



TUBERCULOSIS

M.Emadoleslami MD

بعد از مطالعه این مبحث دانشجو باید بتواند:

- تفاوت مواجهه و عفونت و بیماری را توضیح دهد
- علایم بیماری سل را در سنین مختلف برشمارد
- لیستی از ارگانهای درگیر در بیماری سل را بنویسد
- روش های تشخیص بیماری سل را بیان کند
- کرایتریای تشخیص بیماری سل در کودکان را تشریح کند
- تفاوت تست TST و IGRA را شرح بدهد.
- تاثیر واکسن در تست TST را توضیح دهد
- موارد مثبت و منفی کاذب TST را برشمارد

EPIDEMIOLOGY

- Children <5 y/o, an important demographic group for understanding TB epidemiology, since TB frequently progresses rapidly from latent infection to disease, and severe disease manifestations, miliary TB and meningitis, are more common in this age group
- Therefore, these children serve as sentinel cases, indicating recent and/or ongoing transmission in the community
- Most children are infected by household contacts with TB disease, particularly parents or other caretakers
- When adult index cases are sputum smear negative, transmission to children, in 30-40% of households

What are the differences....

	Exposure	Infection	Disease (TB)
S&S	–	A few/ no S&S	Tackypnea, respiratory distress, fever, weight loss...
CXR	-	Pulmonary infiltration. Hilar lymphadenopathy. Ghon complex	Atelectasis, pleural effusion, infiltration..
TX	-	Prophylaxis in special cases	Ƴ drug treatment
P.P.D	-	+	+/.

CLINICAL MANIFESTATIONS

Pulmonary Tuberculosis

- ✓ Pulmonary disease and associated intrathoracic adenopathy, the most frequent presentations of TB in children
- ✓ Chronic, unremitting cough that is not improving for more than 3 wks
- ✓ Fever $> 38^{\circ}\text{C}$ for at least 3 weeks, other common causes having been excluded
- ✓ Weight loss/ failure to thrive
- ✓ Physical exam findings, the presence of a lower respiratory infection, no specific clinical signs/ findings to confirm pulmonary TB
- ✓ Children ages 5-10 y/o, with clinically silent (but radiographically apparent) disease
- ✓ Infants, more likely to present with signs and symptoms of lung disease

Extrapulmonary Tuberculosis

- The most common forms, TB of the superficial lymph nodes& C.N.S
- Neonates, the highest risk of progression to TB disease with miliary& meningeal involvement
- Tuberculous meningitis, meningitis not responding to antibiotic treatment, with a subacute onset, communicating hydrocephalus, stroke, and/or elevated intracranial pressure
- Pleural TB, Pleural effusion
- Pericardial TB, Pericardial effusion
- Abdominal TB, distended abdomen with ascites, abdominal pain, jaundice, unexplained chronic diarrhea

CONT”

- TB adenitis, Painless, fixed, enlarged lymph nodes, especially in the cervical region, with/without fistula formation
- TB of the joint, Nontender joint effusion
- Vertebral TB, Back pain, gibbus deformity (rarely)
- Skin, Warty lesion(s), papulonecrotic lesions, lupus vulgaris; *erythema nodosum*, a sign of tuberculin hypersensitivity
- Renal, Sterile pyuria, hematuria
- Eye, Iritis, optic neuritis, phlyctenular conjunctivitis

Perinatal Infection

- A life-threatening infection; 50% mortality
- Congenital TB is associated with tuberculous endometritis/ disseminated TB in the mother, hematogenously via the placenta/ umbilical vein/by fetal aspiration (ingestion) of infected amniotic fluid
- Respiratory distress, fever, hepatomegaly, splenomegaly, poor feeding, lethargy, irritability, and low birthweight

Adolescent Infection

- Adolescents with TB can present with features common in children/adults
- Most adolescents presented with clinical symptoms

- Rates of extrathoracic TB, high
- Most cases, AFB sputum smear negative

- Only half of patients with intrathoracic TB, positive cultures
- Antituberculous medications, generally well tolerated

DIAGNOSIS

- ❖ TB in children is often diagnosed clinically
- ❖ Because pulmonary TB in children typically presents with paucibacillary, noncavitary pulmonary disease, lack of sufficient tussive force (differences between adult & childhood T.B)
- ❖ Bacteriologic confirmation, in < 50% of children & 40% of infants
- ❖ Mycobacterial culture of respiratory specimens, for children suspected of having pulmonary TB
- ❖ Obtaining sputum samples from young children is challenging, lack of sufficient tussive force
- ❖ Gastric aspiration is the principal means of obtaining material for culture from young children

CONT”

- Children < 12 months who are suspected of having pulmonary/ extrapulmonary TB undergo L.P, regardless of whether neurological symptoms are present
- For extrapulmonary TB, specimens for culture should be collected from any site
- Each specimen should be cultured regardless of AFB smear result
- The most common extrapulmonary specimens, whole blood, bone marrow, tissue specimens (lymph node/ bone), cerebrospinal fluid, urine, pleural fluid
- In pleural TB, *ADA levels over 10 units/L* in the pleural fluid are observed in the majority of patients

Diagnosis of TB (pulmonary/extrapulmonary) in a child is often based on the presence of the followings: (١) recent close contact with an infectious case, (٢) a positive TST/ IGRA(٣) suggestive findings on chest radiograph(٤)Positive physical examination,(٤)Positive gastric lavage/sputum for T.B

The approach outlined by WHO for evaluation of a child suspected of having TB includes:

- Careful history (history of TB contact and symptoms consistent with TB)
- Clinical examination (growth assessment)
- TST and/or IGRA (both tests, to increase sensitivity)
- Bacteriological confirmation
- Investigations relevant for suspected pulmonary & extrapulmonary TB
- HIV testing (in high HIV-prevalence areas)

CONT''

- ✓ A history of recent close contact with an infectious (sputum smear positive) case of TB is a **critical factor** in making **the diagnosis of TB in children, especially <5y/o**
- ✓ So asking about ill contacts and facilitating evaluation for ill adults can also expedite diagnosis for children
- ✓ In many cases of TB in children, laboratory confirmation is never established (particularly among children<5y/o)
- ✓ A presumptive diagnosis may be made based on clinical and radiographic response to empiric treatment

Screening Tests

Tuberculin Skin Test

- ❑ A positive TST may be present in both contained LTBI and in active TB disease
- ❑ A positive TST alone is not diagnostic of active disease
- ❑ Helpful for diagnosis of TB in children only in circumstances when it is positive
- ❑ A positive TST may be falsely positive due to prior vaccination with BCG, infection with nontuberculous mycobacteria, improper administration or interpretation

*Tuberculin Skin Test**

- A negative TST does NOT rule out TB disease, **false-negative results** can < 9 months, immunosuppression by HIV, other disease or medication, certain viral illnesses or recent live-virus immunization, overwhelming TB infection
- The TST cannot distinguish between TB disease, latent mycobacterium tuberculosis infection, and infection due to nontuberculous mycobacterial infection
- 40% of immunocompetent children with culture-confirmed TB disease, negative TST
- TST positivity rates vary by form of disease; in pulmonary and extrapulmonary TB, the TST, 90% and 80% positive, in miliary TB and TB meningitis, in 50% of cases

Interferon-Gamma Release Assays(IGRA)

- ✓ IGRAs are in vitro blood tests of cell-mediated immune response
- ✓ Greater specificity than TST for diagnosis of LTBI
- ✓ **Most useful for evaluation of LTBI in BCG-vaccinated individuals**(with the TST, IGRAs cannot distinguish LTBI from active disease)
- ✓ **Use of both TST and IGRA** may **increase sensitivity** for diagnostic evaluation of children with suspected T.B

Imaging

C.X.R

- P.A & lateral chest radiography, a very useful tool for diagnosis of TB in children
- The most common chest radiograph findings, a primary complex, which consists of opacification with hilar/subcarinal lymphadenopathy, in the absence of notable parenchymal involvement
- When adenopathy advances, consolidation/ a segmental lesion may occur, leading to collapse in the setting of infiltrate and atelectasis
- A miliary pattern of opacification is highly suspicious for TB, as is opacification that does not improve or resolve following a course of antibiotics
- Adolescents with TB generally present with typical adult disease findings of upper lobe infiltrates, pleural effusions, and cavitations on chest radiograph



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CT Scan

- Further delineate the anatomy for cases in which radiographic findings are equivocal
- Endobronchial involvement, bronchiectasis, and cavitations may be more readily visualized on CT scans than chest radiographs
- No role for routine use of CT scans in the evaluation of an asymptomatic child **since treatment regimens are based on chest radiography findings**
- In tuberculous meningitis, CT scan of the head is useful
- Hydrocephalus and basilar meningeal enhancement are observed in 80% & 90% of cases, respectively; chest radiography may be normal

Laboratory Studies

- Sputum examination: expectorated (for adolescents), swallowed and collected as gastric contents (young children), or induced
- Gastric aspiration is the primary method of obtaining material for AFB smear and culture from young children
- Sputum specimens should be sent for examination by smear microscopy and mycobacterial culture
- Acid-fast bacilli smear and culture, A respiratory specimen should be obtained for AFB smear and mycobacterial culture for children with suspected pulmonary TB

Sputum

- Obtaining expectorated sputum from children for detection of AFB is difficult and its examination is of low yield (<15% for microscopic examination <30% for culture), most adolescents can produce expectorated sputum spontaneously

Gastric Aspirate

- Early morning gastric contents collected from a fasting child contain sputum swallowed during the night. Gastric aspiration specimens may be obtained in the inpatient or outpatient setting
- Ideally, three early morning samples collected on different days before the child eats or ambulates optimize specimen yield
- Gastric aspiration, the most common method for obtaining respiratory samples from children (in facilities where this procedure may be performed)
- Cultures of gastric aspirate specimens are positive for TB (30-40% of cases)
- Smears are even less reliable, with positive results in <10% of cases ; **false-positive smear** results caused by **the presence of nontuberculous mycobacteria**
- Similar yields have been reported with nasopharyngeal aspiration, a less invasive technique that can be performed in the outpatient setting



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