

multi-lobar infiltrates and diffuse interstitial disease.^{5,35} Rapidly progressive disease, including meningitis or mycobacterial sepsis, is more likely among very young children or those who are immunocompromised, including in children with HIV.

The following describes the natural history of childhood TB, although children with HIV of all ages are more likely to have disease manifestations similar to those seen in very young children.^{12,36,37}

- **Aged <1 year:** Infants are at the highest risk for disease following primary infection with *M. tuberculosis*: as many as 50% of infants under 12 months of age might progress to active TB disease. Infants with TB are at high risk for extrapulmonary and disseminated disease, such as miliary TB, tuberculous meningitis (TBM), and extensive pneumonic infiltration.
- **Aged 1 to 4 years:** Compared to adults, young children have an elevated risk of disseminated forms of disease. However, this risk is lower than in infants under 1 year old. Children <5 years are at the greatest risk of complications resulting from airway compression because of their small, pliable airways and exuberant lymph node responses. Extrathoracic manifestations are also common (see below).
- **Aged 5 to 9 years:** Immunocompetent children in this age group have the lowest risk of progression to TB disease after primary infection. Still, depending on the average age at which primary infection occurs, TB among children in this age group may contribute substantially to the total case load of pediatric TB. Clinical manifestations in this age group vary; some patients present clinically with disease patterns more commonly seen in young children while others present with adult-type pulmonary disease, upper lobe infiltration, cavitation, and sputum production.
- **Aged >10 years:** Adult-type pulmonary disease is more common. Children in this age group are more likely to have positive results from acid-fast bacteria (AFB) sputum smear microscopy and should be considered potential infectious sources.³⁸

The reported proportion of children with TB who have extra-thoracic involvement has ranged widely, from approximately 10% to more than 50%, which is likely due to variations in diagnostic capacity and the timing of presentation; disseminated forms appear to be more common in children with HIV.^{33,34,36,37,39,40} Extra-thoracic disease manifestations include:

- **Peripheral lymphadenitis (usually cervical):** Features include a matted mass of lymph nodes >2×2 cm.⁴¹ Axillary adenitis ipsilateral to Bacille Calmette-Guerin (BCG) vaccination site is suggestive of BCG adenitis (also see the Immune Reconstitution Inflammatory Syndrome [IRIS] section below).
- **TBM** is most common in children aged <3 years, but can occur at any age, especially in children with HIV. Although the disease manifestations of TBM in immunocompetent and immunocompromised children are often similar, the list of differential diagnoses is greatly expanded in immunocompromised individuals, including children with HIV.^{42,43}
- **Osteo-articular disease** can involve any bone or joint, but vertebral involvement with typical TB gibbus formation with or without para-vertebral abscess formation is most common.
- **Cold abscesses** can occur at any site, but often develop in association with bone involvement or in deep muscle groups, such as psoas muscle.