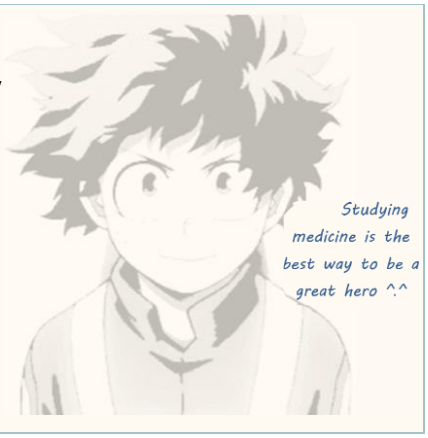
TUBERCULOSIS

435 medicine teamwork

[Important | Notes | Extra | Editing file]

lecture objectives:

- Overview of tuberculosis (TB) epidemiology
- Transmission and TB pathogenesis
- Clinical presentation
- Testing for TB infecting diseases
- Diagnosis of TB disease
- Treatment of latent TB
- Treatment of TB Diseases
- TB infection control



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References: Doctors' Slides + Davidson

Epidemiology + Transmission

General characteristics of TB:

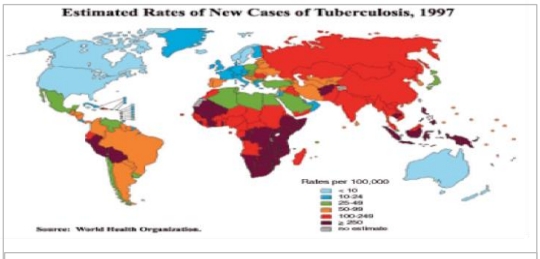
What is it: Tuberculosis is a bacterial infection caused by **Mycobacterium tuberculosis** (also called tubercle bacillus). It damages a person's lungs or other parts of the body. It is fatal if not treated properly.

TB epidemiology:

- It is a worldwide disease
- 90% of cases and 95% of death occurred in **developing** countries.
- Number of cases in **developed** countries has declined because of: case finding & treatment & Improved Nutrition.

Tuberculous infection & tuberculous disease:

Latent TB Infection (LTBI)	TB Disease (in the lungs)
Inactive, contained tubercle bacilli in the body	Active, multiplying tubercle bacilli in the body
TST or blood test results usually positive	TST or blood test results usually positive
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB



Notes

- In saudi Arabia there is 25 - 49 new cases per 100,000
- there are a lot of areas (red / dark red) with high incidence of TB (india, pakistan, south east asia, south africa...). Anyone from these countries can come to us for hajj or just for work!!
- In history-taking, it is important to ask about nationality, residency, and travel history

- 10% of infected people →develop active disease
- 50% of active disease → are contagious (not all TB cases are contagious. Open pulmonary TB is the most contagious type and laryngeal TB is the second most contagious type)

What increases the spread of the disease?

1. Crowding of living -prisons, schools..etc-. it is important to ask about the work, and whether the patient lives alone or with roommates in social history
2. Migration of people from endemic area.

What increases the risk of developing disease after TB infection?

1. Infecting dose
2. Host factors
   - Age: under 5 years, elderly
   - Debilitating illness and poor nutrition
   - Alcoholism
   - Long-term use of steroid
   - Gastrectomy (it can cause poor nutritional status and an associated reduction in immunity / Acid-protective property is lost. Don't forget to ask about it in past surgical history!!)
   - Diabetes mellitus

Mode of spread and transmission:

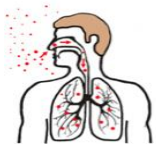
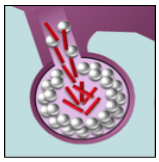
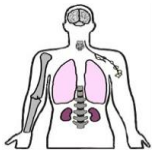
- Mycobacterium tuberculosis spread via **airborne** particles called droplet nuclei (aerosoles) "Airborne spread happens when a germ floats through the air after a person talks, coughs, or sneezes" what type of isolation should be carried to a patient with ACTIVE TB? AIRBORNE isolation with NEGATIVE pressure room. (NOT droplet isolation!)

- Theses droplet nuclei are expelled when person with infectious TB (active TB): Coughs, Speaks, Laughs, Sneezes, or Sings
- Transmission occurs when droplet nuclei inhaled and reach the alveoli of the lungs, via nasal passages, respiratory tract, and bronchi

Pathogenesis

- Droplet nuclei → terminal air space → Multiplication → initial focus
  - the initial focus is usually Subpleural & in 75% it is single
- Migration through blood and lymph node → another focus
- Ingestion of the bacteria by the macrophage → **slow** multiplication (that's why we treat for 6 months)

Pathogenesis:

1	2	3	4	5
				
Exposure to the source (coughing person infected with TB) inhalation of droplet nuclei (aerosols) At this stage >50% will not get the infection, the other < 50% will acquire the infection as bacteria reaches the alveoli.	Tubercle bacilli multiply in the alveoli. The majority of infected individuals their immune system controls the infection and this is the end of the story! the infection remains latent the rest of their lives without causing any symptoms! the unlucky 10%-5% will go on developing TB disease. (mostly secondary after being immunocompromised or primary in children) ممكن تسأل نفسك, هل ممكن انسان تجيه انفكشن TB ويتخلص منها تمامًا بدون ما تكون latent؟ الجواب ممكن, لكن الأغلبية يكونون latent.	TB bacilli infect the **alveoli** and the body immune system begins to fight them. 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, **where bacilli not killed BUT not multiplying. (LTBI).** ✳ "Granuloma is NOT diagnostic of TB since many other diseases manifest granulomas" (sometimes TB spreads through direct extension: vertebral TB (Pott's disease) can spread to psoas muscle) Then, special immune system cells surround and **separate the infected macrophages**. The mass resulting from the separated infected macrophages are hard, grayish nodules called **tubercles**.	If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (TB disease). As more lung tissue is destroyed and granulomas expand, cavities develop in the lungs, which causes more coughing and shortness of breath. Granulomas can also eat away blood vessels which causes bleeding in the lungs, and bloody sputum.	A small number of tubercle bacilli may 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).

الزبدة: مو كل شخص يصير له اكسبوجر يلقط العدوى. أيضًا مو كل شخص يلقط العدوى يمرض. لو مرض إما أنه already immunocompromised فيصير له primary disease (وهذا نادر) أو أنه يمرض لما مناعته بعدين تنزل ويصير reactivation (الأغلب).

Immunological feature:

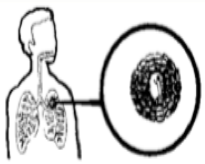
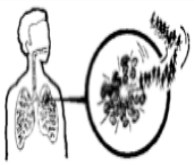
- TB require cell-mediated immunity for its control "delayed hypersensitivity reaction"
- Antibody response is rich but has **no role** "B-cells"
- Multiplication proceeds for weeks Until development of cell mediated immunity both in:
  - Initial focus
  - Lymphohaematogenous metastatic foci

Microbiology:

- Organism: **Mycobacterium tuberculosis**
  - Aerobic (apical part of the lung is the most common site of TB infection / This doesn't mean other sites cannot be involved)
  - Non-spore forming, non-motile
  - Rod: 2 - 5 mm long
  - Resistant to disinfectant (alcohol fast bacilli)
  - Once stained as part of a sample, these organisms can resist the acid and/or ethanol-based decolorization (facultative, meaning they can live both intra and extracellularly)
- Human is the main reservoir of Mycobacterium tuberculosis

Clinical features

Active TB disease Vs. Latent TB infection:

Latent TB infection (LTBI) you have the infection; you don't have the disease	**Active TB disease**
 ⇒ Healthy person ⇒ Initial infection controlled by immune system ⇒ Bacilli remain confined in tubercles for years	 ⇒ Unhealthy person ⇒ Bacilli overwhelm immune system ⇒ Bacilli break out of tubercles in alveoli and spread through bloodstream
• Granulomas may persist (LTBI), or may break down to produce TB disease • 2 to 8 weeks after infection, LTBI can be detected via TST[1]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	• 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 (laryngeal & open pulmonary) • Positive Mycobacterium tuberculosis culture confirms TB diagnosis
A person with LTBI (Infected): • Has a small amount of TB bacteria in his/her body that are alive, but inactive • Cannot spread TB bacteria to others • Does not feel sick, but may become sick if the bacteria become active in his/her body • Usually has a TB skin test or TB blood test reaction indicating TB infection • Radiograph is typically normal • Sputum smears and cultures are negative • Should consider treatment for LTBI to prevent TB disease "prophylaxis in certain conditions - page12 -" • Does not require respiratory isolation • Not a TB case	A person with TB disease (infectious): • Has a large amount of active TB bacteria in his/her body • May spread TB bacteria to others • May feel sick and may have symptoms such as a cough, **fever** (low grade fever) , weight loss. • Usually has a TB skin test or TB blood test reaction indicating TB infection • Radiograph may be abnormal • Sputum smears and cultures may be positive • Needs treatment for TB disease • May require respiratory isolation • A TB case

[1] Tuberculin Skin Test

People at higher risk of TB infection:

- Close contacts with people with infectious TB. (not every TB infection is "infectious", has to be active & spreads via aerosols)
- People born in areas where TB is common (especially Africa, Asia and Latin America)
- Persons who visit TB-prevalent countries
- Residents and employees of high-risk congregate settings
- People with poor access to healthcare
- People who inject illicit drugs (Long-term drug or alcohol use weakens your immune system and makes you more vulnerable to TB)
- People who live or work in residential facilities (crowding!)
- Health care professionals
- The elderly (Older adults are at greater risk of TB because normal aging or illness may weaken their immune systems)

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 (MDR-TB?)
- Illicit drug and alcohol abusers

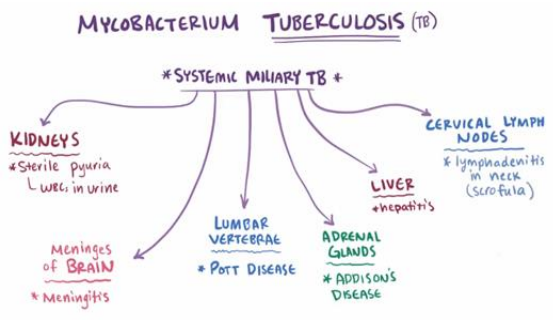
Signs & symptoms:

Pulmonary TB (80%): The FIRST station

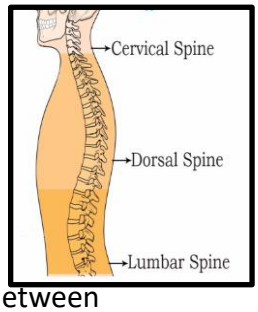
- Symptoms: Fever, night sweat, Weight loss, and Loss of appetite, Cough (non-productive then productive), haemoptysis, Fatigue, Swollen glands (lymph nodes), Chills, Pain while breathing
- Signs: rales in chest exam

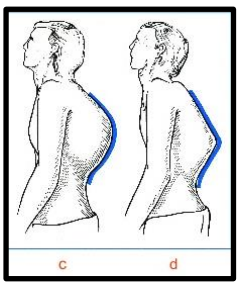
Primary	Post primary
In regions like north america (developed countries), mostly a positive skin test means a primary TB infection "first exposure" Primary TB refers to the infection of a **previously uninfected** (tuberculin -ve) individual. A few patients develop a self-limiting febrile illness but clinical disease only occurs if there is a hypersensitivity reaction or progressive infection. Progressive primary disease may appear during the course of the initial illness or after a latent period of weeks or months. it may manifest in children & elderly. Usually it doesn't manifest in adults except if the person is immunocompromised.	In our region (& in developing countries) most of the adult population have the post primary type (if we did a skin test most of us will have positive result -infection/previous exposure-) Post-primary disease refers to exogenous (**'new' infection**) or endogenous (**reactivation of a dormant primary lesion**) infection in a person who has been sensitised by earlier exposure It is most frequently pulmonary and characteristically occurs in the apex of an upper lobe where the oxygen tension favours survival of the strictly aerobic organism. The onset is usually insidious, developing slowly over several weeks. Systemic symptoms (fever, night sweats, malaise, and loss of appetite…) are accompanied by progressive pulmonary symptoms Radiological changes include ill- defined opacification in one or both of the upper lobes, and as progression occurs, consolidation, collapse and cavitation develop to varying degrees

Extra-Pulmonary TB (20%): here are some examples, any part of the body can be affected. Whenever we find extrapulmonary TB we must check the lungs because they're the FIRST station.



1. **Lymph node (Tuberculous lymphadenitis)**
   - The commonest (25% of thoses 20%)
   - Localized **painless** swelling
   - **Common sites: cervical & supraclavicular**
   - Early: glands are **discrete**
   - Late: glands are **matted** -/+ sinus (open)
   - Dx: Fine-needle aspiration in biopsy for histology and culture (🎗 **Accurate Test:** whole excision biopsy)
2. **Pleural TB**
   - Result form penetration by few bacilli into the pleural space resulting into :
     - pleural effusion and fever
     - Dx: you have to combine **both**:
       - aspirate (thoracentesis): exudate
       - BX [Biopsy of the pleura]: granuloma
     - Acid Fast Bacilli rarely seen
     - culture 30% positive
3. **Bone and joint (skeletal TB)**





   - Source:
     - Reactivation of haematogenous focus
     - Spread from an adjacent lymph node
   - 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 → compression on the spinal cord → paralysis "the condition is more serious with higher lesions"
       - Kyphosis deformity (c) and gibbus deformity (d)
       - Paravertebral abscess (cold abscess): root pain
     - Dx: CT scan and MRI
     - 🎗 Accurate Test **Biopsy**: histopathology & Acid Fast Bacilli stain & culture
4. **Meninges (Tuberculous meningitis)**
   - Most often: children and may affect adult
   - Source:
     - Blood spread "mainly"
     - Rupture of a sub-ependymal tubercle into the subarachnoid space
   - Symptoms:
     - fever, nausea, vomiting
     - headache, photophobia
     - neck rigidity
   - Disease typically evolve in 2 weeks. (**it is chronic unlike other bacterial meningitis which are acute**)
   - Dx: 🎗 **CSF Studies:** AFB stain, WBCs, culture, glucose, protein…
5. **Peritonium**

Conditions that makes the person more prone to Extra-Pulmonary TB:

1. Malnutrition
2. HIV
3. Severe cases of pulmonary TB
   - Primary lesion progress to clinical illness
   - Cavitating pneumonia
   - Lymphatic spread and lobar collapse due to enlarged lymph node
4. 40% haematogenous dissemination

In children:

Asymptomatic state may cause miliary tuberculosis and TB meningitis.

Extra about miliary TB: Blood-borne dissemination gives rise to miliary TB, which may present acutely but more frequently is characterised by 2–3 weeks of fever, night sweats, anorexia, weight loss and a dry cough. Hepatosplenomegaly may develop and the presence of a headache may indicate coexistent tuberculous meningitis. Auscultation of the chest is frequently normal, although with more advanced disease widespread crackles are evident. Fundoscopy may show choroidal tubercles. The classical appearances on chest X-ray are of fine 1–2 mm lesions ('millet seed') distributed throughout the lung fields, although occasionally the appearances are coarser. Anaemia and leukopenia reflect bone marrow involvement.

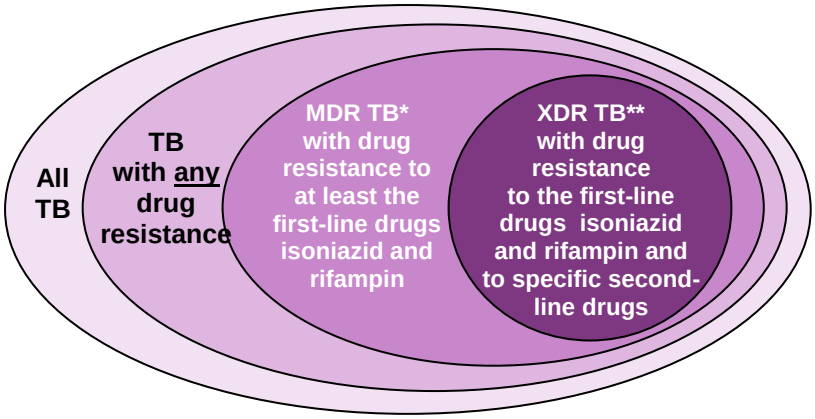
TB & HIV

- 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, intrathoracic lymphadenopathy
- Sputum is less frequent to be + for AFB with HIV than without
- Extra-pulmonary is more common among TB infected HIV-patients, occured in 40%
- Pulmonary TB and HIV --- diagnosis is difficult (why?)
    - sputum (-) in 40 %
    - atypical CXR
    - negative PPD (they lack T cells so there is no cell mediated immunity)

Drug-resistant TB:

لو المريض رفض يعالج الTB غصبن عنه بتعطيه علاج لان ضرره متعدي على الاخرين!

- Caused by organisms resistant to one or more TB drugs (the presence of resistance to any first-line agent)
- Transmitted same way as drug-susceptible TB, and not more infectious
- Delay in detecting drug resistance may prolong period of infectiousness because of delay in starting correct treatment
- Multidrug-resistant (MDR) TB: resistance to at least rifampicin & isoniazid, with or without other drug resistance.
- Extensively drug-resistant (XDR) TB: resistance to at least rifampicin and isoniazid, in addition to any quin olone and at least one injectable second-line agent (amikacin, kanamycin, or capreomycin)
- The prevalence of MDR-TB is more common in those with a prior history of TB, particularly if treatment has been inadequate, and those with HIV infection. Diagnosis is challenging, especially in developing countries, and although cure may be possible, it requires prolonged treatment with less effective, more toxic and more expensive therapies.
- Mortality rate from MDR-TB is high and that from XDR-TB higher still.



Diagnosis

Medical history:

Ask about the symptoms of pulmonary TB:

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

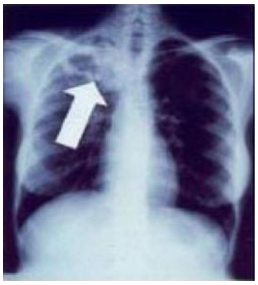
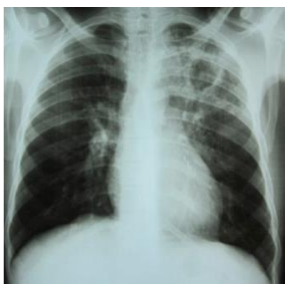
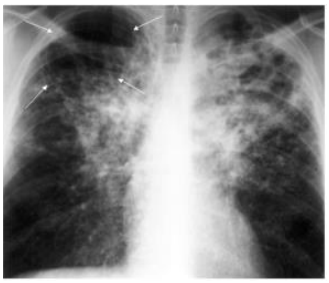
Ask about the symptoms of possible extrapulmonary TB:

- Blood in the urine (TB of the kidney)
- Headache / confusion (TB meningitis)
- Back pain (TB of the spine)
- Hoarseness (TB of the larynx)

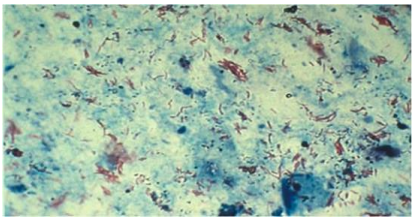
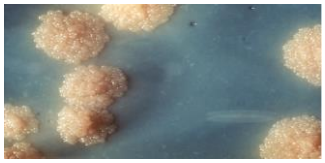
For any respiratory symptoms:

1. **Initial Test:** Do chest x-ray … if abnormal ---
2. Sputum (make sure it is not contaminated with saliva. How? there should be less than 10 epithelial cells and alveolar macrophages should be present). sputum is used for:
    - Ziehl–Neelsen stain → Acid fast bacilli
    - **Accurate Test: culture**
        - Solid media: for example Lowenstein-jansen media: slow growth … takes 3 - 6 weeks (here you can do the sensitivity test)
        - Liquid media (BACTEC): Faster (4 - 14 days) but it is more expensive and require more medical technologists time

Chest radiograph / chest X-Ray:

		
cavity formation in the right upper lobe [cavity = contagious]	cavity formation in the left upper lobe	bilateral upper lobe opacities with multiple cavities including a very large cavity in the right upper lobe

Bacteriology:

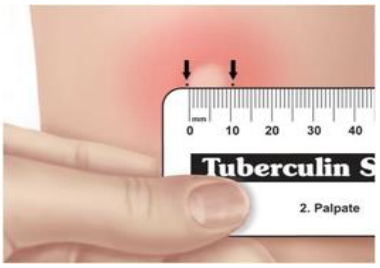
AFB smear	Culture	
 AFB (shown in red) are tubercle bacilli	• Remains **gold standard** for confirming diagnosis of TB • Culture all specimens, even if smear or nucleic acid amplification negative • Culture monthly until conversion, i.e., 2 consecutive negative cultures	 Colonies of M. tuberculosis Growing on Media. (the standard is solid media)

Mantoux Tuberculin Skin Test (TST):

(❌NOT diagnostic!)

- 0.1 ml of purified protein derivative (PPD) (5 tuberculin units), is injected in forearm between skin layers (intradermally) using the Mantoux technique
- Reading and interpretation of TST reaction must be done **within 48–72 hours**
- Infected person's immune cells recognize TB proteins in PPD, respond to site, causing wheal to rise. so induration around injection site indicates injection.
- Takes 2-8 weeks after exposure and infection for the immune system to react to PPD
- it is of limited value because of low sensitivity and specificity (there is high false +ve & false -ve TST)

Reading the TST:



- Trained health care worker assesses reaction 48–72 hours after injection
- Palpate (feel) injection site to find raised area
- Measure diameter of induration across forearm; **only measure induration**, not redness
- Record size of induration in millimeters; record "0" if no induration found

مهم أنك تكتب حجم الإنديوريشن (وليس الإحمرار) بالميللي لا تقول بوسيتف او نيقتف وخلاص.

EXTRA for your curiosity

Classification of the Tuberculin Skin Test Reaction

An **induration of 5 or more millimeters** is considered positive in

-HIV-infected persons

-A recent contact of a person with TB disease

-Persons with fibrotic changes on chest radiograph consistent with prior TB

-Patients with organ transplants

-Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-a antagonists)

An **induration of 10 or more millimeters** is considered positive in

-Recent immigrants (< 5 years) from high-prevalence countries

-Injection drug users

-Residents and employees of high-risk congregate settings

-Mycobacteriology laboratory personnel

-Persons with clinical conditions that place them at high risk

-Children < 4 years of age

- Infants, children, and adolescents exposed to adults in high-risk categories

>An **induration of 15 or more millimeters** is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.

Tuberculin skin testing may be associated with false- positive reactions in those who have had a BCG vaccination and in areas where exposure to non-tuberculous mycobacteria is high. These limitations may be overcome by employing interferon-gamma release assays (IGRAs).

Factors that may affect the skin test reaction:

False - positive	False - negative (in 20% of active disease)
• Nontuberculous mycobacteria (avium,..etc) • BCG vaccination • Problems with TST administration, the most common false diagnosis is false reading!!	• Anergy: absence of normal immune response to particular antigen or allergen • Viral, bacterial, fungal coinfection • Recent TB infection • Very young age; advanced age • Live-virus vaccination • Overwhelming TB disease • Renal failure/disease • Lymphoid disease / Lymphoproliferative disease (lymphoma) • Low protein states (malnutrition) • Immunosuppressive drugs (steroid) • Problems with TST administration • Sarcoidosis

Interferon Gamma Release Assays (IGRAs):

ماتنعمل الا لمرضى معينين

- IGRAs detect MTB 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: QuantiFERON-TB Gold In-Tube test (QFT-GIT) & T-SPOT.TB test (T-Spot)

General recommendation 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

Direct Detection Using Nucleic Acid Amplification Test (NAAT):

- NAAT 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

Management

Chemotherapy:

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):

First line	Second line
• Isoniazid (INH) • Rifampin (RIF) • Pyrazinamide (PZA) • Ethambutol (EMB) • Rifapentine (RPT) • Streptomycin (SM) sometimes it replaces ethambutol	• Cycloserine • Capreomycin • *p*-Aminosalicylic acid • Ethionamide

Regimen 1 for Treatment of Pulmonary, Drug-Susceptible TB (6-Month Standard Regimen for Most Patients):

لا تعطي دواء واحد بس لازم تكون عدة ادوية!! - لا تحفظون الdoses

- Initial phase: INH, RIF, PZA, EMB daily (7 or 5 days/week) for 8 weeks
    - Why do we use multiple drugs (?) This will:
        - Rapidly reduce the number of viable organism
        - Kill the bacilli
        - slow rate of induction of drug resistance
- 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
- 9–12 months of therapy should be considered if the patient is HIV-positive, or if drug intolerance occurs and a second-line agent is substituted.
- Treatment regimen is the same, the difference is only in the duration of treatment, in pulmonary TB you treat for 6 months, in Tuberculous meningitis you treat for at least 12 months.
- Pyridoxine should be prescribed in pregnant women and malnourished patients to reduce the risk of peripheral neuropathy with isoniazid
- Patients treated with rifampicin should be advised that their urine, tears and other secretions will develop a bright orange/red coloration, and women taking the oral contraceptive pill must be warned that its efficacy will be reduced and alternative contraception may be necessary.
- Ethambutol should be used with caution in patients with renal failure, with appropriate dose reduction and monitoring of drug levels.
- Usually Ethambutol is used as the forth drug, sometimes it is replaced by streptomycin
- Adverse drug reactions occur in about 10% of patients, but are significantly more common in the presence of HIV co- infection

19.62 Main adverse reactions of first-line antituberculous drugs

	Isoniazid	Rifampicin	Pyrazinamide	Streptomycin	Ethambutol
Mode of action	Cell wall synthesis	DNA transcription	Unknown	Protein synthesis	Cell wall synthesis
Major adverse reactions	Peripheral neuropathy[1] Hepatitis[2] Rash	Febrile reactions Hepatitis Rash Gastrointestinal disturbance	Hepatitis Gastrointestinal disturbance Hyperuricaemia	8th nerve damage Rash	Retrobulbar neuritis[3] Arthralgia
Less common adverse reactions	Lupoid reactions Seizures Psychoses	Interstitial nephritis Thrombocytopenia Haemolytic anaemia	Rash Photosensitisation Gout	Nephrotoxicity Agranulocytosis	Peripheral neuropathy Rash

[1]The risk of peripheral neuropathy may be reduced by prescribing pyridoxine.
[2]Hepatitis is more common in patients with a slow acetylator status and in alcoholics.
[3]Reduced visual acuity and colour vision may be reported with higher doses and are usually reversible.

Drug failure:

- **Non compliance** "most common cause of drug failure"
- Inappropriate drug "if someone had Nontuberculous mycobacteria and you used anti-TB drugs"
- Drug resistance (MDR-TB: culture +ve after 2 months on treatment, or contact with known MDR)

The effectiveness of therapy for pulmonary TB may be judged by a further sputum smear at 2 months and at 5 months. A positive sputum smear at 5 months defines treatment failure.
Extrapulmonary TB must be assessed clinically or radiographically as appropriate.

Control & prevention

TB infection control measure:

- 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

Infection control:

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

Detection & treatment of latent TB infection (LTBI) -chemoprophylaxis- :

- 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 (Rifampicin + isoniazid for 3 months or isoniazid for 6 months)

Candidates for treatment of LTBI:

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

- 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

Chemoprophylaxis is also recommended for:

- Asymptomatic **contact** with a positive tuberculin skin test but a normal chest X-ray
- Children aged less than 16 years identified during contact tracing to have a strongly positive tuberculin test
- Children aged less than 2 years in close contact with smear-positive pulmonary disease, those in whom recent tuberculin conversion has been confirmed
- Babies of mothers with pulmonary TB.
- HIV-infected close contacts of a patient with smear- positive disease

BCG Vaccine:

- Vaccine made from live, attenuated (weakened) strain of M. bovis
- It is administered by intradermal injection and is highly immunogenic.
- BCG appears to be effective in preventing disseminated disease, including tuberculous meningitis, in children, but its efficacy in adults is inconsistent and new vaccines are urgently needed
- Early version first given to humans in 1921
- Many TB-prevalent countries vaccinate infants to prevent severe TB disease

BCG contraindication:

- 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.

At the end of this lecture, REMEMBER investigations of Pulmonary TB

- Initial Test: **CXR**
- **Mainstay: Sputum smear**
- Accurate Test: **Sputum culture**

Note:

- PPD (also known as Mantoux test or, Tuberculin test) -> used only when "at risk" but asymptomatic & CXR is negative. (if symptomatic or CXR is positive sputum sample should be next)
- Other specimens taken depend on the sites affected, but may include cerebrospinal fluid (CSF), blood, peritoneal and pericardial fluid, early morning urine, lymph node aspirates or tissue samples.

MCQs

1. A 30--year--old man IV drug abuser came complaining of fever, night sweats and hemoptysis. AFB stain was positive. Also blood test revealed that he is positive to HIV with 50 cell CD4+. What is your next step in management?
A. Start antiretroviral then after that start TB medications.
B. Start antiretroviral till CD4+ become 350 cell then start anti TB.
C. Now treat only the HIV infection
D. Start anti TB medication at the same time with antiretroviral therapy

2. Which one of the following patient requires respiratory isolation?
A. 24 years old man admitted with weight loss, fever, oral & esophageal candidiasis, enlarged cervical node. Biopsy of which shows smear positive for acid fast bacilli.
B. 18 years old girl who was admitted with generalized lymphadenopathy, the FNA (fine needle aspiration) reveals hictiocytic necrotizing lymphadenitis.
C. An aquarium sheep worker who present with hand discharging ulcer, biopsy of which shows mycobacterium marinum as culture.
D. 65 year old man with mediastinal lymphadenopathy.

3. Which of following individual is at increased risk of mycobacterium tuberculosis infection?
A. A classmate of the patient with mycobacterium osteomyelitis.
B. Mother of a teenager with Mycobacterium meningitis.
C. Roommate of a patient with pulmonary tuberculosis.
D. A health care worker who interviewed a patient with pleural tuberculosis.

Answer key:

1 (D) | 2 (A?) | 3 (C)