell–mediated immune response is initiated leading to inflammation. Calcium deposits, *cavitation* (i.e., cavities left by drained fluid), *caseation* (i.e., dry, porous lung tissue), and/or tissue death can result. TB usually affects the respiratory system, particularly the lungs (i.e., pulmonary TB), but can spread to the musculoskeletal, lymphatic, cardiovascular, neurological, gastrointestinal, or genitourinary systems (referred to as *extrapulmonary* TB); wide dissemination of TB throughout the body (i.e., *miliary* TB) is also possible. TB infection can remain dormant and asymptomatic (i.e., *latent* TB), or become infectious (i.e., *active* TB). TB is prevalent in many areas of the world, particularly sub-Saharan Africa. It is making a comeback in industrialized countries due to the rise in immunocompromised individuals (e.g., those with HIV infection/AIDS) who are more vulnerable to TB infection and due to emigration of people from developing countries in which TB is endemic (e.g., China, Ethiopia).

The natural history and clinical presentation of TB in children and adolescents (collectively called “youth”) differs from that of TB in adults. Children are usually infected with TB through household or community contact with infected adults. The risk of developing *active* TB is higher in infants, young children, and older adolescents, compared with youth aged 5–14 years. The interval between infection and the onset of the *active* form of TB can be several months to years. Activation of the *latent* form of TB to the *active* form is rare in children aged younger than 10 years. Most youth with TB have the *latent* form, and even those with abnormal X-ray findings are often asymptomatic. Children < 10 years of age with active TB tend to be less contagious than older patients because they usually have a reduced cough and minimal expulsion of bacilli. Further, young children, and particularly neonates, infants, and toddlers, are at much higher risk of developing severe disease, such as disseminated TB and tuberculosis meningitis.

Diagnosis of TB among youth is complicated by several factors, including the absence of symptoms or the presence of nonspecific symptoms and the difficulty in obtaining sputum samples. Diagnosis relies mainly on clinical presentation, tuberculin skin testing (TST), and chest X-rays. In some cases, culture and drug susceptibility results from the adult source case have to be relied on for diagnosis and proper treatment of TB in this population. Diagnosis of TB is particularly difficult in HIV-infected youth because of the similarity in the symptoms caused by both diseases and the fact that the TST is less sensitive in immunocompromised patients. Treatment of TB in youth is the same as in adults and involves long-term antibiotic treatment (e.g., 12 weeks to 9 months with isoniazid/rifapentine or isoniazid alone) and supportive care. Potential complications include multorgan involvement, particularly of the lymph nodes and/or the central nervous system (e.g., meningitis, vasculitis, hydrocephalus, and brain ischemia/infarction), and tuberculous pneumonia; however, with adherence to medical treatment, the prognosis is good. The bacillus Calmette-Guérin (BCG) vaccine is the only vaccination available against TB infection and is the most widely used vaccination in the world. In the United States, however, the BCG vaccine is not generally utilized because of low infection rates with *M. tuberculosis*, inconsistent efficacy, and risk for false-positive TST results.
Facts and Figures
Worldwide, there are at least 1 million cases of TB among children < 15 years of age each year; this age group represent 15–20% of TB cases in countries with high TB prevalence. In 2014, an estimated 140,000 children died of TB worldwide. In the U.S., children < 15 years of age accounted for 5% of the TB cases reported in 2013. Tuberculosis meningitis develops in 5–10% of children younger than 2 years old and in 1% of older children. Regions that contribute to the highest TB burden are South-East Asia (35%), Africa (30%), and Western Pacific areas (20%).

Risk Factors
Close or prolonged exposure to high-risk adults is the main risk factor for TB acquired by youth. High-risk adults include those who use intravenous drugs and/or corticosteroids; live in or were born in a region with a high prevalence of TB; are homeless or incarcerated; are immunocompromised (e.g., due to HIV infection/AIDS); have a history of alcohol and/or drug abuse; or reside in long-term care facilities. TB disproportionately affects individuals from disadvantaged populations, such as those who lack health care, are from low-income areas, are malnourished, and/or reside in crowded or unsanitary areas with inadequate ventilation. Outbreaks of TB among youth can occur wherever children and adolescents congregate.

Latent TB can become active TB in patients who have non-TB type infections (e.g., measles, varicella, pertussis). Patients receiving steroid or chemotherapy, or diagnosed with hematological malignancies, severe malnutrition, or poor cell-mediated immune response (e.g., due to HIV infection) that results in severe disease (e.g., AIDS) have an increased risk of developing active TB infection. Patients with certain types of human leukocyte antigen (HLA) genes have a predisposition to TB.

Signs and Symptoms/Clinical Presentation
Most youth with TB infection are asymptomatic. Infants are more likely to have signs and symptoms, which can include fever of unknown origin, cough, malaise, night sweats, low weight gain, loss of appetite, failure-to-thrive, pallor, weakness, chest pain, and multiorgan involvement. Signs and symptoms depends on the site infected (e.g., pulmonary, extrapulmonary).

Assessment

› Physical Findings of Particular Interest
  • Note decreased breath sounds and/or localized wheezing or crackling

› Laboratory Tests
  • Following TST, an induration of 5 mm or greater is generally interpreted as a positive test result and can reflect TB infection as early as 2–12 weeks after initial exposure. (Note: This test has poor sensitivity when used in HIV-infected children)
  • Sputum culture and smear are used to diagnose active TB. Scant sputum production in children can make samples difficult to obtain; bronchoscopy and early morning gastric washings can be necessary to obtain fluids
    – Bronchial secretions can be obtained in older children by using an aerosol solution of propylene glycol in 10% sodium chloride to stimulate coughing
  • Acid-fast staining of sputum or other tissue specimens using the Ziehl-Neelsen method reveals mycobacteria. Acid-fast staining does not differentiate M. tuberculosis from other acid-fast organisms (e.g., M. avium)
  • Nucleic acid amplification tests (e.g., polymerase chain reaction [PCR], loop-mediated isothermal amplification [LAMP]) can detect M. tuberculosis
  • Serum calcium and erythrocyte sedimentation rate (ESR) can be elevated
  • Pleural fluid analyses and staining might reveal elevated WBC, decreased glucose, and the presence of M. tuberculosis

› Other Diagnostic Tests/Studies
  • Chest X-rays reveal enlarged hilar lymph nodes, lung nodules (i.e., granuloma), lung tissue cavitation (particularly in the lung apices), or atelectasis. Lymph node calcification might be seen
    – Cavity lung lesions are highly infectious; lesions can contain 10 million to 1 billion bacilli; nodular lung lesions can contain 100–10,000 organisms
  • CT or MRI scans show granulomas and presence of lung damage
  • Contrast-enhanced sonography is used as an alternative to contrast-enhanced CT for patients with contraindications to contrast-enhanced CT and can show lesions suggestive of TB

Treatment Goals

› Promote Optimum Physiologic Status, Provide Supportive Care, and Reduce Risk of Complications
• Monitor vital signs, intake/output, respiratory and nutritional status, weight, sputum, and cough; provide a well-balanced diet and encourage adequate hydration
• Administer combination treatment of isoniazid, rifampin, pyrazinamide, and ethambutol, as prescribed by the treating clinician; crushed pills or suspension can be needed depending on the age of the patient; a consultation with a TB expert can be helpful if drug resistance is suspected
  – Monitor for medication side effects, including liver toxicity (e.g., from pyrazinamide, rifampin, or isoniazid), auditory nerve damage (e.g., from streptomycin), and/or color blindness (e.g., from ethambutol); report these and other serious side effects to the treating clinician
• Encourage complete bed rest for patients with severe TB infection; the need for bed rest varies with type and severity of disease

Prevent Further Transmission and Educate
• Follow facility protocols to maintain airborne infection isolation precautions and, if possible, to place the patient in a private room with negative airflow; follow facility infection control protocols to properly dispose of all materials that could be contaminated with secretions and apply airborne precautions to all visitors
• Assess anxiety level and coping ability of the patient and/or family members; educate and encourage discussion about TB pathophysiology, medications used to treat TB, and the need to maintain isolation precautions to limit the spread of infection
• Follow facility protocols for mandatory disease reporting to the local public health department so a contact investigation can be initiated to determine TB source and screen other contacts

Food for Thought
• Interferon gamma release assays (IGRAs) measure the host’s immune response to TB. Unlike TST, a blood sample is required, which can limit the use of this test in children
• Children < 6 years of age usually do not have a cough that is deep enough to produce sputum so gastric aspirates are usually obtained for analysis
• Several new vaccines are undergoing clinical trials. Vaccines being developed for use in infants include pre-exposure prime vaccines that could replace the current BCG vaccine and pre-exposure booster vaccines that would be given in addition to BCG. In addition, post-exposure vaccines that would be given during adolescence or adulthood are also being tested. Therapeutic vaccines for use in combination with chemotherapy are being investigated for the treatment of active TB (Weiner et al., 2014)

Red Flags
• Children < 4 years of age with untreated TB are at risk of developing tuberculous meningitis, which can result in death if not promptly diagnosed and treated
• Nasopharyngeal secretions and saliva are not acceptable samples for analysis
• The emergence of MDR-TB (TB infection that does not respond to standard anti-TB treatment) and XDR-TB (TB infection that does not respond to any anti-TB treatment) has raised concern among public health authorities
• Anti-TB medications must be taken correctly to reduce the risk of the development of drug resistance, which increases the cost and length of treatment (up to 18–24 months)

What Do I Need to Tell the Patient/Patient’s Family?
• Provide written information on TB to reinforce verbal education, including prevention strategies (e.g., proper hand hygiene, disposal of tissues), signs and symptoms of active TB, when to seek urgent medical attention, and follow-up screening of household members
• Inform parents that strict adherence to the medication regimen and follow-up laboratory/diagnostic testing are essential

Note
• Recent review of the literature has found no updated research evidence on this topic since previous publication on February 17, 2017
References


