Gram positive Bacterial Infections

Tuberculosis

DEFINITIONS AND EPIDEMIOLOGY:

Robert Koch (1843–1910) discovered that *Mycobacterium tuberculosis* causes TB. The agent is pleomorphic bacilli, weakly gram positive curved rods 2-4 Mm long. Children in endemic areas carry a huge disease burden and experience considerable TB-related morbidity and mortality. In addition, Poor countries carry the bulk of the TB disease burden. The risk to develop active TB following infection is mainly determined by the age and immune status of the child. The highest risk occurs in very young (Immune immature) and/or immune-compromised Children, Malnutrition, Cigarette smoking and Crowding. If children do progress to active TB, it usually occurs within 12 months of primary infection.

PATHOGENESIS:

TB is spread via tiny aerosol droplets, predominantly produced by adults with cavitary TB. The risk of infection following TB exposure depends on the infectiousness of the index case, as well as the proximity and duration of contact. In highly endemic areas, the majority of transmission occurs outside the household, but this does not reduce the importance of household exposure, especially in young and vulnerable children.

CLINICAL PRESENTATION:

Intrathoracic manifestations include mediastinal lymph node disease, pleural and pericardial effusion, disseminated or miliary disease. Extrathoracic manifestations include cervical lymphadenitis, tuberculous meningitis, and other organ involvement.

**Primary pulmonary tuberculosis** in older infants and children is usually an asymptomatic infection. Often the disease is manifested by positive TST with minimal abnormalities on CXR, such as an infiltrate with hilar LAP or GHON COMPLEX. Malaise, low grade fever, failure to gain weight, erythema nodosum, or symptoms resulting from LN enlargement may occur. **Progressive primary disease** is characterized by a primary pneumonia that develops shortly after initial infection. Progression to pulmonary disease or disseminated
miliary disease, or progression of CNS granulomas to meningitis occurs most commonly in the first year of life. Hilar LAP may compress the bronchi or trachea. **Tuberculous pleural effusion** generally represents the immune response to the organisms and most commonly occurs in older children and adolescent. **Reactivation pulmonary tuberculosis** usually confined to apical segments of upper lobes or superior segments of lower lobes. There is usually little LAP and no extrathoracic infection. Advanced disease is associated with cavitations and endobronchial spread of bacilli, which will be manifested by productive cough and hemoptyis. **LAP and Cervical lymphadenitis** is common in primary disease and the most common nodes involved are the cervical, submandibular and supraclavicular areas (Scrofula). Isolated involvement of a single node is rare. Nodes are usually matted because of considerable periadenitis. A cold abscess results when the caseous material liquefies, and this is signified by a soft fluctuant node with violaceous discoloration of the overlying skin; spontaneous drainage and sinus formation may follow. **Miliary TB** means wide spread hematogeneous dissemination to multiple organs. It's characterized by fever, malaise, weight loss, LAP, night sweat and hepatosplenomegaly. It's more common in very young (2–3 years of age) and immune-compromised children. The TST may be non reactive because of anergy. Typical radiologic signs include the presence of even-sized miliary lesions (2 mm), which are distributed bilaterally into the very periphery of the lung. **Tuberculous meningitis** most commonly occurs in children below 5 years age and often within 6 months of primary infection. The condition may have insidious onset, characterized by low grade fever, head ache and subtle personality change. Progression leads to basilar meningitis, increase ICP, deterioration of mental state and coma. CT shows hydrocephalus and infarction. **Tuberculous pericarditis** usually occurs when organisms from the lung or pleura seeds to the adjacent pericardium. Persistence of the infection may leads to constrictive pericarditis. **Skeletal tuberculosis** results from either hematogenous spread or direct extension from caseous lymph nodes. It's usually chronic disease with insidious onset. Radiograph shows cortical destruction. TB of the spine, POTT’S disease is the most common site followed by the hip, finger and toes (dactylitis). **Abdominal TB** occurs from swallowing of infected material. Its relatively uncommon if dairy herds are inspected for bovine TB. **Tuberculous peritonitis** is associated with abdominal TB and presents as fever, anorexia, ascites and abdominal pain. **Renal TB** is a late reactivation complication and is rare in children. It presents with dysuria, frequency, urgency, hematuria and sterile pyuria. Newborn babies may acquire **congenital TB** via the placenta, in which case the primary (Ghon) focus is usually located in the liver, if the mother develops active TB or *M. tuberculosis* infection with hematogenous dissemination during pregnancy.
**DIAGNOSIS:**

Tuberculous Skin Test (TST)
Its T cell-mediated delayed hypersensitivity reaction to the organism.

The **MANTOUX TEST**
is the intradermal injection of 0.1 mL containing 5 tuberculin units of purified protein derivative (PPD). The amount of induration in response to the test should be measured by a trained person 48–72 hr after administration. Occasional patients will have the onset of induration >72 hr after placement; this is also a positive result. Tuberculin sensitivity develops 3 wk to 3 months, most often in 4–8 wk—after inhalation of organisms. Host-related factors, including very young age, malnutrition, immunosuppression by disease or drugs, viral infections (measles, mumps, varicella, influenza), vaccination with live-virus vaccines, and overwhelming tuberculosis can depress the skin test reaction in a child infected with M. tuberculosis. Corticosteroid therapy may decrease the reaction to tuberculin. False-positive reactions to tuberculin can be caused by cross sensitization to antigens of nontuberculous mycobacteria

Definitions of Positive Tuberculin Skin Test (TST) Results in Infants, Children, and Adolescents

**INDURATION ≥5 MM**
- Children in close contact with known or suspected contagious people with tuberculosis disease.
- Children suspected to have tuberculosis disease:
  1. Findings on chest radiograph consistent with active or previously tuberculosis disease
  2. Clinical evidence of tuberculosis disease.

- Children receiving immunosuppressive therapy or with immunosuppressive conditions, including HIV infection.

**INDURATION ≥10 MM**
- Children at increased risk of disseminated tuberculosis disease:
  1. Children younger than 4 yr of age
  2. Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition.
  3. Children born in high-prevalence regions of the world
  4. Children frequently exposed to adults who are HIV infected, homeless, users of illicit drugs, residents of nursing homes, institutionalized, or migrant farm workers.
  5. Children who travel to high-prevalence regions of the world
INDURATION ≥15 MM
- Children 4 yr of age or older without any risk factors.

QuantiFERON-TB Gold, detect Gamma interferon (INF-γ) a cytokine which's generated by the patient's T cells in response to specific M. tuberculosis antigens is the recommended test for children older than 5 yr.
Culturing of the organism from biopsies of the tissue is the ultimate confirmatory to the diagnosis.
Induced Sputum or gastric fluid obtained via an NG tube with samples taking before or immediately on waking contains swallowed sputum, provides appropriate samples for gram stain and culturing.

Diagnostic Imaging:
Radiography is essential tool for diagnosis. All lobes of the lung may involved. Hilar lymphadenitis with paranchymal focus (Ghon complex) with or without calcification can be seen. Hilar LAP must be present always. Hyperinflated lung, pleural effusion and tuberculous cavity are other radiological findings.
CT scan, MRI and plain XR are also useful in diagnosing extra pulmonary TB.
LN fine needle and excisional biopsy are also confirmatory to diagnosis.

DIFFERENTIAL DIAGNOSIS:
It includes; pneumonia, malignancy and systemic diseases. For the enlarged LN, it includes: infection by atypical Mycobacteria, cat – scratch disease, toxoplasmosis, malignancy and drug reaction.

TREATMENT:
A 9 month regimen of isoniazide and rifampin cures >98% of drug susceptible pulmonary TB. The addition of pyrazinamide for the first 2 months of the regimen reduces the total duration to 6 months.
Improves of compliance occurs with DOT (Directly Observed Therapy).
Extrapulmonary TB needs prolonger and addition of further drugs to the treatment course.
**PREVENTION:**
BCG vaccine given in the first week of life by intradermal injection to the left shoulder provides 80-90% protection against the disease.
Case findings, treatment and screening of at risk children by TST interrupts disease transmission. Prevention of transmission in health care setting involves appropriate physical ventilation of air around the source case.
Mycoplasma Pneumoniae

Mycoplasma pneumoniae is the only recognized human pathogen. It is a major cause of respiratory infections in school-aged children and young adults.

ETIOLOGY:

Mycoplasmas are the smallest self-replicating biologic system. They are distinguished by the complete absence of a cell wall, double-stranded DNA, and small genomes.

EPIDEMIOLOGY:

M. pneumoniae infections occur worldwide and throughout the year. Infection is endemic in larger communities, with epidemic outbreaks occurring every 4–7 yr.

TRANSMISSION:

Infection occurs through the respiratory route by large droplet spread. The incubation period is 1–3 wk. High transmission rates have been documented within families, with a high proportion of secondary cases developing lower respiratory tract infections.

CLINICAL MANIFESTATIONS:

Bronchopneumonia is the most commonly recognized clinical syndrome associated with M. pneumoniae infection. Although the onset of illness may be abrupt, it is usually characterized by gradual onset of headache, malaise, fever, and sore throat, followed by progression of lower respiratory symptoms including hoarseness and cough. Coryza is unusual with M. pneumoniae pneumonia and usually suggests a viral etiology. Coughing usually worsens during the 1st wk of illness, with all symptoms usually resolving within 2 wk. The cough is initially nonproductive, but older children and adolescents may produce frothy, white sputum. Crackles or rales, which are fine, are the most prominent signs. With progression of the disease, the fever intensifies, the cough becomes more troublesome, and the patient may become dyspneic. Radiographic findings are not specific. Involvement is most common in the lower lobes, with unilateral, centrally dense infiltrates described in 75% of cases. Hilar lymphadenopathy may occur in up to 33% of patients. The white blood cell and differential counts are usually normal, whereas the erythrocyte sedimentation rate is usually elevated. Additional respiratory illnesses caused infrequently by M. pneumoniae include undifferentiated upper respiratory tract infections, pharyngitis, sinusitis, croup, and bronchiolitis.
DIAGNOSIS:

Pneumonia in school-aged children and young adults, especially if cough is a prominent finding, is always suggestive of M. pneumoniae disease. Cultures on special media of the throat or sputum may demonstrate M. pneumoniae. Positive IgM M. pneumoniae antibody identified by enzyme-linked immune assay (EIA) supports the diagnosis. PCR for M. pneumoniae DNA is very specific (>97%).

TREATMENT:

M. pneumoniae illness is usually mild, and hospitalization is infrequently required. M. pneumoniae is exceptionally sensitive to erythromycin, clarithromycin, azithromycin. The recommended treatment is clarithromycin (15 mg/kg/day divided bid PO for 10 days) or azithromycin (10 mg/kg once PO on day 1 and 5 mg/kg once daily PO on days 2–5) eradicate M. pneumoniae in 100% of patients.