

• Tuberculosis

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- Learning objectives
- epidemiology
- Tuberculosis remains worlds deadliest communicable disease.
- TB is present in all regions of the world.
- WHO estimates that 1/3 of worlds population is infected.
- 95% of cases occur in developing countries.
- 9 million people developed TB in 2013.

- 56% of these were in south east Asia and west pacific region.
- epidemiology
- One quarter in African region, also had highest death rate.
- 1.5 million people died of TB last year.
- 360,000 were HIV positive.
- About 60% of cases and deaths occur in males.
- 37 million lives were saved during last 13 years with effective treatment.
- Globally 3.5% of new and 20.5% of old patients were found to have MDR-TB in 2013.
- 9.0% of MDR patients had XDR TB.(EXTENSIVELY resistant)
- etiology
- *M.tuberculosis*. *M.bovis*. *M.africanum*. *M.microti*. *M.canetti*.
- *M.tuberculosis* is the most important cause of tuberculosis in humans.

- Non spore forming, nonmotile, pleomorphic, weakly gram positive rods.
 - May appear beaded or clumped .
 - Obligate aerobes.
 - Grow on Loewenstein-Jansen culture media.
 - Best grown at 37-41 C.
 - Acid fastness is hallmark of all mycobacteria.
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- Isolation from clinical specimens takes 3-6 weeks and drug susceptibility further takes 4 weeks.
 - Can be detected within hours using **nucleic acid amplification.NAA and PCR.**
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- transmission
 - Usually occurs by airborne mucus droplets 1-5 um.

- Rarely through direct contact with infected discharge or contaminated fomites.
- Adult patients usually don't transmit within days to 2 weeks after treatment.
- **Chance of transmission increases when...**
 - Patient has positive acid-fast smear of sputum.
 - Extensive upper lobe infiltrate or cavity.
 - Copious production of thin sputum.
 - Severe and forceful cough.
 - Poor air circulation.
- Risk factors
 - Concentration of organisms expelled.
 - Length of exposure time to contaminated air.
 - Immune status of exposed individual.
 - HIV.
 - IV DRUG ABUSE.
 - ALCOHALISM

- DIABETES MELLITUS
- AGE BELOW 5 YEARS.
- pathogenesis
- The lung is portal of entry in > 95% of cases.
- Tubercle bacilli multiply initially within alveoli and alveolar ducts.
- Mostly killed, some survive in nonactivated macrophages ,carrying to regional lymph nodes.
- **PRIMARY COMPLEX (GHON COMPLEX) is combination of parenchymal pulmonary lesion and corresponding lymph node site.**
- **Viable M. tuberculosis can persist for decades in lymph nodes but parenchymal lesions usually heal.**
- Tubercle bacilli are taken to most tissues by blood and lymphatics most favorably in **lung apices, brain, kidneys and bones.**
- TB lesions

- Epithelioid granuloma with central caseation necrosis.
 - Early tubercles are spherical with 3 or 4 cellular zones..
 - Central caseation necrosis
 - An inner cellular zone of epithelioid macrophages and Langerhan giant cells with lymphocytes.
 - An outer zone of lymphocytes, plasma cells and immature macrophages.
 - A rim of fibrosis in healing lesions.
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- Clinical manifestations
 - **Latent TB**; reactive tuberculin skin test and absent clinical and radiological findings.
 - Untreated infants have up to 40% risk of developing tuberculosis while 5-10% in adults.
 - Classic clinical features with **active pulmonary TB** are...
 - Cough
 - Weight loss/anorexia
 - Fever

- Night sweats
- Hemoptysis

- Clinical manifestations
- Chest pain
- Fatigue
- Pneumonia, collapse, consolidation and cavitary lesions.
- Pneumothorax , pleural effusion.
- Miliary pattern.
- **PERICARDIAL DISEASE**
- Pericarditis
- Systemic features
- Pericardial friction rub.

- Clinical features
- Pericardial effusion.
- **DISSEMINATED DISEASE(LYMPHOHEMATOGENOUS)**
- Multiple organs involvement.
- Hepatomegaly, splenomegaly, lymphadenitis, papulonecrotic skin lesions.

- Miliary disease
- **Upper respiratory disease**
- Observed in developing countries
- Croupy cough
- Painless unilateral otorrhea
- Facial paralysis

- **Lymph node disease(scrofula)**
- Most common form of extra pulmonary disease in children
- Mostly 6-9 months after primary infection
- Firm, not hard, discrete and nontender.
- Systemic signs and symptoms except low grade fever are generally absent.
- **Central nervous system disease**
- Most serious complication in children and is fatal without treatment.
- Tuberculous meningitis
- Brainstem is often site of greatest involvement.

- Cranial nerves 3, 6, 7, most commonly involved.
- Communicating hydrocephalus.
- **1st stage**
- Lasts 1-2 week, nonspecific symptoms like fever, headache, irritability, drowsiness, may be present.
- Focal neurological signs are absent.
- **2nd stage**
- Lethargy, nuchal rigidity, seizures, positive Kernig and Brudzenski signs.
- Hypertonia, vomiting, cranial nerve palsies.
- May have signs of encephalitis.
- **3rd stage**
- Coma, hemiplegia or paraplegia, decerebrate posturing.
- Deterioration of vital signs and eventually death.
- **Bone and joint disease**
- Takes several years to develop.
- Most likely to involve vertebrae

- Spondylitis progresses to Pott disease (destruction of vertebral bodies leading to gibbus formation and kyphosis)
- Bone lesions may present as tumors or infections.
- Arthritis presents mostly as single joint involvement, mostly hip or knee.

- Clinical presentation
- **Abdominal and gastrointestinal**
- Tuberculous peritonitis
- Abdominal pain, tenderness, ascites.
- Abdominal mass, enlarged lymph nodes.
- Enteritis may present with pain, diarrhea or constipation.
- **Genitourinary**
- May become evident decades after infection.
- Early stage is clinically silent, only has sterile pyuria and microscopic hematuria.

- Dysuria, flank pain and gross hematuria in later stages.
- Hydronephrosis and ureteral strictures .
- Fallopian tubes are most often involved.
- Lower abdominal pain, dysmenorrhea or amenorrhea.
- Orchitis , epididymitis, painless scrotal swelling.
- **Disease in HIV patients**
- More severe, progressive and extra-pulmonary sites.
- Lobar disease and cavitation more common.
- Drug resistance more common.

- **Perinatal disease.**
- Congenital TB may be present at birth.
- Most common at 2nd or 3rd week of life.
- Respiratory disease, hepatomegaly, splenomegaly, poor intake, ear drainage and skin lesions.

- Abnormal chest radiograph and miliary pattern mostly.
 - Generalized lymphadenopathy and meningitis occurs in 30-50%
 - diagnosis
 - Mantoux tuberculin skin test.(primary screening test)
 - Interferon-gamma release assays .
 - QuantiFERON-TB Gold & T-SPOT.TB assay.
 - Gram staining and ZN staining to see acid-fast bacilli.
 - All specimens should be cultured.
 - Nucleic acid amplification (NAA) testing..PCR.
 - Drug susceptibility testing .
 - Chest radiograph.PA and lateral view.
 - CT scan.
 - Lumbar puncture.
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- Mantoux Tuberculin skin test
Intradermal injection of 0.1 ml containing 5 tuberculin units of purified protein derivative PPD.

Amount of induration in response to the test is measured 48-72 hr. after, by a trained person.

- goals of tuberculosis (TB) treatment
- Eradicating *M. tuberculosis* infection
- Preventing development of drug resistance
- Preventing relapse of disease

- treatment
- Treatment requires careful monitoring for adverse drug effects.
- Baseline laboratory evaluation.
- Hepatic enzymes (transaminases, bilirubin, and alkaline phosphatase), complete blood count, serum creatinine, and uric acid.
- Patients must be educated about the symptoms of hepatic toxicity.
- Sputum acid-fast bacilli (AFB) smears and cultures should be obtained at the time of initiation and completion of the initial phase of treatment.

- Second line drugs are levofloxacin, moxifloxacin, cycloserine, paraamino salicylic acid, amikacin.
- prevention
- Case finding & treatment interrupts transmission to close contacts.
- All suspected, and close contacts should be tested with tuberculin skin test.
- Hospital-based infection control programs are critical for limiting nosocomial transmission of TB.
- Suspected or confirmed cases of TB should be reported promptly to the local public health department.
- Patient should be provided with an adequate supply of medication (not just prescriptions).
- Directly observed therapy (DOT) should be arranged if feasible.
- prevention
- Drug susceptibility data for TB cases should be reviewed.

- Healthcare workers should undergo annual serial testing for latent TB infection.
 - Contact investigation is also warranted .
 - **Bacille Calmette-Guerin vaccine.**
 - The only available vaccine for tuberculosis.
 - Live attenuated, given intradermal at birth.
 - Most protective against disseminated and meningeal TB.
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- summary
 - Tuberculosis is a potential risk to global health.
 - Mycobacterium tuberculosis is responsible for the most of cases.
 - These are acid fast, gram positive rods and obligate aerobes.
 - Transmission is air born mostly.
 - Initially lungs are infected and then it may spread to distant sites.

- Extra pulmonary TB is more common in children.
- Tuberculus meningitis is the most serious form of the disease.
- Diagnosed by organism isolation, cultures, rapid tests like PCR.
- First line anti tuberculus drugs are the most important for treatment.
- With active treatment and education TUBERCULOSIS can be eradicated.
- Suggested readings
- **WHO site.**
- **Up to date.com**
- **Nelson Text book of pediatrics.**