LATENT TUBERCULOSIS INFECTION

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Latent Tuberculosis Infection

- What?
- Why?
- How many? (One third)
- How Identify? (TBT, IGRA)
- Who Should Be Tested?
- the “booster” phenomenon
- Ruling out Active Tuberculosis
Have all infected individuals the same risk of contracting disease?

- **An immunocompetent adult:**
  - approximately a **5 to 10 percent lifetime** risk of developing disease
  - The **half** the risk exists in **the first 2 to 3 years** after infection occurs.

- **Adults with tuberculosis infection & HIV**
  - A **5 to 10 % annual risk** of developing tuberculosis

- **Immunocompetent infants:**
  - as many as **40 %**
  - often serious, life-threatening forms,
  - within **1 to 2 years**.
**Determining Whom to Treat**

**TABLE 1. PERSONS AT INCREASED RISK WHO SHOULD BE TESTED FOR LATENT TUBERCULOSIS INFECTION.**

<table>
<thead>
<tr>
<th><strong>RISK</strong></th>
<th><strong>EXAMPLES OF PERSONS WITH RISK</strong></th>
</tr>
</thead>
</table>
| Increased risk of exposure to infectious cases| Persons with recent close contact with persons known to have active tuberculosis*  
|                                               | Health care workers who work at facilities where patients with tuberculosis are treated  
| Increased risk of tuberculosis infection      | Foreign-born persons from countries with a high prevalence of tuberculosis  
|                                               | Homeless persons  
|                                               | Persons living or working in facilities providing long-term care  
|                                               | HIV-infected persons  
| Increased risk of active tuberculosis once infection has occurred | Persons with recent tuberculosis infection†  
|                                               | Injection-drug users  
|                                               | Patients with end-stage renal disease  
|                                               | Patients with silicosis  
|                                               | Patients with diabetes mellitus  
|                                               | Patients receiving immunosuppressive therapy  
|                                               | Patients with hematologic cancers  
|                                               | Malnourished persons or those with a recent weight loss of more than 10% of their ideal body weight  
|                                               | Persons who have undergone gastrectomy or jejunostomal bypass  

Remember

“A decision to test is a decision to treat.”
Early detection by Tuberculin Test
BOX 197–2. Definition of a Positive Tuberculin Skin Test Reaction Result in Infants, Children, and Adolescents

**INDURATION ≥5 mm**
- Close contacts of known or suspected case of tuberculosis disease
- Children having clinical or radiographic findings of tuberculosis disease
- Children with immunosuppressive conditions, including HIV and organ transplantation
- Patients receiving immunosuppressive therapy, including immunosuppressive doses of corticosteroids (≥15 mg/24 hr prednisone or equivalent for ≥1 mo)

**INDURATION ≥10 mm**
- Infants and children ≤4 yr of age
- Children with underlying medical conditions or behaviors that increase risk: renal disease, hematologic disorders, diabetes mellitus, malnutrition, injection drug use
- Children with frequent exposure to adults at high risk
- Birth or recent immigration (<5 yr) from a high-prevalence country
- Children with travel to or exposure to visitors from high-prevalence countries

**INDURATION ≥15 mm**
- Children >4 yr of age and older without any risk factors
The QuantiFERON-TB Gold In-Tube test (QFT)

- \textit{in vitro} cell-mediated immune response
- measuring IFN-g in whole blood
- \textit{M. tuberculosis} antigens
  - early secretory antigenic target – 6 (ESAT-6)
  - culture filtrate protein-10 (CFP-10)
  - peptide from the TB antigen TB7.7
● Enzyme-linked immunospot (ELISPOT)

● Number of mononuclear cells that produce INF
QuantiFERON-TB Gold and Tuberculin Skin Test for the Diagnosis of Latent Tuberculosis Infection in Children

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- Hossein Masoumi Asl
- Mehdi Kalani,
- Jalal Mardaneh
- Zhahra Rezaee
Methods

Study Design

- A cross-sectional study.
- 967 children 1-15 year-old in the city of Shiraz
- All the participants were selected by stratified multistage random sampling in sex and age layers
- Children with acute febrile diseases, immunocompromised, on drug medications, contact history, and the immigrants were excluded.
Results

The prevalence of LTBI with TST

- Prevalence of LTBI with TST among all the cases was 3.8% (37 positive/967)
  - The highest rate was 7.8% in 15 year olds and the lowest rate (1.6%) was in the one year old group
  - Males and females were 3.7% and 4%,

- The prevalence of LTBI by QFT-GIT was 2.2% (21 positive /967)
  - The highest rate of 2.8% in 1-5 year olds and the lowest rate of 1.5% in the 6-10 year old group
  - 3.3% in males and 1% in females
Comparison of QFT-GIT with TST

- one case was positive for TST and QFT-GIT
- 20 cases were QFT-GIT positive but TST negative
- 36 cases were TST positive but QFT-GIT negative

Comparison of the two tests indicated a poor agreement between TST and QFT-GIT in the diagnosis of LTBI among low risk children (1.8%, 95%, CI: 0%- 5.3%) and (k= 0.007)
Reproducibility of QFT-GIT

- 32 Individuals (17 negative and 15 positive at first visit) were retested after 3 months
  - 2/17 (11.8%) of those initially QFT-GIT negative converted, and 10/15 (66%) of those initially QFT-GIT positive reverted
Conversion & Reversion

- 2/17 (11.8%) QFT-GIT negative converted, and 10/15 (66%) of QFT-GIT positive reverted, were retested after 3 months
  - A higher reversion rate among children may also reflect the variability of IFN-γ responses during the adaptation of the cellular immune system.

- QFT-GIT may more quantitative and dynamic measurement of cellular immune response than TST,
  - Important for serial-testing studies.
EXTRA PULMONARY TUBERCULOSIS
In some individuals, disease symptoms appear, as a mature tubercle is formed. The disease progresses as the caseous center enlarges in the process termed liquefaction. The caseous center now enlarges and forms an air-filled tuberculous cavity in which the aerobic bacilli multiply outside macrophages.

Liquefaction continues until the tubercle ruptures, allowing bacilli to spill into a bronchiole (see Figure 24.2) and thus be disseminated throughout the lungs and then to the circulatory and lymphatic systems.
The primary complex of tuberculosis
The timetable of tuberculosis

- Renal
- Skeletal
- Bronchial perforation
- Primary complex
- Plural effusion
- Miliary and meningeal
- Initial fever
- Hypersensitivity

1–5 years
33% of cases

Months after infection
Distribution of tuberculosis cases by anatomical site in HIV-positive patients

in HIV-negative patients
the site of extrapulmonary disease in children and adults
- Scrofula
- tuberculous adenitis
Tuberculous lymphadenitis. Computed tomographic scan of the neck reveals a heterogeneous mass in the right posterior cervical space (arrow) with central necrosis.
Tuberculous empyema. Computed tomographic scan showing loculated pleural fluid and pleural thickening (arrow) in the right chest with associated right lower lobe atelectasis.
• Spinal tuberculosis. Magnetic resonance imaging of the spine revealing osteomyelitis involving T10 and T11 vertebral bodies and disc space (A; arrow) and an adjacent multiloculated paravertebral abscess (B; arrow).
- Osteoarticular tuberculosis. Radiograph of the right knee showing a large effusion, osteopenia, joint space narrowing, and lucencies in the distal femur.
Psoas abscess. Computed tomographic scan of the abdomen showing a left iliopsoas abscess (arrow) that likely originated from tuberculous osteomyelitis involving the T12, L1, and L2 vertebrae.
Testicular tuberculosis. Computed tomographic scan of the pelvis showing a large, irregular, mixed solid and cystic left testicular mass (arrow).
Miliary tuberculosis. Chest radiograph (A) and chest computed tomographic scan (B) showing bilateral miliary nodular pattern.
a round lesion deep in the right hemisphere, with ring enhancement. The ventricles are grossly enlarged, and the sulci over the hemispheres widened.
• An optic funds shows fluffy patches due to localised tuberculous lesions in the choroid.

• In the older literature, these were stated to be present in 60% of cases of TBM and miliary TB.
- Papulonecrotic tuberculide
- multiple seeding of organisms to the skin with an exaggerated inflammatory response, resulting in multiple indolent skin nodules
- erythema nodosum
- raised, tender, bruise-like areas over the shins.
- The commonest manifestation of TB in the skin
- a phenomenon of hypersensitivity
Lupus vulgaris

seldom encountered in children.
Case 1
A Case of Primary Gastric Tuberculosis Mimicking Gastric Cancer

A 43 year old male presented with epigastric and periumblical pain, anorexia, intermittent constipation and nausea for 1 year.

exhibited significant weight loss in 4 months and denied having fever, cough, vomiting, passing tarry stools, or diarrhea.
There was a family history of pulmonary tuberculosis in his brother 5 years ago, who was treated successfully.

Chest X ray, liver and renal function tests were normal.
- Hgb = 9.5 mg/dl
- ESR = 58 mm/h
- WBC = 8800/mm³
- neutrophils 50%
- lymphocytes 45%
- monocytes 5%.

- His upper gastrointestinal endoscopy:
  - severe thickening of antrum and distal body of stomach which was suggestive of malignancy.

- Gastric mucosal biopsy
  - severe acute inflammation, necrosis, ulceration and granuloma tissue formation with a few highly atypical cells
- CT scan of abdomen
  - Thickening of gastric antral wall suggestive of gastric antral mass indicative of infiltrative process.

- total gastrectomy and omentectomy.

- Histopathological examination:
  - Chronic caseating granulomatous inflammation

- Acid-fast staining: -
  - PCR test for Mycobacterium tuberculosis complex DNA was positive

- Tuberculin skin test= 10 mm in diameter.
Case 2
Case presentation

A young adult man with lymphadenopathy, diffuse bilateral interstitial pneumonia, and splenomegaly
A young adult man with swellings in left submandibular area and lateral of left side of neck, intermittent fever and occasional productive cough since 2 months ago.

A young man tall and thin, not toxic but seems ill.

Temp: 38.5 oral, RR: 15/min, PR: 85/min
• Throat exam: purulent post nasal discharge
• Nose: crusted pussy discharge of both nostrils
• Lymphadenopathy:
  • A rubbery, not erythematous, mildly tender mobile lymph node, 3 x 3.5 cm in left submandibular area
  • a 2 x 2 cm in right submandibular area with the same characters
  • a 2 x 2 cm one in anterior upper cervical area with the same characters
  • A few 1 x 0.5 cm and 0.5 x 0.5 cm lymph nodes in both axillary areas with the same characters
- **Chest:** symmetric expansion, no retraction, no rales or wheezing

- **Abdomen:** no organomegaly
Lab work-up

- Hb: 10.5 mg/dl
- MCV: 80
- WBC: 7600/µL
- ESR: 50 mm/hr
- TB test: negative
- Toxoplasma titer: negative
- Wright test: negative
- Fine needle aspiration:
  - nonspecific chronic inflammation, necrotic material
Treatment

- Subacute sinusitis (3-10 weeks)
- Chest Xray → Chest Ct
- Abdominal sonography: splenomegaly
Case 3

14 y/o female from Gheshm Island

Anorexia Nervosa
Vs
Tuberculous Meningitis
Tuberculin positivity in various forms of extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Tuberculosis type</th>
<th>Tuberculin positive (%)</th>
<th>Abnormal C-XRAY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph node</td>
<td>74-98</td>
<td>5-44</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>73-93</td>
<td>30-50</td>
</tr>
<tr>
<td>Abdominal</td>
<td>58-100</td>
<td>20-28</td>
</tr>
<tr>
<td>Pericardial</td>
<td>75-100</td>
<td>32</td>
</tr>
<tr>
<td>Cutaneous tuberculosis</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Disseminated &amp; miliary</td>
<td>21-62</td>
<td></td>
</tr>
</tbody>
</table>
Yield of various tissues and body fluid specimens by the conventional smear and culture methods in patients with extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pleural fluid</th>
<th>Pericardial fluid</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear microscopy</td>
<td>&lt; 10%</td>
<td>&lt; 1%</td>
<td>5-37%</td>
</tr>
<tr>
<td>Mycobacterial culture</td>
<td>12-70%</td>
<td>25-60%</td>
<td>40-80%</td>
</tr>
</tbody>
</table>
Characteristic body fluid findings in patients with various forms of extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pleural fluid</th>
<th>Pericardial fluid</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Straw coloured</td>
<td>Straw coloured or serosanguinous</td>
<td>Clear early; Turbid with chronicity</td>
</tr>
<tr>
<td>pH</td>
<td>7.3-7.4</td>
<td>Not well described</td>
<td>Not well described</td>
</tr>
<tr>
<td>Rarely &lt;7.3, Never &gt;7.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cell count</td>
<td>1000-5000, 50-90% lymphocytes, eosinophils &lt;5% Few mesothelial cells</td>
<td>Leukocyte count is usually ↑ PMN preponderant early. Later, up to mononuclear cells predominate</td>
<td>100-500, Rarely &gt;1000 PMN preponderant early. Later, up to 95% Mononuclear</td>
</tr>
<tr>
<td>Total count Cytology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>Usually high (&gt;2.5g/dl)</td>
<td>Usually high (100-500 mg/dl) Can be very high with blockage or extreme chronicity</td>
<td>Usually high (100-500 mg/dl) Can be very high with blockage or extreme chronicity</td>
</tr>
<tr>
<td>Glucose</td>
<td>Usually less than serum</td>
<td></td>
<td>Usually 40-50 mg/dl</td>
</tr>
</tbody>
</table>
Method of confirmation of diagnosis in patients with disseminated/miliary tuberculosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>yield (%)</th>
<th>Variable</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum</td>
<td>41.4</td>
<td>Urine</td>
<td>32.0</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>35.7</td>
<td>Bone marrow</td>
<td>58.1</td>
</tr>
<tr>
<td>Gastric lavage</td>
<td>61.1</td>
<td>Liver biopsy</td>
<td>88.9</td>
</tr>
<tr>
<td>CSF</td>
<td>20.5</td>
<td>Lymph node biopsy</td>
<td>90.3</td>
</tr>
</tbody>
</table>
Sensitivity and specificity of immunodiagnostic and molecular methods applied to the pleural fluid and cerebrospinal fluid

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>Pleural fluid</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ELISA:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of antibody in the fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.22 - 0.68</td>
<td>0.60 - 0.90</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.90 - 1.00</td>
<td>0.58 - 1.00</td>
</tr>
<tr>
<td>Detection of antigen in the fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.48 - 1.00</td>
<td>0.61 - 0.79</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.98 - 1.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Molecular methods:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.22 - 0.81</td>
<td>0.50 - 0.90</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.77 - 1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Sensitivity and specificity of some commonly used non-conventional diagnostic tests in the diagnosis of extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Pleural effusion ADA (IU/l)</th>
<th>Cut-off ≥</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Villegas et al</td>
<td>45.5</td>
<td>0.88</td>
<td>0.86</td>
</tr>
<tr>
<td>Reechaipichitkul et al</td>
<td>48</td>
<td>0.8</td>
<td>0.81</td>
</tr>
<tr>
<td>Sharma et al</td>
<td>35, 100</td>
<td>0.83, 0.40</td>
<td>0.67, 1.00</td>
</tr>
<tr>
<td>Perez-Rodriguez et al</td>
<td>40</td>
<td>0.89</td>
<td>0.92</td>
</tr>
<tr>
<td>Ocana et al</td>
<td>45</td>
<td>1.00</td>
<td>0.97</td>
</tr>
<tr>
<td>Burgess et al</td>
<td>50</td>
<td>0.91</td>
<td>0.81</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Pericardial fluid</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA (IU/l)</td>
<td>≥</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dogan</td>
<td>50</td>
<td>1.00</td>
<td>0.83</td>
</tr>
<tr>
<td>Burgess et al</td>
<td>30</td>
<td>0.94</td>
<td>0.68</td>
</tr>
<tr>
<td>Aggeli et al</td>
<td>72</td>
<td>1.00</td>
<td>0.94</td>
</tr>
</tbody>
</table>
Sensitivity and specificity of some commonly used non-conventional diagnostic tests in the diagnosis of extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Cerebrospinal fluid ADA (IU/l)</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gambhir et al</td>
<td>≥8</td>
<td>0.44</td>
<td>0.75</td>
</tr>
<tr>
<td>Mishra et al</td>
<td>5</td>
<td>0.89</td>
<td>0.92</td>
</tr>
</tbody>
</table>
The End
Pathophysiology of EXTRA PULMONARY TUBERCULOSIS

- Spread of infectious pulmonary secretions via respiratory & gastrointestinal tract
- Swallowing: Before chemotherapy, 70% advanced pul TB acquired GI TB

- Contagious spread
  - Pleurisy
  - pericarditis

- Lymphohematogenous spread
  - Miliary
  - genitourinary
Pathophysiology

- Latent TB infection $\rightarrow$ 10% of those people will be reactivation later in their life if they do not receive prophylaxis therapy

- 50% of these occur in the next 2 years after the primary infection
Pathophysiology

- Tubercle bacilli reach the alveoli ➔ ingested by alveolar Macrophages
- Infection occurs if the inoculums escapes alveolar macrophage microbiocidal activity
- Once infection occur, lymphatic and hematogenous dissemination typically occurs before an effective immune response take place
- Primary TB is typically silent
- If cell mediated and macrophages are intact, they surround the organisms in granulomas limiting their multiplication and spread. The organism is contained but not eradicated
- Viable organisms may remain dormant within the granuloma for years –decades, such people do not have active disease, they do not transmit the infection to others
- Latent TB infection ➔ 10% of those people will be reactivation later in their life if they do not receive prophylaxis therapy
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“A decision to test is a decision to treat.”
Increase risk of reactivation

- HIV
- corticosteroid and other suppressive agents
- DM
- silicosis
- gastrectomy
- In 5%, if the immune response is not adequate, progressive primary TB take place
- 90% of TB cases in adults are due to reactivation
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(a) Primary tuberculosis infection

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Granuloma in TB
EXTRA PULMONARY TUBERCULOSIS

Dr Adil Khazindr
Consultant Medicine & Infectious disease
KAUH
Tuberculosis

- One of the commonest and most serious infections in the world
- Aerolized droplet inhalation of mycobacterium tuberculosis
- 1/3 of cases is transmitted from person to person, the majority of the rest by reactivation
- Life time risk of developing active TB in an infected immunocompetent person
Epidemiology facts

- 20 – 43% of the population maybe infected
- Anually 3 million die
- Cell mediated immunity (CMI) is critical to host defence during TB. This regulated by Th1/Th2 balance
- INH prophylaxis in +ve tuberculin test, liver transplanted patients well tolerated
- 90% of people exposed Mycobacterium TB, do not develop disease. Immune system and virulence of the pathogen play a role in the disease
- INH since 50s
- Rifampcin since 70s
- MDR TB in Eastern Europe, India, part of China
Pathophysiology

- Tubercle bacilli reach the alveoli → ingested by alveolar Macrophages
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- DM
- silicosis
- gastrectomy

In 5%, if the immune response is not adequate, progressive primary TB take place.

90% of TB cases in adults are due to reactivation.
(a) Primary tuberculosis infection
AFB
Granuloma in TB
Other diagnostic methods

- Boprobe Tec. is useful for rapid detection of MTP
- BACTEC- MGIT 960 AFB liquid culture system, in respiratory sample. Result within 4 hours. Sensitivity 87%, specificity 99% can be used as alternative to AFB (ZN stain) in TB screening
- PCR – detection of MTB from fine needle aspiration for diagnosis of TB, sensitive, specific and fast. It reduce the need for open biopsy
- MB/BCCT is an accurate method for rapid susceptibility testing of MTB (multi-center study)
- Molecular Beacons → rapid detection of INH and Rifampcin resistance
- ELIZA → method to measure antibodies for 7 antigens (MTB- genes), specificity is low in endemic area as prior exposure to MTB occur
Tubercles Meningitis

- Tubercle bacilli from pulmonary focus → milliary spread leading to tuberculoma

- **Clinically**
  - Gradual onset of irritability, progressive headache, anorexia followed by vomiting and seizure
  - Behavioural changes common in elderly
  - With progression of disease nuchal rigidity and cranial nerves palsies
  - Evidence of TB else where or past medical history of TB
TB Meningitis cont.

Investigations

- Chest Xry may be +ve for TB
- Tuberculin test may be +ve
- CSF finding: yellow color, increase pressure, high protein, low glucose, WBC $\rightarrow$ 100 – 500 cells predominantly lymphocyte
- CT scan of head $\rightarrow$ hydrocephalus
TB meningitis cont.

- Nonenhanced CT scan shows hydrocephalus and ependymal calcification (arrow), which represent sequelae of tuberculosis. A chronic infarct of the internal capsule secondary to prior tuberculous arteritis is also shown (arrowhead).
TB meningitis cont.

- **Differential diagnosis**
  - fungal infection
  - neurosyphilis

- **Complications**
  - seizure
  - cranial nerves palsies

- **Therapy**
  - same regimen for pulmonary tuberculosis but longer duration 1 year
  - Ethambutol → variable penetration into CSF
  - Corticosteroid → Dexamethasone 0.15mg/kg/d, 1 – 2 weeks then taper over 4 weeks
  - supportive as indicated
Intestinal tuberculosis

- Common in developing countries
- Caused by both *mycobacterium TB* and *Bovis*
- < 50% of patients have active pulmonary TB
- Commonest site is the ileocecal region
Intestinal TB cont.

- **Pathologically**
  - mucosal ulceration → scaring → fibrosis with narrowing of the lumen

- **Clinically**
  - Chronic abdominal pain
  - Obstructive symptoms
  - Weight loss
  - Fever
  - Abdominal mass
  - Fistula formation may be seen
  - Low grade fever
  - Malabsorption
  - Bacterial overgrowth with
Intestinal TB cont.

- **Differential diagnosis**
  - Inflammatory bowel disease
  - Intestinal amoebiasis
  - Carcinoma of colon

- **Investigations**
  - Chest Xray may be normal or show old TB or active TB
  - PPD skin test may be –ve
  - Double contrast barium enema → mucosal ulceration, mucosal thickening or stricture formation
  - Diagnosis is established by endoscopic or surgical biopsy → AFB or granulomas

- **Therapy**
  - Standarded anti TB is effective
Intestinal TB cont.

- Ileocecal tuberculosis in a 51-year-old man. Anteroposterior image from an enteroclysis study shows thickened folds in the cecum and an irregular cecal contour.
Intestinal TB cont.

- CT scan shows minimal thickening of the cecum with pericecal inflammatory changes. Mesenteric lymph nodes are also evident (arrows).
TB Lymphadenitis

- Is relatively common disorder
- Clinically present as a neck mass, persistant adenopathy which may be fixed with or without external drainage
- Usually no constitutional symptoms
- Pulmonary TB may be absent
TB lymphadenitis cont.

- **Differential diagnosis**
  - Atypical mycobacterium adenitis
  - Staph. Aureus
  - Sarcoidosis
  - Cat-scratch fever

- **Diagnosis**
  - fine needle aspiration → granulomatous origin. Acid fast staining if –ve aspirate for PCR

- **Therapy**
  - four anti TB drugs for 2 months, then 2 drugs (INH & Rifampcin) for 4 months more
TB Pericarditis

- Is caused by direct lymphatic or hematogenous spread; pulmonary TB is commonly absent but pleural effusion is common.

- **Clinically**
  - Subacute, low grade fever, night sweating, fatigue, FUO
  - Pericardial effusion if large → tamponade

- **Diagnosis**
  - Pericardiocentesis for AFB → yield is low
  - Pericardial biopsy → high yield
  - Pericardiectomy may be needed for both diagnosis and therapeutic reasons

- **Therapy**
  - Anti TB for 9 – 12 months + steroid
TB Peritonitis

- Relatively common in developing countries. Common in HIV patients.

- **Clinically**
  - Non-specific low-grade fever, weight loss, and abdominal pain with distension then ascitis in > 95%.

- **Investigations**
  - Ascitic aspiration → protein > 2.5 g/dl, LDH > 90 units/l, mononuclear leukocytosis > 500.
  - This gives 70% – 80% sensitivity, but non-specific.
  - Sensitivity decline with liver cirrhosis.
  - Smear for acid-fast bacilli is rarely +ve.
  - Peritoneal culture in only 20% (4-6 wks).
  - **Laparoscopy** → definitive test for diagnosis > 90% characteristic.
  - Peritoneal nodules are visible, granuloma is seen in peritoneal biopsy.
  - **PPD** skin test +ve in 50%.
  - **CXR** is abnormal in 70% – 80% of patients.

- **Therapy**
  - Ant-TB medication up to one year.
TB peritonitis

- Peritoneal tuberculosis (wet type) in a 27-year-old woman with ileocecal tuberculosis.
- CT scan shows a high-attenuation, loculated fluid collection and mesenteric lymph nodes (arrow) with fine nodular irregularity of the mesenteric surface. Marked thickening of the cecum and terminal ileum is also shown. The diagnosis was confirmed with culture of peritoneal fluid.
Renal TB

- Microscopic pyuria without bacteruria and with or without hematouria
- Progression of the disease → urine culture may be +ve for tubercle bacilli
- Cavitation of renal parenchyma may be seen
- Standered anti TB therapy
Ovarian TB

- Fallopian tubes are affected in 94% of women with genital tuberculosis. Salpingitis caused by hematogenous dissemination is almost always bilateral.
- A tubo-ovarian abscess that extends through the peritoneum into the extraperitoneal compartment suggests tuberculosis.
Ovarian TB

- Tuberculous tubo-ovarian abscess in a 21-year-old woman with lower abdominal pain and fever. *(a)* Contrast-enhanced CT scan shows a multiloculated mass with peripheral enhancement around centers of low, soft-tissue attenuation. The lesion extends to the iliac muscle (arrow). *(b)* Coronal T2-weighted MR image (7,200/90) shows the abscess (arrows). The diagnosis was confirmed with culture of a US-guided aspiration sample.
TB of the Musculoskeletal System

- Is caused by hematogenous spread from a primary lesion of the respiratory tract, a short time after infection or several years later.
- Children, the elderly and HIV patients are mainly affected.
- A single site of bone or joint is infected.
- Lower thoracic and knee mostly affected.
- Pott’s disease → TB of spine, most of the time there is no evidence of extraspinal infection.
Clinical manifestation

- Insidious onset, no fever, sweating or weight loss. Pain is limited to the site.
- Classically worsened at night with or without stiffness, with progression of the disease there is limitation in joint movement.
- It may present as monoarthritis (mostly knee joint).
- With time muscle atrophy and deformity is apparent.
- Abscess formation with external drainage → sinus formation.
- Gibbus formation result from chronic disease of the thoracolumbar region, destruction of bone or joint.
- Paraplegia is the most serious complication.
Diagnosis

- Finding AFB from joint fluid aspirate, pus or tissue specimen
- Biopsy of the bone, synovium or regional lymph node: caseation necrosis and giant cells
- Spinal TB: CT scan show paraspinal soft tissue extension of infection (e.g., psoas abscess, epiduralextension)
- Differential diagnosis include other chronic infection like brucellosis, RA, gout, metastatic tumor
Tuberculous spondylitis in a 17-year-old girl with low back pain. (a, b) Anteroposterior (a) and lateral (b) plain radiographs of the lower lumbar spine show loss of vertebral body height (arrowhead in a), sclerosis of the end plates, and anterior scalloping (arrowheads in b).
TB Spine MRI

- Sagittal T1-weighted magnetic resonance (MR) image shows focal decreased signal intensity (arrow).
Sagittal T2-weighted and contrast material-enhanced coronal T1-weighted MR images show increased signal intensity (arrow). Tuberculous disease was confirmed with bone biopsy.
Management

- Always with 4 drugs INH + Rifampcin + Ethambutol + Pyrazinamide
- Chemotherapy is effective even in advanced disease without need for surgical intervention
- Supportive measures
  - In acute infection: immobilization by splint of large joint or plaster, aspiration of the joint
- Surgical
  - Synovectomy is indicated for hypertrophy of the tendon sheet, hypertrophy of the bursae, hypertrophy of the joint
Therapy for TB

- **INH+ Rif+ PZA** can be given as initial therapy if strain are known to be sensitive to INH (resist. >4%) or patient immunocompetent, no HIV, dose not live in area with high resistance to INH.
- **DOT** (directly observed therapy) is preferred for all patients.
- Test for susceptibility initially and after 3 months of therapy (failure to convert).
- **MDR** treat with the classical 4 drugs + 3 other (Ciprofloxacin, Ethionamide, Capreomycin, Cycloserine, Kanamycin, Amikacin).
- Resistance is high in Africa, Far Asia, exposure to drug resistant strain, prior drug therapy.
- Duration for pulmonary TB → 6 months + 3 months after conversion. Test for conversion after 3 months, if still +ve → resistance is the case.
Monitoring therapy

- LFT, uric acid (Pyrazinamide) 1-3 months
- Ethambutol → visual activity
- INH hepatitis → by age 35-49 → 1.2%
  50-64 → 2.3%, >65 → 1% more with alcohol abuse
- Rifampcin → cholstatic changes during 1st month
- If transaminase > 5 times normal → DC INH, Rifampicin and Pyrazinamide
Response to therapy

- Symptoms improve in 4 weeks
- Conversion → 2 months
- Chest Xry → 2 -3 months after therapy
  - if no improvement? Old TB or another cause.

Extra pulmonary → same, prolonged duration
  - 9 – 12 months

Some experts give Pyrazinamide through out in meningitis
Risk factors for MDR

- Immigration from parts of the world with high prevalence of MDR-TB
- Close and prolong contact with TB patient
- MDR is associated with high mortality 70 – 90%
- Survival rate of 4 – 16 weeks only
- Relapse rate with current anti TB therapy < 5% mainly due non adherence to therapy
New therapy

- Moxifloxacin → in animal models is most effective Quinolone for mycobacterium TB
- Enhancement of cell mediated immunity as a therapeutic strategy for TB through activation NK (natural killing cell) is proven successful by using alpha Galactosyceramide in mice – models
- Immuno stimulatory DNA sequences and their synthetic oligonucleotide analoges (ISS-ODN) can improve the ability of human MDT (monocyte derived macrophages) to contain growth of virulent MTB in mice - study
THANK YOU
Because most persons who receive BCG vaccine are from countries with a high incidence of tuberculosis, it is recommended that the history of BCG vaccination be ignored when tuberculin tests are interpreted.

Targeted tuberculin testing and treatment of latent tuberculosis infection.

Am J Respir Crit Care Med 2000;161:S221-S247.
ارزیابی از طریق اخذ شرح حال، انجام معاونه بالینی، رادیوگرافی قفسه سینه و آزمون پوستی توبرکولین

آیا علائم مشکوک به سل وجود دارد؟

خیر

آیا عکس قفسه سینه غیر طبیعی است؟

خیر

آیا آزمون توبرکولین مثبت است (بیش از 5 میلی متر)؟

خیر

پیشگیری با ایزونیازید

برای شش ماه

پیشگیری با ایزونیازید برای سه ماه و سپس انجام آزمون پوستی توبرکولین

آیا آزمون توبرکولین مثبت است (بیش از 5 میلی متر)؟

بلی

آیا رادیوگرافی قفسه سینه نگران شود

آیا رادیوگرافی قفسه سینه غیر طبیعی است؟

خیر

قطع ایزونیازید و در صورت مشاهده علائم بیماری سریعاً گزارش شود

ایزونیازید را برای سه ماه دیگر ادامه دهید.
TB manifestations in children

- Primary TB diseases
  - Unilateral lymphadenopathy
  - Primary complex
    - Mediastinal or hilar lymphadenopathy and primary lesion
  - Lobar or segmental lesion

- Post-primary TB
  - Acute disseminated
    - Milliary TB ± meningitis
  - Pulmonary
  - Extra pulmonary
Granuloma in TB
Distribution of tuberculosis cases by anatomical site in HIV-negative patients.
Distribution of tuberculosis cases by anatomical site in HIV-positive patients

PTB only (30%)

EPTB only (20%)

Both (50%)

Pleural effusion (20%)

Others (45%)

LNTB (35%)