In the Name of GOD

Tuberculosis

Epidemiology and Symptoms

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Introduction

- Tuberculosis is a major cause of death worldwide.
- This disease, which is caused by bacteria of the *Mycobacterium tuberculosis* complex, usually affects the lungs.
- If untreated, the disease may be fatal within 5 years in 50–65% of cases.
- Transmission usually takes place through the airborne spread of **droplet** nuclei produced by patients with infectious pulmonary tuberculosis.

Etiology

- ***M. tuberculosis*** is a rod-shaped, non-spore-forming, thin aerobic bacterium measuring 0.5 μm by 3 μm.

- **M. tuberculosis**, are often neutral on Gram's staining. However, once stained, the bacilli cannot be decolorized by acid alcohol; this characteristic justifies their classification as *acid-fast* bacilli .

- **M. tuberculosis** comprises 4043 genes encoding 3993 proteins and 50 genes encoding RNAs .

Epidemiology

- **Epidemiology** is the study of diseases and other health problems in groups of people.
- **Epidemiologists** determine the frequency and pattern (the distribution) of health problems in different communities.

- **Epidemiologists** find out **who** has a specific health problem, **how** often the problem occurs, and **where** the problem occurs. Using this information about **who**, **when**, and **where.**
- **Epidemiologists** try to determine why the health problem is occurring, to **prevent and control the diseases.**

TB Epidemiology

- It is estimated that nearly **2 billion people** (about one fourth of the world's population) are infected with **M. tuberculosis.**
- Every year, about **10 million people** develop TB disease and **1.6 million people die** of it. 95% of them in developing countries.
- Reported cases represent only ~60% of total estimated cases (**Under estimated**).
- TB disease is the leading cause of death due to infectious disease in the world.

TB Epidemiology

- In **Eastern Mediterranean** region, in 2020, Pakistan accounted for 70% of tuberculosis cases, Afghanistan for 9%, Iraq for 1.3% and **Iran for 1.3% .**
- The incidence of the disease in the Iran was reported at **16 cases per 100 000 population in 2015**, which decreased to **13 cases per 100 000 in 2019**.
- **Pulmonary** TB is bacteriologically confirmed in **84%** of patients (smear-positive tuberculosis), the remaining **16%** pulmonary tuberculosis cases are **confirmed clinically.**

GIS map of the incidence of new cases of tuberculosis in 100 thousand populations in 2016

Number of incidence in 100000 population	
	Less than 5
	5-10
	10-15
	15-20
	20-25
	25-30
	30 and above

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From Exposure to Infection

- ***M. tuberculosis*** is most commonly transmitted from a person with infectious pulmonary tuberculosis to others by droplet nuclei.

- **There may be as many as 3000 infectious nuclei per cough.**

Risk of Infection Given Exposure:

Particle/Volume X Exposure time e time

- **Particle** Production of infectious droplet nuclei
- **Volume** Volume of air and ventilation
- **Exp. time** Time of inhaling air with droplet nuclei

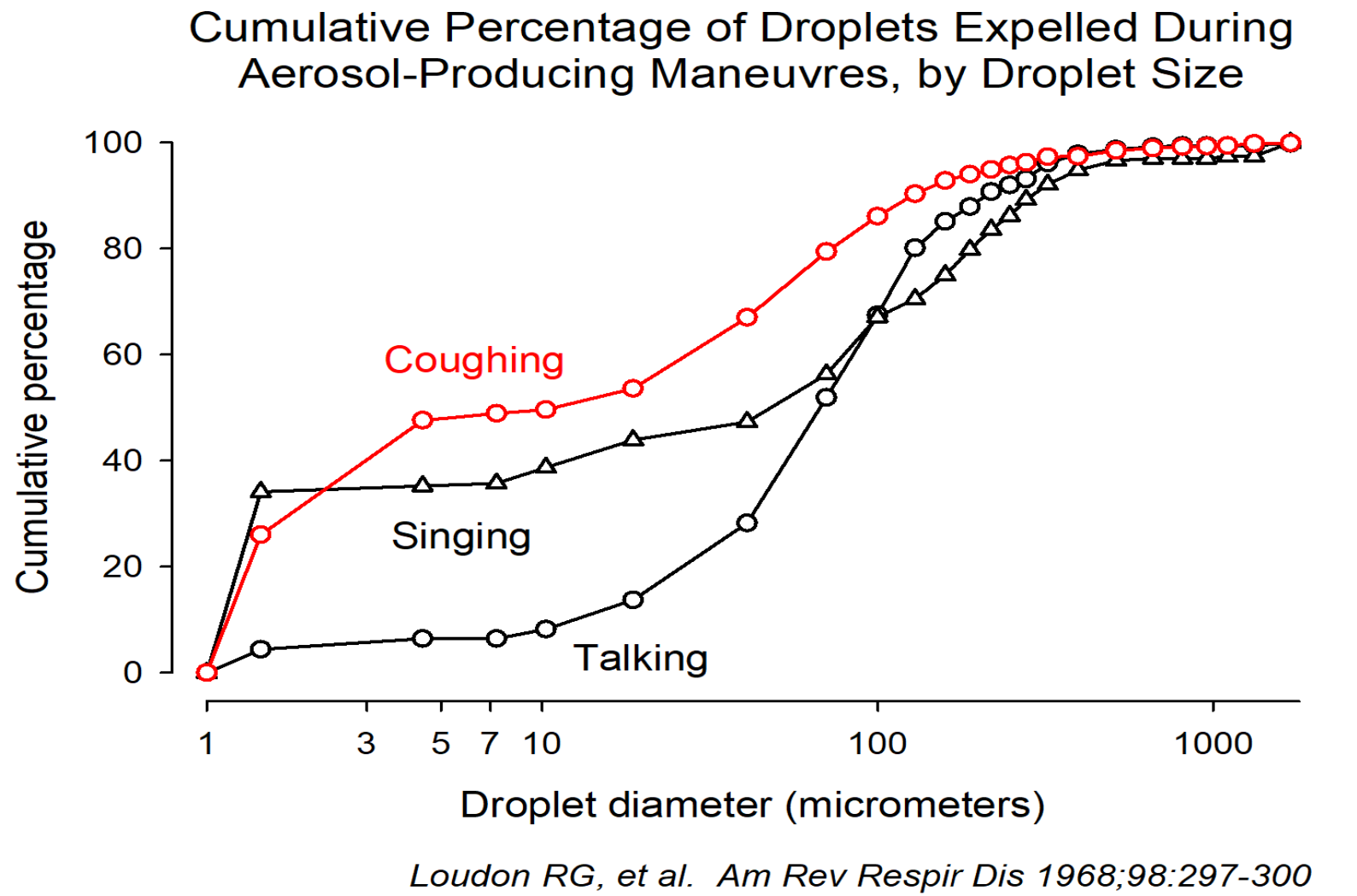
Production of Infectious Droplets

- Aerosolization
- Site and form of disease

TB Spreads Through the Air

TB spreads from person to person when someone with active TB disease coughs, speaks, or sings

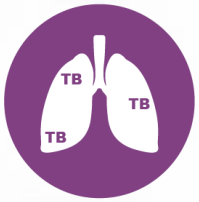
Aerosol Producing Maneuvers



From Exposure to Infection - 2

- The most infectious patients have **cavitary** pulmonary disease and produce sputum containing as many as **10^5–10^7 AFB/ml**.
- Persons with both HIV infection and tuberculosis are less likely to have cavitations, they may be less infectious than persons without HIV co-infection.
- **Crowding** in **poorly ventilated** rooms is one of the most important factors in the transmission of tubercle bacilli.
- In short, the risk of acquiring *M. tuberculosis* infection is determined mainly by exogenous factors.

Two TB-Related Conditions



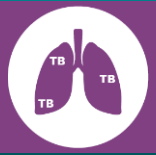
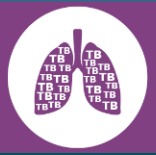
Inactive TB

- People with latent TB infection or inactive TB
- Do not feel sick, do not have symptoms, and cannot spread TB germs to others
  - Can have inactive TB for years
  - Have a small amount of TB germs in their bodies that are alive but inactive
- Inactive TB **can** develop into TB disease

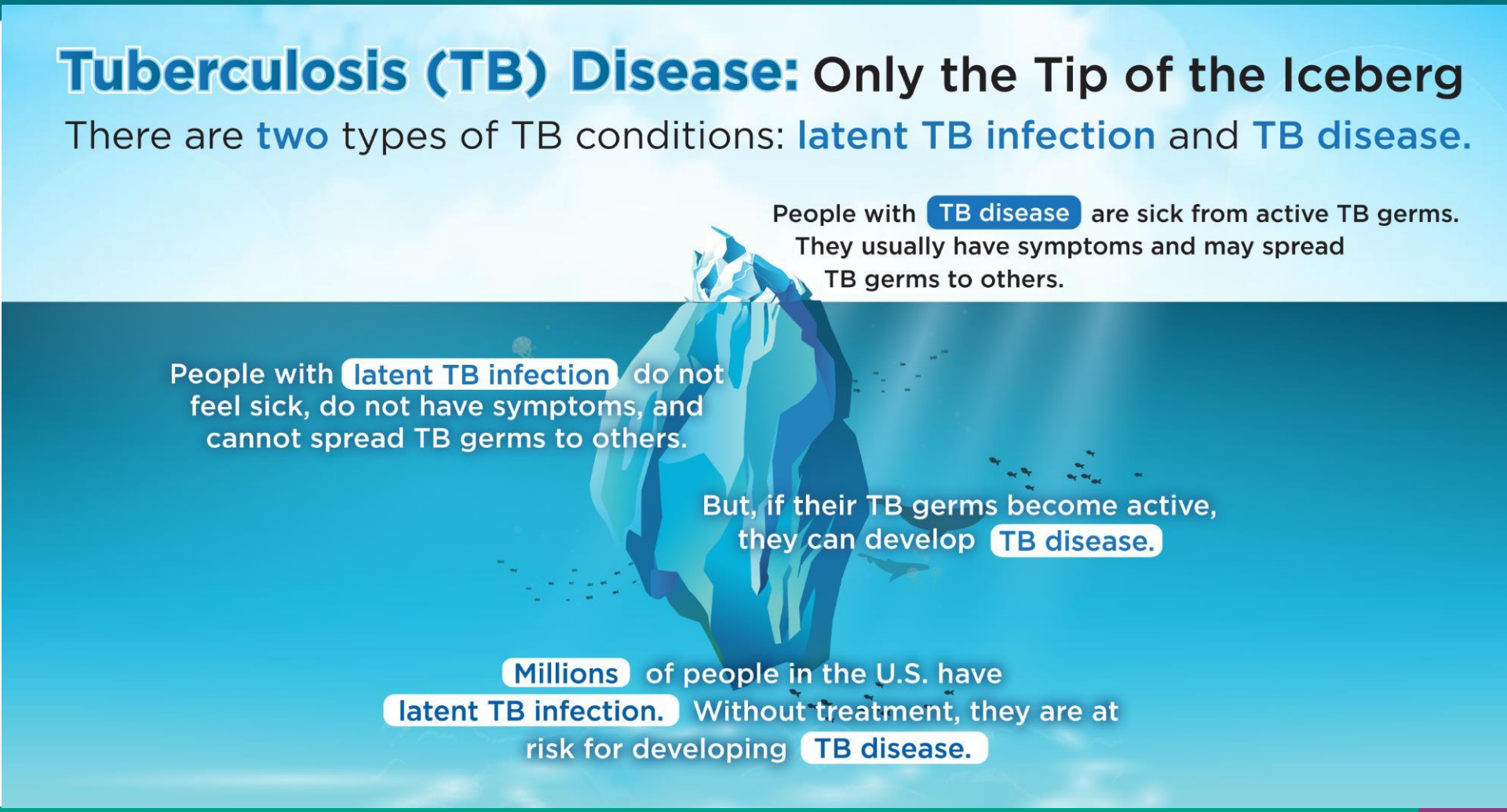
TB Disease

- If TB germs become active and multiply, inactive TB can turn into TB disease

Not Everyone Who Is Infected with TB Becomes Sick

 Person with **Inactive TB**	 Person with **TB Disease**
Has a small amount of TB germs in their body that are alive but inactive	Has a large amount of active TB germs in their body
Cannot spread TB germs to others	May spread TB germs to others
Has no symptoms and does not feel sick, but may become sick if the germs become active in their body	Feels sick and has symptoms such as a cough, fever, and/or weight loss
Usually has a positive TB skin test or TB blood test result indicating TB infection	Usually has a positive TB skin test or TB blood test result indicating TB infection
Has a normal chest x-ray and a negative sputum smear	May have an abnormal chest x-ray, or positive sputum smear or culture
Needs treatment for inactive TB infection to prevent TB disease	Needs treatment for active TB disease

Tuberculosis (TB) Disease: Only the Tip of the Iceburg



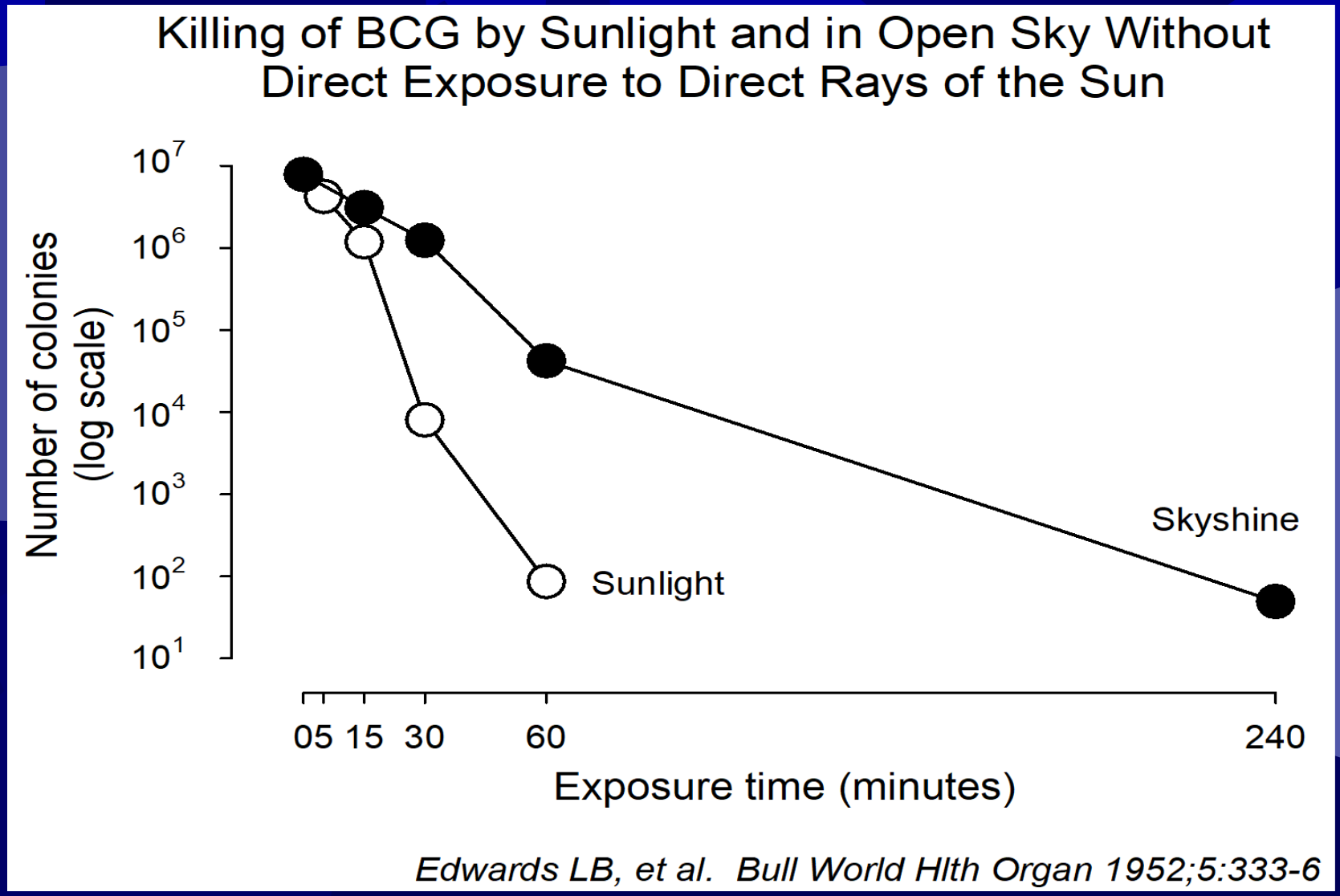
From Infection to Disease

- **The risk of developing disease after being infected depends largely on endogenous factors.**
- Clinical illness following infection is classified as ***primary tuberculosis*** and is common among children up to 4 years of age and among HIV persons.
- Dormant bacilli, however, may persist for years before reactivating to produce ***secondary or post primary tuberculosis.***
- Overall, it is estimated that up to 10% of infected persons will develop active tuberculosis in their lifetime.

From Infection to Disease - 2

- **Age** is an important determinant of the risk of disease after infection.
- Among infected persons, the incidence of tuberculosis is highest during **late adolescence** and **early adulthood**.
- **The incidence among women peaks at 25–34 years of age.**
- The risk may increase in the elderly, possibly because of waning immunity and comorbidity.

killing time of bacilli



Edwards LB, et al. Bull World Hlth Organ 1952;5:333-6

Risk Factors for Tuberculosis

- Recent infection (<1 year)
- Fibrotic lesions
- HIV infection
- Silicosis
- Chronic renal failure / Hemodialysis
- Diabetes
- Intravenous drug use
- Immunosuppressive treatment
- Gastrectomy / Jejunoileal bypass
- Posttransplantation period
- Malnutrition and severe underweight
- Homeless, 10 times higher

Who Is at Risk for Developing TB Disease?

People at high risk for developing TB disease generally fall into two categories:

- Those who have been recently infected with TB germs
- Those with medical conditions that weaken the immune system, such as:

HIV infection

Diabetes

Specialized treatment for rheumatoid arthritis or Crohn's disease

Organ transplants

Severe kidney disease

Head or neck cancer

Substance abuse

Medical treatments such as corticosteroids

Silicosis

Low body weight

Skin Test Reactivity

- **DTH** to *M. tuberculosis* is the basis of the **TST**.

- The cellular mechanisms responsible for **TST** reactivity are related mainly to previously sensitized

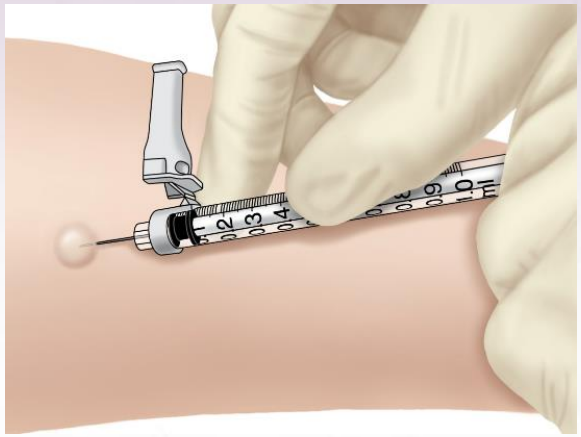
CD4+ T lymphocytes .

- TST-positive persons being less susceptible to a new M. tuberculosis infection .

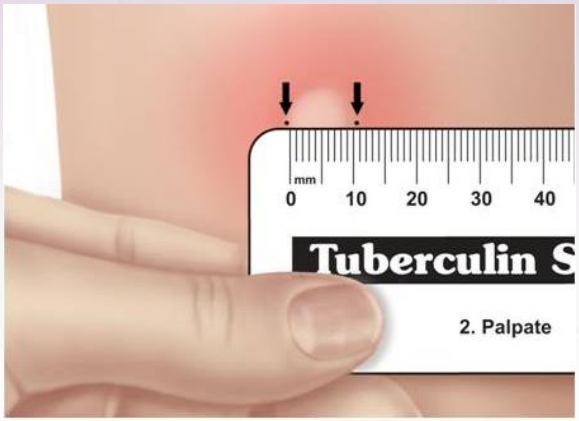
TB Skin Test

The TB skin test, also called the Mantoux tuberculin skin test (TST), requires two visits with a health care provider

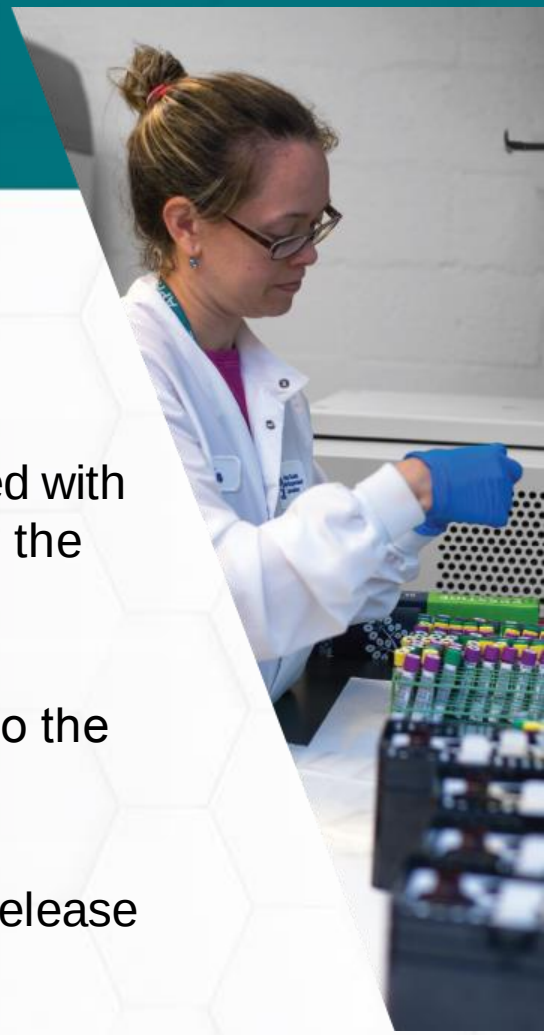
On the **first visit,** a test is **placed**



On the **second visit,** the test is **read**



TB Blood Test



Blood is drawn and sent to a lab for analysis.

- **Positive blood test:** A person *likely* has been infected with TB germs. Additional tests are needed to determine if the person has inactive TB or TB disease.
- **Negative blood test:** A person's blood did not react to the test and inactive TB, or TB disease is not likely.

The TB blood test is also known as an Interferon-Gamma Release Assay (IGRA).

Clinical Manifestations

- Tuberculosis is classified as

  1-Pulmonary, 2-Extrapulmonary

- Pulmonary TB can be categorized as

  1-Primary, 2-Postprimary (secondary).

Primary Disease

- **Primary pulmonary** tuberculosis occurs soon after the initial infection with tubercle bacilli.
- In areas of high tuberculosis transmission, this form of disease is often seen in children.
- **Middle and lower lung zones are most commonly involved in primary tuberculosis.**
- The lesion forming after infection is usually peripheral and accompanied by hilar or paratracheal lymphadenopathy.

Primary Disease - 2

- In the majority of cases, the lesion heals and may later be evident as a small calcified nodule (***Ghon lesion***).
- **Pleural effusion**, which is found in up to two-thirds of cases, results from the penetration of bacilli into the pleural space from an adjacent subpleural focus.
- **Enlarged lymph nodes** may compress bronchi, causing obstruction and subsequent segmental collapse.
- In immunocompromised persons (e.g., patients with HIV infection) may develop **miliary TB** and/or **meningitis**.

Postprimary Disease

- **Postprimary disease** results from endogenous reactivation of latent infection and is usually localized to the apical and posterior segments of the upper lobes.
- The extent of lung parenchymal involvement varies greatly, from small infiltrates to extensive caviars disease.
- With **cavity formation**, liquefied necrotic contents are ultimately discharged into the airways, resulting in satellite lesions within the lungs that may in turn undergo cavitation.
- Some pulmonary lesions become **fibrotic** and may later calcify, but cavities persist in other parts of the lungs.
- Most patients respond to treatment, with defervescence, decreasing cough, weight gain, and a general improvement in well-being within several weeks.

Symptoms & Signs

- Early in the course of disease, symptoms and signs are often nonspecific and insidious,

  fever , night sweats, weight loss, anorexia, general malaise, hemoptysis, and weakness.

- Physical findings are of limited use in pulmonary tuberculosis.

  rales in the involved areas, rhonchi due to partial bronchial obstruction, In some cases, pallor and finger clubbing develop.

Possible TB Disease Symptoms

Night Sweats

Weakness or fatigue

Cough lasting longer than 3 weeks

Fever

Weight loss

Pain in the chest

Chills

No appetite

Coughing up blood or sputum (phlegm from inside the lungs)

Pleural Tuberculosis - 1

- Involvement of the **pleura** is common in primary tuberculosis and may result from either contiguous spread of parenchymal inflammation or, actual penetration by tubercle bacilli into the pleural space.
- **Pleural effusion** may resolve spontaneously or may be sufficiently large to cause symptoms such as fever, pleuritic chest pain, and dyspnea.
- The fluid is an exudate with a protein concentration >50% of that in serum , a normal to low glucose concentration, a pH of ~7.3 (occasionally <7.2),
- A chest radiograph reveals the effusion and, in up to one-third of cases, also shows a parenchymal lesion.
- Neutrophils may predominate in the early stage, while mononuclear cells are the typical finding later.

Pleural Tuberculosis - 2

- **Mesothelial cells are generally rare or absent.**
- **AFB** are seen on direct smear in only 10–25% of cases, but cultures may be positive for *M. tuberculosis* in 25–75% of cases; positive cultures are more common among post-primary cases.
- Determination of the pleural concentration of **adenosine deaminase (ADA)** is a useful screening test .
- Needle biopsy of the pleura is often required for diagnosis and reveals granulomas and/or yields a positive culture in up to 80% of cases.
- This form of pleural tuberculosis responds well to chemotherapy and may resolve spontaneously.

Pleural Tuberculosis - 3

Tuberculous empyema

- **Tuberculous empyema** is a less common complication of pulmonary tuberculosis.
- It is usually the result of the rupture of a cavity, into the pleural space.
- A chest radiograph shows hydro-pneumothorax with an air-fluid level.
- The pleural fluid is purulent and thick and contains large numbers of lymphocytes.

Pleural Tuberculosis – 4

Tuberculous empyema

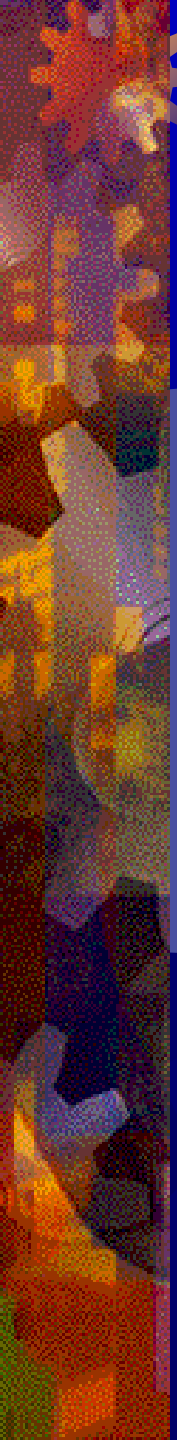
- Acid-fast smears and mycobacterial cultures are often positive.
- Surgical drainage is usually required as an adjunct to chemotherapy.
- Tuberculous empyema may result in severe pleural fibrosis and restrictive lung disease.
- Removal of the thickened visceral pleura (decortication) is occasionally necessary

HIV-Associated Tuberculosis

- Tuberculosis is one of the most common diseases among HIV-infected persons worldwide.
- A person with a positive TST who acquires HIV infection has a 3–13% annual risk of developing active tuberculosis.
- Tuberculosis can appear at any stage of HIV infection, and its presentation varies with the stage.
- Overall, sputum smears may be positive less frequently among tuberculosis patients with HIV infection than among those without HIV .
- Extra pulmonary tuberculosis is common among HIV-infected patients.

Diagnosis

- *AFB Microscopy*
- *Mycobacterial Culture*
- *Nucleic Acid Amplification*
- *Radiographic Procedures*
- *Additional Diagnostic Procedures*



THE END

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توخشنود باشی و ما رستگار