Team Medicine

26#

TB

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■ Slides ■ Doctors notes ■ Additional

431 Teams

TB

❖ Overview of Tuberculosis (TB) Epidemiology

- Bacterial infection.
- Caused by Mycobacterium tuberculosis (also calledtubercle bacillus).
- Damages a person's lungs or other parts of the body.
- Fatal if not treated properly.

- There are many Mycobacterium species.
- There is Mycobacterium tuberculosis and there is something called MOTT: Mycobacterium Other Than Tuberculosis but the most common is Mycobacterium tuberculosis.
- Whenever you send a sample to the lap you must ask for a culture to know the species - because some of these Mycobacterium do not respond to usual treatment of anti TB.
- Mycobacterium marinum causes abscess to the hand.

❖ Epidemiology

- It is a worldwide disease.
- TB infects 1.7 billion with 3 million deaths/yr.
- UK: 1st half of 20th century: a lot of death secondary to TB epidemic.
- 90% of cases and 95% of death occurred in developing countries.
- No. of cases in developed countries has declined because of:
- Case Finding&RX
- Improved Nutrition

Don't remember these numbers

- Q:What is the different between tuberculous infection and disease?

Infection: is the presence of the organism in your body without causing disease "latent tuberculosis" the patient does not have disease and he can'tspread the disease to the others.

- **Tuberculous infection:** a state in which the tubercle bacillus is established in the body without symptoms.
- **Tuberculous disease**: a state in which one or more organs of the body becomes diseased by the disease.

- **What increases the spread of the disease:**

1) Crowding of living
2) Migration of people from endemic area.

It is important when you ask about the situation and home circumstance

- 10% of infected people⇒active disease
- 50%of active disease ⇒ contagious

Gastrectomy: because they lost the protection path "gastric acidity".

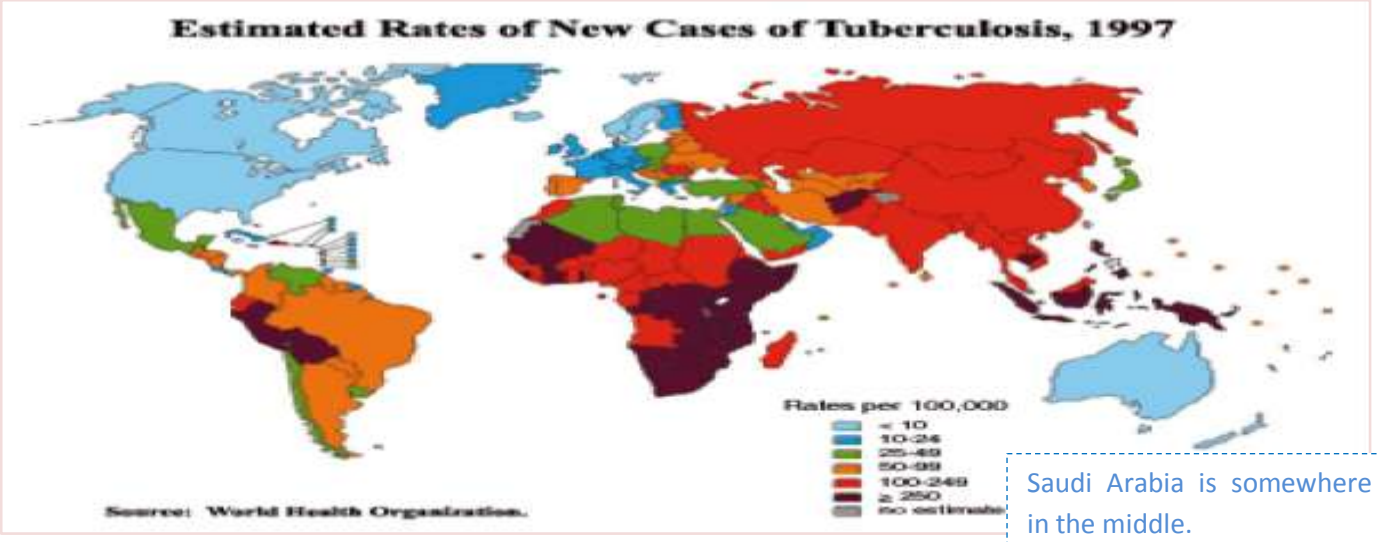
- **What increases the risk of developing disease after TB infection ?**

1-Infecting dose
2-Host factors

- age(under 5 yrs) - debilitating illness and poor nutrition - alcoholism -gastrectomy
- diabetes mellitus – immunosuppressed.

When a person inhales the infected respiratory droplets, it first affects the lung (local focus) however it could spread by overcoming your body's immunity.

Also a person might not manifest the disease from the first exposure. Children usually manifest it from the first exposure.



Saudi Arabia is somewhere in the middle.

❖ Transmission of M. tuberculosis

- M. tb spreads via airborne particles called "droplet nuclei".
- Expelled when person with infectious TB coughs, sneezes, shouts, or sings.
- Transmission occurs when droplet nuclei are inhaled and reach the alveoli of the lungs, via nasal passages, respiratory tract, and bronchi.

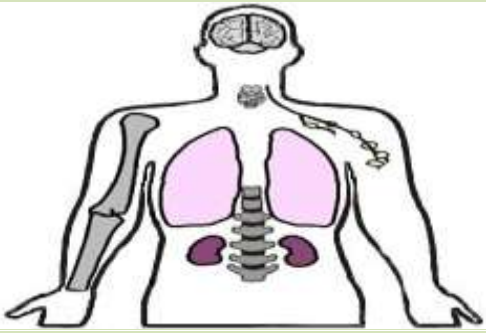
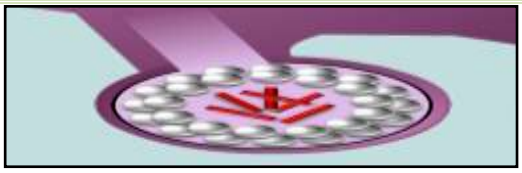
❖ Pathogenesis

- Droplet nuclei ---terminal air space ---
- Multiplication … initial focus
  - Subpleural
  - 75%single
- Migration through blood and lymph node --- another focus
- Ingestion of the bacteria by the macrophage --- slow multiplication

Negative room pressure is an isolation technique used in hospitals and medical centers to prevent cross-contaminations from room to room

When you get someone who is suspected for TB you must isolate him in a negative air pressure room.

Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli

	Tubercle bacilli multiply in the alveoli.
	A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the brain, larynx, lymph node, lung, spine, bone, or kidney).
	Within 2 to 8 weeks, special immune cells called macrophages ingest and surround the tubercle bacilli. The cells form a barrier shell, called a granuloma, that keeps the bacilli contained and under control (LTBI).
	If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (TB disease). This process can occur in different areas in the body, such as the lungs, kidneys, brain, or bone.

❖ **Inside the Body**

- Breathe in infected air and bacilli enter the lungs through bronchioles.
- Bacilli infect alveoli.
- Macrophages attack bacteria, however some survive.
- Infected macrophages separate and form tubercles.
- Dead cells form granulomas.
- As a person breathes in infected air, the bacilli go to the lungs through the bronchioles. At the end of the bronchioles are alveoli, which are balloon-like sacs where blood takes oxygen from inhaled air and releases carbon dioxide into the air exhaled.
- TB bacilli infect the alveoli and the body immune system begins to fight them. Macrophages — specialized white blood cells that ingest harmful organisms — begin to surround and "wall off" the tuberculosis bacteria in the lungs, much like a scab forming over a wound.
- Then, special immune system cells surround and separate the infected macrophages. The mass resulting from the separated infected macrophages are hard, greyish nodules called tubercles.
- Active TB spreads through the lymphatic system to other parts of the body. In these other parts, the immune system kills bacilli, but immune cells and local

tissue die as well. The dead cells form masses called granulomas, where bacilli survive but don't grow.

- As more lung tissue is destroyed and granulomas expand, cavities develop in the lungs, which causes more coughing and shortness of breathe. Granulomas can also eat away blood vessels, which cause bleeding in the lungs, and bloody sputum.

❖ Immunological Feature

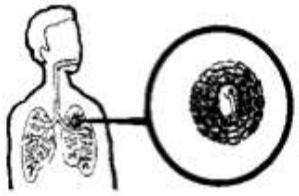
- TB requires CMI for its control.
- Ab response is rich but has no role.
- Multiplication proceeds for weeks both in:
  - Initial focus.
  - lymphohaematogenous metastatic foci.
- Until development of ... cell mediated immunity.

Which type of immune system control is required to control tuberculosis? T-cells, that's why Ab has no role.
When somebody with AIDS has tuberculosis the case is worse because HIV destroy the T cells.

❖ Microbiology

that's why it prefers the upper lobe of the lung however it can be in any lobe ex "middle lobe syndrome"

- Organism:
- Mycobacterium tuberculosis.
- Aerobic.-Non-spore forming ,non-motile.
- Rod..: 2—5 mm long. - Resistant to disinfectant.
- Once stained it resists decolorization with acid and alcohol facultative intracellular organism.
- Human is the main reservoir of MTB.

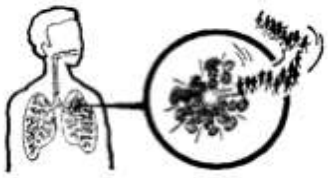


❖ Clinical Features

Active VS. Latent Infection

➢ Unhealthy person

- Bacilli overwhelm immune system.
- Bacilli break out of tubercles in alveoli and spread through bloodstream.
- This is (active) TB.



➢ Healthy person

- Initial infection controlled by immune system.
- Bacilli remain confined in tubercles for years.
- This is(latent) TB.

❖ Symptoms

- Cough
- Fever
- Weight loss

-There are no specific symptoms for tuberculosis
-The contagious disease is in few site:
1- pulmonary tuberculosis "cough"
2- laryngeal tuberculosis "sputum" extremely contagious brain, heart is not contagious

-Night sweats. - Swollen glands (lymph nodes)

- Loss of appetite. - Chills.

- Fatigue. - Pain while breathing.

❖ Clinical Features

Pulmonary 80%

Extra pulmonary 20%

- Lymph node
- Pleural
- Pericardial
- Bone and joint
- Meninges
- Peritonium

Pulmonary tuberculosis	
Primary	Post primary
the lung is the 1st organ involved ... middle and lower lobe • Health: asymptomatic • Heals spontaneously • CXR normal	• Result from endogenous reactivation of latent infection and manifest clinically: - Fever and night sweat - Weight loss - Cough… non-productive then productive • May have haemoptysis • Signs: rales in chest exam

Extra pulmonary			
Tuberculous lymphadenitis 25 %	Pleural Tb	Skeletal Tb	Tuberculous meningitis
• The commonest • Localized painless swelling • Common sites: cervical & supraclavicular • Early: glands are discrete • Late: glands are matted -/+ sinus • Dx: FNA 30% in biopsy for histo and culture	• Result form penetration by few bacilli into the pleural space resulting into : - pleural effusion and fever - DX; aspirate , exudate - AFB rarely seen - culture 30% positive - BX 80% granuloma	• Source: - reactivation of haematogenous focus - spread from an adjacent LN • Common sites: spine ,hips , knees • **Spinal Tb:** • Dorsal site is the commonest site • Involve two vertebral bodies and destroy the disc in between • Advance disease • Collapse fracture of the bodies • Kyphosis and gibbus deformity • Paravertebral abscess(cold abcess) • Dx: CT scan and MRI Biopsy: histopath	• Most often: children and may affect adult • Source: - Blood spread - Rupture of a sub-ependymal tubercle • Symptoms: - fever - headache - neck rigidity • Disease typically evolve in 2 wks. • Dx: CSF
In lymphoma and Tb If the biopsy is negative, that doesn't mean anything, because you take a small part and sometime it's not sufficient. The best thing to do is to have an excision biopsy and take theentire lymph nodes. Remember! Make sure you put it in saline and not in formalin, you will lose the microbiology part in formalin.	-negative culture does not rule out the disease. -todiagnose tuberculosis from pleura you must compare in fluid aspiration +pleural biopsy.	You must act very, diagnose and stabilize them early.	Major difference between Tuberculosis meningitis and Neisseria meningitides. Neisseria: acute, sudden onset. Tuberculosis: chronic. In CSF>> high protein, high leukocytes, normal glucose, and most imp AFB

Remember pleura is extra pulmonary

- Malnutrition
- HIV
- Severe cases
  - primary lesion progress to clinical illness
  - cavitating pneumonia
  - lymphatic spread and lobar collapse due to LN
- 40% haematogenous dissemination

In children

- Asymptomatic state may cause miliary tuberculosis and TB meningitis

❖ TB & Aids

- Person with active TB are more frequent to have HIV than general population.
- AIDS in HAITIANS: almost all children are positive for PPD →active TB in 60%.
- New York: 50% of active TB patients are HIV+.
- Africans: 60% of active TB patients are HIV+.
- TB can appear at any stage of HIV infection.
- But presentation varies with the stage:
  - Early:
    - Typical pattern of upper lobe infiltrate -+cavitation …
  - Late:
    - Diffuse infiltrate ..no cavitation .. LN
- Sputum is less frequent to be + for AFB with HIV than without.
- Extra pulmonary is more common40%.
- Pulmonary TB and HIV --- diagnosis is difficult
  - sputum (-) in 40 %
  - atypical CXR
  - negative PPD

You must test patient with HIV for TB.
HIV pts with TB present differently, clinically and radiologically

❖ Latent TB Infection (LTBI)

- Granulomas may persist (LTBI), or may break down to produce TB disease
- 2 to 8 weeks after infection, LTBI can be detected via TST or interferon-gamma release assay (IGRA)
- The immune system is usually able to stop the multiplication of bacilli
- Persons with LTBI are not infectious and do not spread organisms to others

❖ TB Disease

- In some, the granulomas break down, bacilli escape and multiply, resulting in TB disease
- Can occur soon after infection, or years later
- Persons with TB disease are usually infectious and can spread bacteria to others
- Positive *M. tb* culture confirms TB diagnosis

❖ LTBI vs. TB Disease

Person with LTBI (Infected)	Person with TB Disease (Infectious)
Has a small amount of TB bacteria in his/her body that are alive, but inactive	Has a large amount of active TB bacteria in his/her body
Cannot spread TB bacteria to others	May spread TB bacteria to others
Does not feel sick, but may become sick if the bacteria become active in his/her body	May feel sick and may have symptoms such as a cough, fever, and/or weight loss
Usually has a TB skin test or TB blood test reaction indicating TB infection	Usually has a TB skin test or TB blood test reaction indicating TB infection
Radiograph is typically normal	Radiograph may be abnormal
Sputum smears and cultures are negative	Sputum smears and cultures may be positive
Should consider treatment for LTBI to prevent TB disease	Needs treatment for TB disease
Does not require respiratory isolation	May require respiratory isolation
Not a TB case	A TB case

❖ Most Susceptible

- People at higher risk of TB infection
    - Close contacts with people with infectious TB
    - People born in areas where TB is common
    - People with poor access to health care
    - People who inject illicit drugs
    - People who live or work in residential facilities
    - Health care professionals
    - The elderly

➢ People at higher risk of active TB disease

- People with weak immune systems (especially those with HIV or AIDS)
- People with diabetes or silicosis
- People infected within the last 2 years
- People with chest x-rays that show previous TB disease
- Illicit drug and alcohol abusers

❖ Persons at Higher Risk for Exposure to or Infection with TB

- Close contacts of person known or suspected to have active TB
- Foreign-born persons from areas where TB is common
- Persons who visit TB-prevalent countries
- Residents and employees of high-risk congregate settings

❖ Drug-Resistant TB

- Caused by organisms resistant to one or more TB drugs
- Transmitted same way as drug-susceptible TB, and no more infectious
- Delay in detecting drug resistance may prolong period of infectiousness because of delay in starting correct treatment

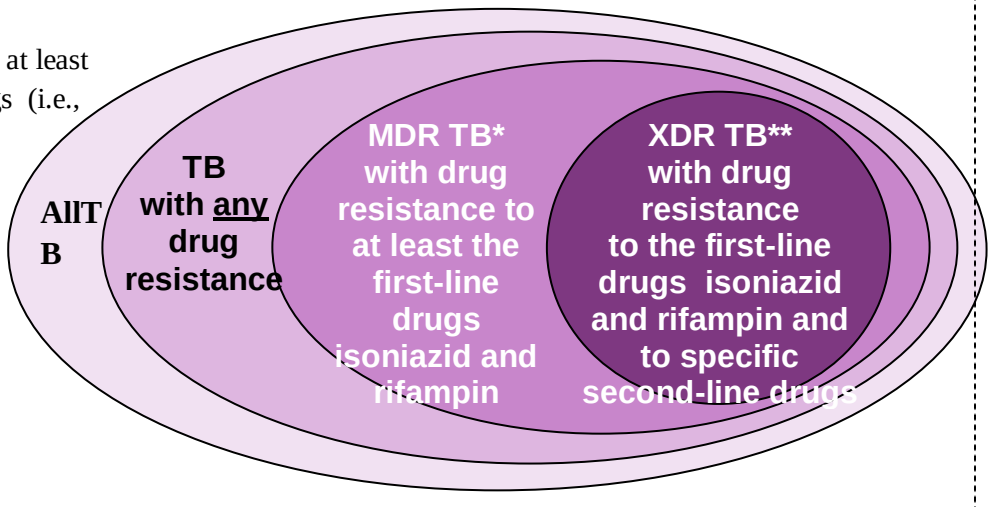
-multidrug resistant organism was not create like this we made it resistant because of using antibiotics
-two types of drug resistant
primary: that when the patient is infected with an organism which already drug resistant to antibiotic
secondary: when the patient while he is on treatment he develop resistance

❖ Multidrug-Resistant (MDR) and Extensively Drug-Resistant (XDR) TB

- MDR TB caused by bacteria resistant to best TB drugs, isoniazid and rifampin.
- XDR TB caused by organisms resistant to isoniazid and rifampin, plus fluoroquinolones and ≥1 of the 3 injectable second-line drugs."most serious patient"

*Often resistant to additional drugs

**Resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)



Diagnosis

- Medical Evaluation for TB
  - Medical history
  - Physical examination
  - Test for TB infection
  - Chest radiograph
  - Bacteriologic examination

❖ Medical History

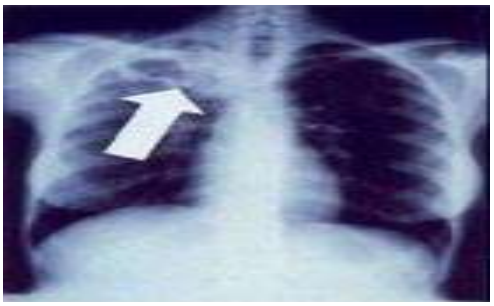
➢ Symptoms of pulmonary TB:

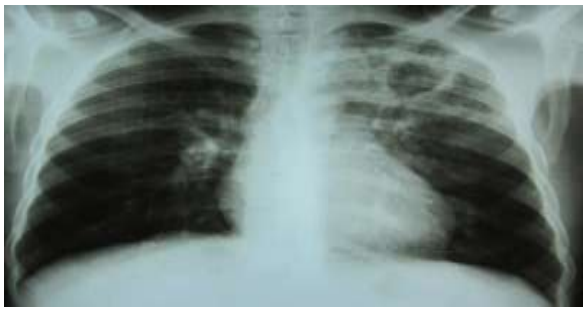
- Prolonged cough (3 weeks or longer), hemoptysis
- Chest pain
- Loss of appetite, unexplained weight loss
- Night sweats, fever
- Fatigue

❖ Chest radiograph

- For any respiratory symptoms:
- Do chest x-ray … if abnormal ---
  - Sputum for:
    - Zn stain
    - culture ..definite diagnosis
  - Use lowenstein-jansen media
- Slow growth … 3 - 6 wks
- Bactic liquid media ...

- CXR: Most common infiltrate is in the apical area, however it can occur anywhere.
- Sputum: The best specimen for sputum is the one you send the moment the pt gets to the hospital, before he gets colonized by hospital flora.
- Culture is imp to know the organism and its sensitivity.





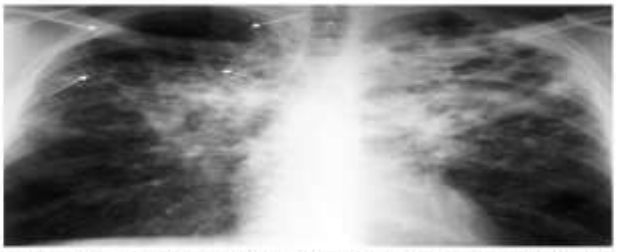
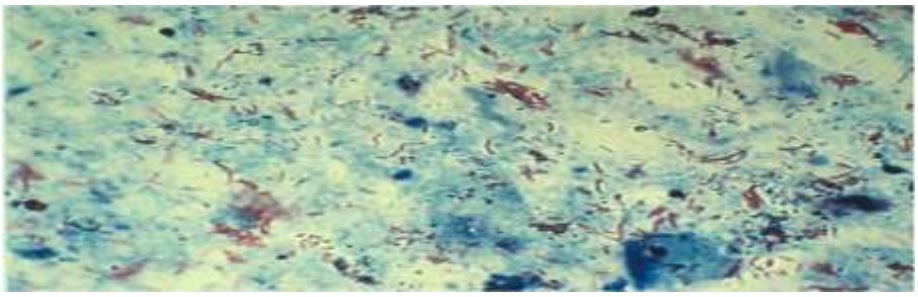


Figure 8. Chest x-ray with bilateral upper lobe opacities (white areas) with multiple cavities including a very large cavity in the right upper lobe (arrows).

AFB Smear

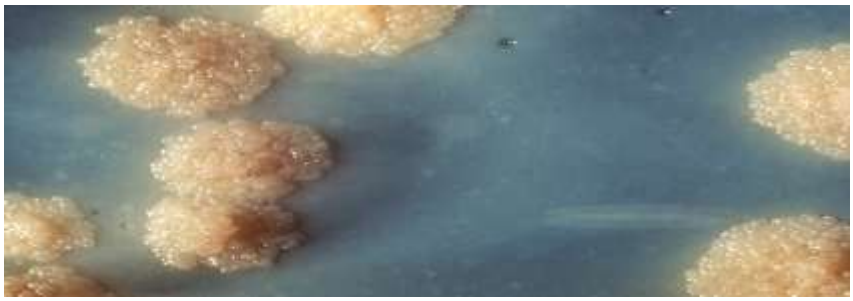
AFB (shown in red) are tubercle bacilli



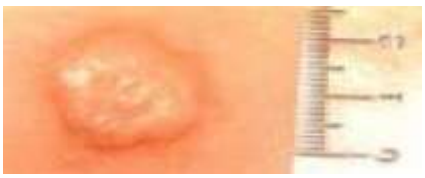
❖ Culture

- Remains gold standard for confirming diagnosis of TB
- Culture all specimens, even if smear or NAA negative
- Results in 4–14 days when liquid medium systems used
- Culture monthly until conversion, i.e., 2 consecutive negative cultures

Colonies of *M. tuberculosis* Growing on Media



❖ Test for TB infection



- PPD … intradermally …
- 5 unit in o.1 ml
- 10 mm: 90 % infected
- More than 15 mm: 100% infected
- BCG and positive PPD:
- Unless very recent: positive PPD of more than 10mm should not be due to BCG
- TST (Mantoux test),(PPD)
- PPD injected in forearm and examined 2-3 days later(24,48&72hrs)
- Induration around injection site indicatesinfection
- Measure Induration NOT redness
- Examine medical history, x-rays, and sputum
- Blood tests(B-interferone)
- PCR

The most common cause of negative PPD is wrong technique. It is very important to know how to do it. This test should be done under the skin “intradermal”, if you went slightly to the subcutaneous tissue you lose it

❖ Administering the TST

- Inject 0.1 ml of PPD (5 tuberculin units) into forearm between skin layers
- Produce wheal (raised area) 6–10 mm in diameter
- Follow universal precautions for infection control

❖ Reading the TST

- Trained health care worker assesses reaction 48–72 hours after injection
- Measure diameter of induration across forearm; only measure induration, not redness
- Record size of induration in millimeters; record "0" if no induration found

There are criteria:
1 - painful
2- swelling
3- when you take out the needle there should be no blood, if there is blood it is mean you passed the epidermis(avascular) and into the subcutaneous tissue.

❖ Mantoux Tuberculin Skin Test (TST)

- Purified protein derivative (PPD), derived from tuberculin, is injected between skin layers using the Mantoux technique.
- Infected person's immune cells recognize TB proteins in PPD, respond to site, causing wheal to rise.
- Takes 2-8 weeks after exposure and infection for the immune system to react to PPD.
- Reading and interpretation of TST reaction must be done within 48–72 hours.
- False negative TST:
  - 20 % of active disease
  - Malnutrition
  - Sarcoid
  - Lymphoproliferative disease.(lymphoma)
  - Viral infection
  - Steroid
- PPD: is of limited value because of
- Low sensitivity and specificity

❖ Factors that May Affect the Skin Test Reaction

Type of Reaction	Possible Cause
False-positive	• **Nontuberculous mycobacteria** • **BCG vaccination** • **Problems with TST administration**
False-negative	• **Anergy** • **Viral, bacterial, fungal coinfection** • **Recent TB infection** • **Very young age; advanced age** • **Live-virus vaccination** • **Overwhelming TB disease** • **Renal failure/disease** • **Lymphoid disease** • **Low protein states** • **Immunosuppressive drugs** • **Problems with TST administration**

❖ Interferon Gamma Release Assays (IGRAs)

- IGRAs detect *M. tb* infection by measuring immune response in blood.
- Cannot differentiate between TB and LTBI; other tests needed.
- May be used for surveillance/screening, or to find those who will benefit from treatment.
- FDA-approved IGRAs are QFT Gold In-Tube and T-Spot.*TB* test.

❖ BCG Vaccination

- Vaccine made from live, attenuated (weakened) strain of *M. bovis.*
- Early version first given to humans in 1921.
- Many TB-prevalent countries vaccinate infants to prevent severe TB disease.

If somebody at our age is positive to PPD this is because latent tuberculosis not because of the previous vaccination

❖ BCG Contraindications

- Contraindicated in persons with impaired immune response from:
  - HIV infection, congenital immunodeficiency.

  - Leukemia, lymphoma, generalized malignancy.
  - High-dose steroid therapy.
  - Alkylating agents.
  - Antimetabolites.
  - Radiation therapy.
- BCG vaccination should not be given to pregnant women.

❖ General Recommendations for Using IGRAs

- May be used in place of, but not in addition to, TST.
- Preferred when testing persons:
  - Who might not return for TST reading.
  - Who have received BCG vaccination.
- Generally should not be used to test children <5 years of age, unless used in conjunction with TST.

❖ Symptoms of possible extrapulmonary TB:

- Blood in the urine (TB of the kidney).
- Headache/confusion (TB meningitis).
- Back pain (TB of the spine).
- Hoarseness (TB of the larynx).
- Loss of appetite, unexplained weight loss.
- Night sweats, fever.
- Fatigue.

Remember the treatment of every types of tb is the same the difference in the duration.

Pulmonary tb :6 months

Other types: around 9 months

❖ Direct Detection Using Nucleic Acid Amplification (NAA)

- NAA tests rapidly identify a specimen via DNA and RNA amplification
- Benefits may include
  - Earlier lab confirmation of TB disease
  - Earlier respiratory isolation and treatment initiation
  - Improved patient outcomes; interruption of transmission
- Perform at least 1 NAA test on each pulmonary TB suspect
- A single negative NAA test does not exclude TB.

❖ Treatment for Latent TB Infection (LTBI)

- Treatment of LTBI essential to controlling and eliminating TB disease
- Reduces risk of LTBI to TB disease progression
- Use targeted testing to find persons at high risk for TB who would benefit from LTBI treatment
- Several treatment regimens available

❖ Candidates for Treatment of LTBI (cont.)

High-risk persons with positive IGRA test or TST reaction of ≥10 mm (cont.):

- Persons with conditions that increase risk for TB:
  - Silicosis
  - Diabetes mellitus
  - Chronic renal failure
  - Certain cancers (e.g., leukemia and lymphomas, or cancer of the head, neck, or lung)
  - Gastrectomy or jejunoileal bypass
  - Weight loss of at least 10% below ideal body weight
  - Children <4 yrs of age; children/adolescents exposed to adults in high-risk categories

❖ Major Goals of TB Treatment

- Cure patient, minimize risk of death/disability, prevent transmission to others
- Provide safest, most effective therapy in shortest time
- Prescribe multiple drugs to which the organisms are susceptible
- Never treat with a single drug or add single drug to failing regimen
- Ensure adherence and completion of therapy.

❖ Current Anti-TB Drugs

- **10 drugs FDA-approved for treatment of TB**
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)
  - Rifapentine (RPT)
  - Streptomycin (SM)
  - Cycloserine
  - Capreomycin
  - ρ-Aminosalicylic acid
  - Ethionamide

❖ Treatment

- Chemotherapy: cure
- Isonised
- Rifampicin
- Pyrazinamide
- Ethambutol/streotomycin
  - rapidly reduce the number of viable organism
  - kill the bacilli
  - slow rate of induction of drug resistance

Regimen 1 for Treatment of Pulmonary,

- Drug-Susceptible TB
  6-Month Standard Regimen for Most Patients.

Initial phase

INH, RIF, PZA, EMB daily (7 or 5 days/week) for 8 weeks.

4-month continuation phase options

1) INH, RIF daily (7 or 5 days/week) for 18 weeks.
2) INH, RIF intermittently (2 days/week or 1 day/week for INH, rifapentine) for 18 weeks.

- Drug failure
  - None compliance
  - Inappropriate drug
  - Drug resistance

❖ Infection Control

- Active pulmonary tuberculosis:
  - Isolation of the patient (2wks).
  - Isolation room should be negative pressure.
  - Patient remains until 3 negative smears and there is clinical improvement.

❖ TB Infection Control Measures

- TB infection control (IC) measures should be based on TB risk assessment for the setting.
- The goals of IC programs are:
  - Detect TB disease early and promptly.
  - Isolate persons with known/suspected TB.
  - Start treatment in persons with known/suspected TB.

SUMMARY

- Most commonly caused by Mycobacterium tuberculosis
- Transmission via inhalation of aerosolized droplets containing the active organism.
- Bacilli are inhaled and deposited into the lung, then ingested by alveolar
- Macrophages.
- Granulomas form and "wall off" the mycobacteria.After the resolution of the primary infection, the organism remains dormant within the granuloma.
- An insult to the immune system may activate the TB at any time.
- Only those people with active TB are contagious (e.g., by coughing, sneezing).
- People with primary TB are not contagious.
- Tuberculousinfection :a state in which the tubercle bacillus is established in the body without symptoms.
- Tuberculous disease: a state in which one or more organs of the body becomes diseased by the disease.
- Secondary TB (reactivation) Occurs when the host's immunity is weakened (e.g., HIV infection, malignancy, immunosuppressants, substance abuse, poor nutrition).
- Extrapulmonary TB occurs in individuals with impaired immunity, this may result in active disease throughout the body. It is common in patients with HIV because their cellular immunity is impaired.
- Risk factors include (HIV-positive patients ,Recent immigrants (within the past 5 years) Prisoners , Health care workers, Close contacts of someone with TB, Alcoholics, Diabetics, Glucocorticoid use, Hematologic malignancy, Injection drug users).
- Diagnosis :

➢ CXR
  - Classic findings are upper lobe infiltrates with cavitations.

➢ Sputum studies (sputum acid-fast testing)
  - Definitive diagnosis is made by sputum culture—growth of M. tuberculosis.

➢ Tuberculin skin test (PPD test)
  - Tuberculin skin test is a screening test to detect those who may have been exposed to TB.

- Treatment :

✓ Patients with active TB must be isolated until sputum is negative for AFB.

▪ First-line therapy is a four-drug regimen: **isoniazid (INH), rifampin, pyrazinamide, and ethambutol or streptomycin.**

▪ The initial treatment regimen consists of 2 months of treatment with the four-drug regimen. After this initial 2-month phase, a phase of 4 months is recommended using INH and rifampin.

MCQs

1-The most common site of skeletal involvement in patients with tuberculosis is:

A. Skull
B. Pelvis
C. Ribs
D. Spine

2- Which of the following is a primary site for mycobacterium tuberculosis(MBT):

A. extra pulmonary
B. meningeal
C. pulmonary
D. visceral

3-The following individual is at increased risk of mycobacterium tuberculosis (MIB) infection:

A. a class mate of the patient with mycobacterium osteomyelitis
B. mother of a teenager with mycobacterium meningitis
C. room mate of a patient with pulmonary tuberculosis
D. a health care worker who interviewed a patient with pleural tuberculosis

4-A 54 year old Saudi taxi driver from jazan has a 6 week history of a dry cough , fatigue and poor appetite and night sweating for the last 5 days . He also complains of mild right side stabbing chest pain and shortness of breath . No significant past medical history apart from a history of smoking 15 cigarettes per day for 5 years . He stopped smoking 10 years ago .Chest x-ray showed right pleural effusion .
what is the most probable diagnosis?

A. hemothorax
B. pulmonary embolism
C. bronchogenic carcinoma
D. pulmonary TB

5-30 years old patient had kidney transplant one year ago. He is doing well on standard immunosuppressive therapy.
He is at high risk to develop which of the following infections?

A. recurrent urinary tract infections
B. infectious mononucleosis
C. pulmonary tuberculosis
D. recurrent cellulites