* **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 Loewnstein-Jansen culture media.
* Best grown at 37-41 C.
* Acid fastness is hallmark of all mycobacteria.
* 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.**
* 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
* Epitheliod granuloma with central caseation necrosis.
* Early tubercles are spherical with 3 or 4 cellular zones..
* Central caseation necrosis
* An inner cellular zone of epitheliod macrophages and Langerhan gaint cells with lymphocytes.
* An outer zone of lymphocytes, plasma cells and immature macrophages.
* A rim of fibrosis in healing lesions.
* 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
* Spondilitis 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.
* Mantoux Tuberculin skin test

Intradermal injection of 0.1ml 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.
* 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.**