



# Tuberculosis

## TB

- Understand the epidemiology and global burden of TB
- List the sign and symptoms and risk factors of different types of TB, with particular emphasis on pulmonary TB
- Describe trends and state reasons for resurgence of pulmonary TB
- List population subgroups at risk for pulmonary TB
- Draw the cycle of infection of pulmonary TB
- Outline procedures for community diagnosis of pulmonary TB with emphasis on the limitation of each procedure
- Describe measures for prevention and control for pulmonary TB
- Describe the role of WHO to address the global burden of TB, particularly directly observed therapy short course (DOTS) for pulmonary TB

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- Golden notes
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- Extra



# Epidemiology and global burden of TB

TB IS THE TOP INFECTIOUS KILLER IN THE WORLD

IN 2017

1.6 MILLION TB DEATHS



INCLUDING 0.3 MILLION DEATHS AMONG PEOPLE WITH HIV

10 MILLION PEOPLE FELL ILL WITH TB



TB IS THE LEADING KILLER OF PEOPLE WITH HIV

AND MAJOR CAUSE OF DEATH DUE TO ANTIMICROBIAL RESISTANCE

5.8 MILLION MEN 3.2 MILLION WOMEN 1 MILLION CHILDREN

## TREATMENT OF TB INFECTION (LATENT TB)



1/4 of the global population is infected with latent tuberculosis



10-15% will go on to develop TB disease

### PRIORITY RISK GROUPS

- CHILD CONTACTS UNDER 5 YEARS
- RECEIVING ORGAN OR HEMATOLOGICAL TRANSPLANTATION
- PEOPLE LIVING WITH HIV
- RECEIVING ANTI-TB TREATMENT
- RECEIVING DIALYSIS
- HAIR SILENCERS



### SETTING/CONTEXT

- CONTACTS 5 YEARS OLD AND OLDER
- HOMELESS
- HEALTHCARE WORKERS
- PEOPLE WHO USE DRUGS
- IN PRISON

World Health Organization

## EXPANDING ACCESS TO TB PREVENTIVE TREATMENT



ONLY 36% OF PEOPLE NEWLY ENROLLED IN HIV CARE WERE STARTED ON TB PREVENTIVE TREATMENT



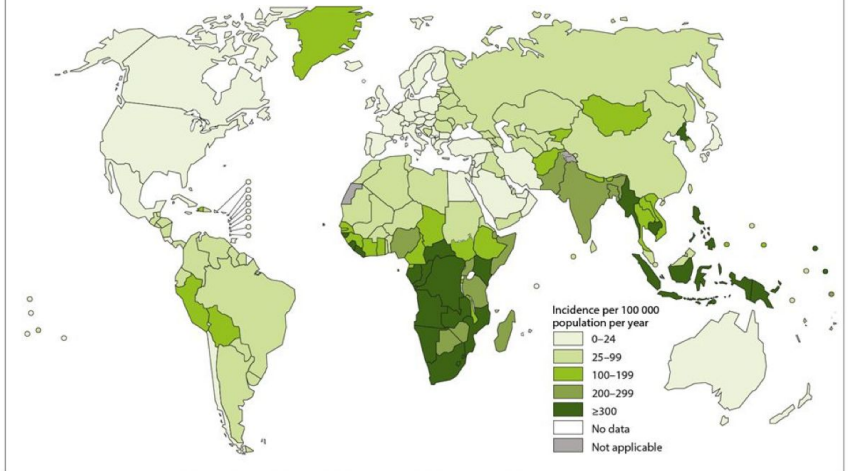
ONLY 23% OF CHILDREN UNDER 5 YEARS, ESTIMATED TO BE ELIGIBLE FOR TB PREVENTIVE TREATMENT WERE STARTED ON IT.



WHO recommends preventive treatment for people living with HIV and all contacts living in households with TB (including children under 5 years)

World Health Organization

## Estimated TB incidence rates, 2017



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

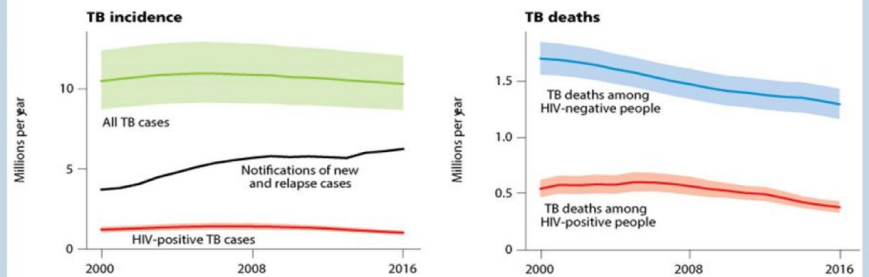
Data Source: Global Tuberculosis Report 2018, WHO, 2018.

World Health Organization

South Africa and Southeast Asia have the highest incidence of TB, although no country is spared.

World Health Organization

Global trends in the estimated number of incident TB cases and the number of TB deaths (in millions), 2000-2016



Source: Global Tuberculosis Report 2017, WHO

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# Transmission of TB

## Transmission of M. Tuberculosis

Spread by droplet nuclei<sup>1</sup>

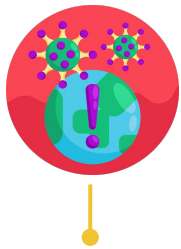
Expelled when person with infectious TB coughs, sneezes, speaks, or sings.

Close contacts at highest risk of becoming infected and prolonged exposure usually needed to establish infection.

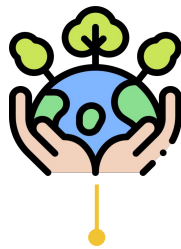
Transmission occurs from person with infectious TB disease (not latent TB infection).

Risk of transmission outdoors is reduced because of dilution and bacilli are killed by ultraviolet light.

## Probability TB Will Be Transmitted



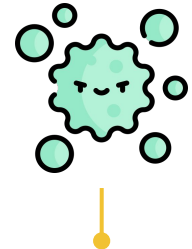
Infectiousness of person with TB.



Environment in which exposure occurred.



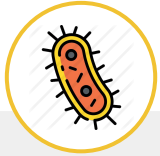
Duration of exposure



Virulence of the organism<sup>2</sup>.

1: M. Tuberculosis is transmitted in airborne particles called droplet nuclei; it can stay in the air for a long time.  
2; Highly virulent organisms will almost always lead to a disease. Factors that regulate the virulence are: the genetic makeup of the organism and the genetic makeup of the susceptible host.

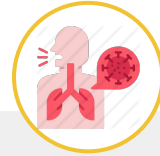
# CYCLE OF INFECTION OF PULMONARY TUBERCULOSIS



**Agent:**  
Mycobacterium tuberculosis



**Reservoir:**  
man in the form of a case

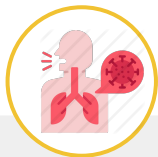


**Portal of exit:**  
Respiratory tract.

**Source of infection:**  
sputum and contaminated articles, dust.



**Transmission:**  
1- contact : Direct, indirect & droplet.  
2- Airborne: droplet nuclei and dust transmission



**Portal of entry (inlet):**  
Respiratory tract.



**Susceptible host:**  
Low standard of living, malnutrition, alcoholism, HIV/AIDS.



**Incubation period:**  
4-12 weeks

## Conditions That Increase the Risk of Progression to TB Disease



HIV infection



Diabetes mellitus



Substance abuse



Silicosis



Recent infection



Prolonged corticosteroid therapy



Chest radiograph finding suggestive of previous TB

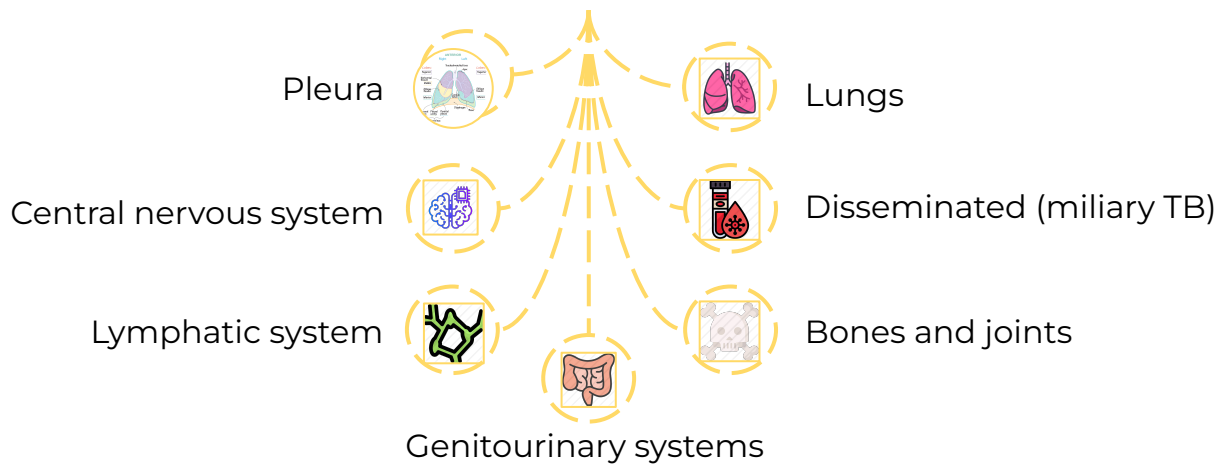


Other immunosuppressive therapy

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

Close contacts of persons known or suspected to have TB
Residents and employees of high-risk congregate settings
Health care workers (HCWs) who serve high-risk Clients
Medically underserved, low-income populations
Persons with malnutrition
Children exposed to adults in high-risk categories
Persons who inject illicit drugs

## Common Sites of TB Disease



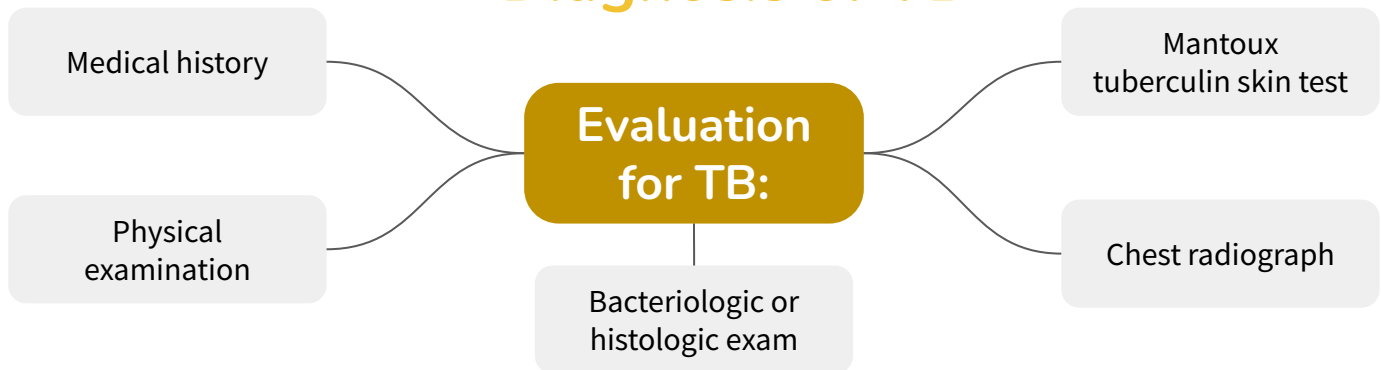
Extra		Diagnosis of TB	
Latent	Tuberculin skin test		
	Interferon- $\gamma$ release assay (IGRA)		
Active	Bacteriological confirmation (Sample obtained by 3 early morning sputum)	Acid-fast bacilli smear microscopy	
		PCR	
		Culture	
Chest X-Ray			

# Latent Tuberculosis Infection (LTBI)



- 1 defined as a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB.
- 2 There is an increased chance of developing active TB disease from the infection.
- 3 **Treatment:** Isoniazid (has been the standard treatment) for 6-9 months

## Diagnosis of TB



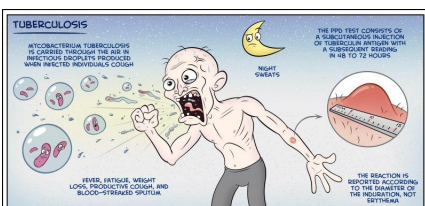
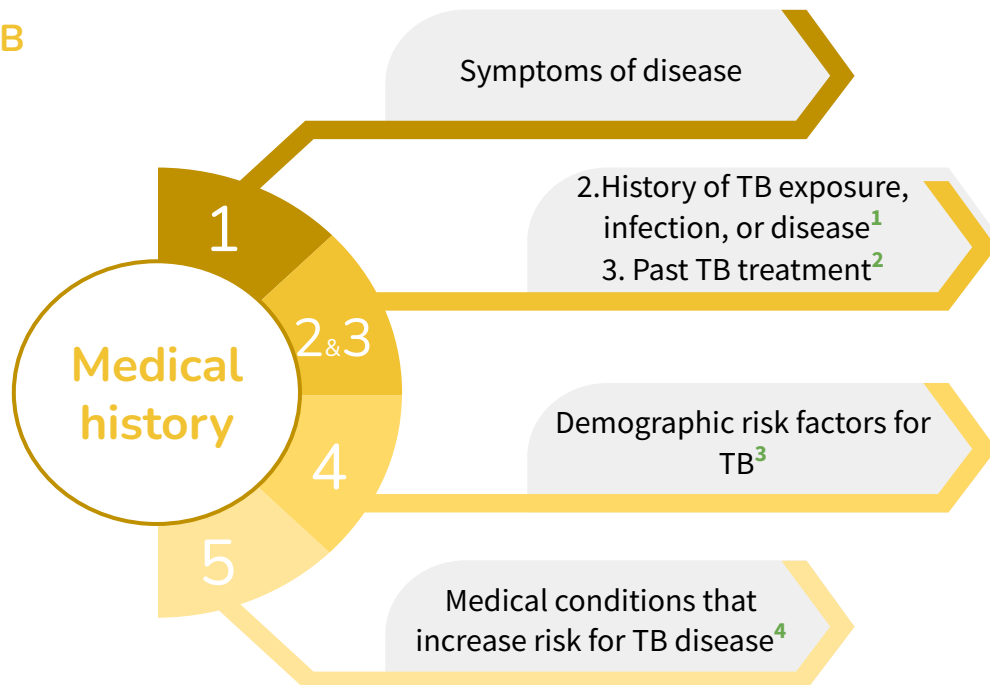
## Symptoms & medical history

### 1. Symptoms of pulmonary TB

- Productive, prolonged cough
- (duration of >3 weeks)
- Chest pain
- Hemoptysis

### 2. Systemic symptoms

- Fever
- Chills
- Night sweats
- Appetite loss
- Weight loss
- Easy fatigability



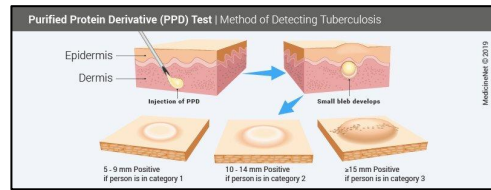
- 1: Ask about HIV, drug abuse, smoking history and pregnancy.
- 2: Or steroids therapy (as they are known to reduce the immune system).
- 3: Travel history, living in a high prevalence area.
- 4: Sarcoidosis, silicosis, prolonged COPD, chest infections, smokers, etc..

# Testing for TB Disease and Infection

- All testing activities should be accompanied by a plan for follow-up care

## Tuberculin skin test (Universal test)

Administration	Reading
<p>Steps :</p> <ul style="list-style-type: none"> <li>Inject intradermally 0.1 ml of 5 TU PPD tuberculin</li> <li>Produce wheal 6 mm to 10 mm in diameter</li> <li>Do not recap, bend, or break needles, or remove needles from syringes</li> <li>Follow universal precautions for infection control</li> </ul>	<p>Instruction :</p> <ul style="list-style-type: none"> <li>Read reaction 48-72 hours after injection</li> <li>Measure only induration not the redness</li> <li>Record reaction in millimeters.</li> </ul>
<p>Interpretation:</p> <p>- A tuberculin skin test reaction is considered positive if the transverse diameter of the indurated area reaches the size required for the specific group.</p>	



Induration size <sup>1</sup>	Group
≥5mm	<ul style="list-style-type: none"> <li>HIV-positive persons.</li> <li>Patients with organ transplants and other immunosuppressed patients.</li> </ul>
≥10mm	<ul style="list-style-type: none"> <li>Recent immigrants from countries with a high prevalence of TB.</li> <li>HIV-negative injection drug users.</li> <li>Laboratory personnel.</li> <li>Health care worker. (commonly exposed)</li> <li>Persons with increased risk of TB e.g. DM, silicosis, ...</li> </ul>
≥15mm	<ul style="list-style-type: none"> <li>Persons with no risk factors for tuberculosis</li> </ul>

## Factors that May Affect the Skin Test Reaction

Type of reaction:

**False-positive**

Possible causes:

- Non-tuberculous mycobacteria
- BCG vaccination

**False-negative**

Possible causes:

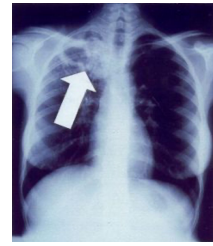
- Recent TB infection
- Very young age (< 6 months old)
- Live-virus vaccination
- Overwhelming TB disease
- HIV positive people

<sup>1</sup>: If a person was in contact with TB we should do a skin test: if it's negative (no reaction, 0mm) then we should repeat the test; if negative again we give the vaccine but if positive we give chemoprophylaxis.

# Testing for TB Disease and Infection

## Chest Radiograph (TB x-rays images are important)

- 1 Abnormalities often seen in apical or posterior segments of upper lobe or superior segments of lower lobe.
- 2 May have unusual appearance in HIV-positive persons.
- 3 Cannot confirm diagnosis of TB



Arrow points to cavity in patient's right upper lobe

## Sputum Specimen Collection



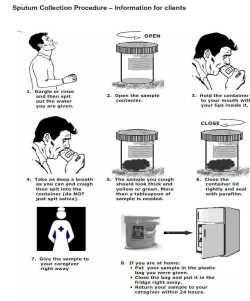
Obtain 3 sputum specimens for smear examination and culture.



Persons unable to cough up sputum, induce sputum, bronchoscopy or gastric aspiration

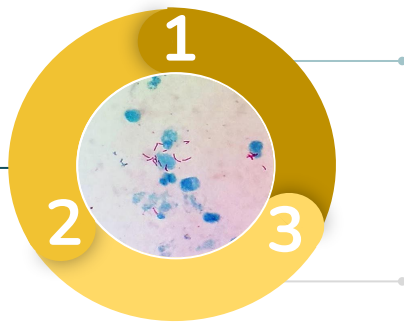


Follow infection control precautions during specimen collection



## Smear Examination

Results should be available within 24 hours of specimen collection.



Strongly consider TB in patients with smears containing alcohol acid-fast bacilli (AAFB).

Presumptive diagnosis of TB.

## Culture

- Use to **confirm** diagnosis of TB.
- Culture all specimens, even if smear negative.
- Results in 4 to 14 days when liquid medium systems used.



## Blood Tests for TB Infection

### Interferon Gamma Release Assays (IGRA)

#### Quantiferon

#### Definition

is a simple-blood test, a modern alternative to the tuberculin skin test that can aid in diagnosing M. tuberculosis infection. highly specific and sensitive

#### Advantages

- Requires a single patient visit to conduct the test.
- Results can be available within 24 hours.
- Prior BCG (Bacille Calmette-Guérin) vaccination does not cause a false-positive Quantiferon result. (Whereas in tuberculin test, prior BCG vaccination did cause a false-positive result.)
- A positive test result suggests that M. tuberculosis infection is likely; a negative result suggests that infection is unlikely. (Due to its high sensitivity and specificity.)
- Used to detect persons with Latent TB infection.

#### Disadvantage

They **do not** help differentiate latent tuberculosis infection (LTBI) from tuberculosis disease.



# Treatment of TB Infection

## DIRECTLY OBSERVED TREATMENT, SHORT COURSE (DOTS) CHEMOTHERAPY

- Health care worker watches patient swallow each dose of medication.
- Consider DOT for all patients. (Treatment with the DOTS strategy is the current WHO recommended tuberculosis control strategy)
- DOT can lead to reductions in relapse and acquired drug resistance.
- Use DOT with other measures to promote adherence.

### The five elements of DOTS:

1. Political commitment with increased and sustained financing
2. Case detection through quality-assured bacteriology
3. Standardized treatment, with supervision and patient support
4. An effective drug supply and management system
5. Monitoring and evaluation system, and impact measurement

### TB for HIV-Negative persons



- **Include four drugs of initial regimen:**

1. Isoniazid (INH)
2. Rifampicin (RIF)
3. Pyrazinamide (PZA)
4. Ethambutol (EMB) or Streptomycin

- Adjust regimen when drug susceptibility result are known

### Extra-pulmonary TB



(Bone and Joint TB, Miliary TB, or TB Meningitis in Children)

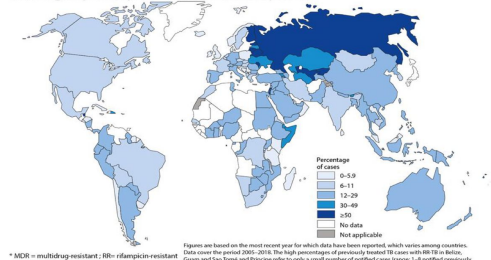
- In most cases, treat with same regimens used for pulmonary TB
- Treat for a minimum of 12 months

### Multidrug-Resistant TB (MDR TB)



- Presents difficult treatment problems
- Treatment must be individualized
- Clinicians unfamiliar with treatment of MDR TB should seek expert consultation
- **Always use DOT to ensure adherence**

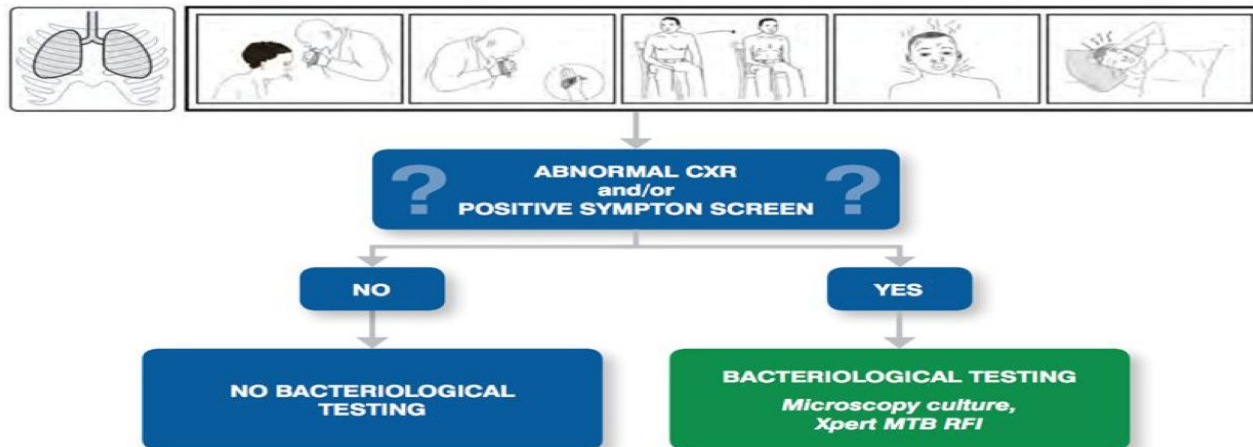
Percentage of previously treated TB cases with MDR/RR-TB\*



[Click here to go to the WHO website](#)

# Screening

FIG. 3. WHO's recommended screening strategy for TB prevalence surveys (21)

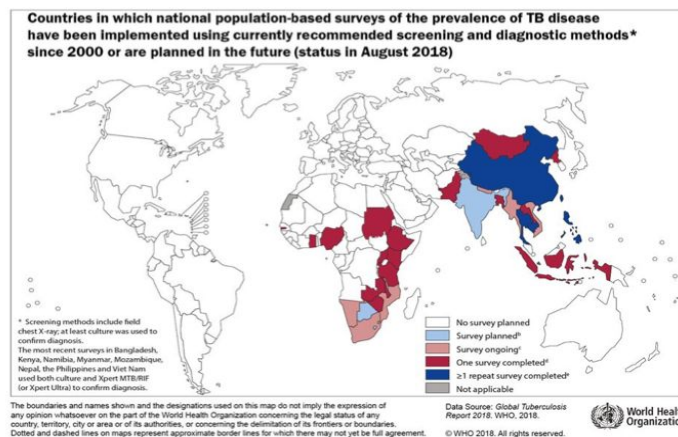


CXR: chest X-ray.

## WHO EFFORTS

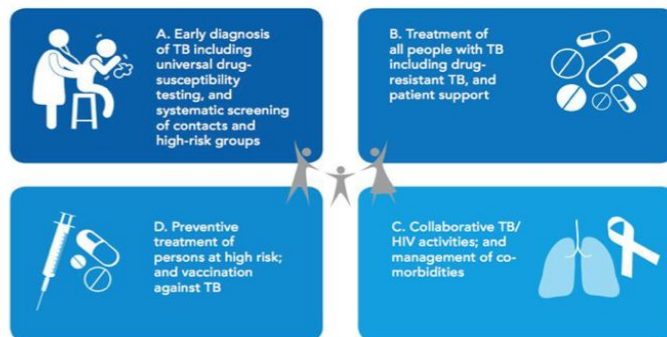
### STRATEGY

**A WORLD FREE OF TB**  
**ZERO deaths, disease, and suffering due to TB**  
**END THE GLOBAL TB EPIDEMIC**



## INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

### How pillar 1 works : Key actions



	MILESTONES		TARGETS	
	2020	2025	SDG* 2030	END TB 2035
<b>Reduction in number of TB deaths</b> compared with 2015 (%)	35%	75%	<b>90%</b>	<b>95%</b>
<b>Reduction in TB incidence rate</b> compared with 2015 (%)	20%	50%	<b>80%</b>	<b>90%</b>
<b>TB-affected families facing catastrophic costs due to TB (%)</b>	0%	0%	<b>0%</b>	<b>0%</b>

\* The United Nations Sustainable Development Goals (SDGs) include ending the TB epidemic by 2030 under Goal 3.

# Preventing and Controlling TB

## Three priority strategies:

# 1

Identify and treat all persons with TB disease

# 2

Identify contacts to persons with infectious TB; evaluate and offer therapy

# 3

Test high-risk groups for latent TB infection (LTBI); offer therapy as appropriate

## BCG Vaccination

In countries where tuberculosis is prevalent and the risk of childhood infection is high.

the national policy is to administer **BCG** very early in infancy either:

At **birth** or at **6 weeks of age** with other immunizing agents such as DPT and polio. (In KSA, BCG vaccine is given at 6 months.)

## Health care providers should work with health department in the following areas :

- Overall planning and policy development
- Identification of persons with clinically active TB
- Management of persons with disease or TB suspects
- Identification and management of persons with TB
- Laboratory and diagnostic services
- Data collection and analysis
- Training and education

### Data Collection and Analysis

- TB reporting required in every state.
- All new cases and suspected cases promptly reported to health department.
- All drug susceptibility results sent to health department.

### Training and Education

TB control programs should:

1. Provide training for program staff.
2. Provide leadership in TB education to the community.
3. Ensure community leaders, clinicians, and policymakers are knowledgeable about TB.
4. Educate the public.

# Why is it a concern for Saudi Arabia? <sup>1</sup>

## THE DUAL EPIDEMIC OF TB AND DIABETES - A deadly linkage

- People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active tuberculosis.
- Diabetes triples a person's risk of developing TB. About 15% of TB cases globally may be linked to diabetes
- TB can temporarily cause impaired glucose tolerance which is a risk factor for developing diabetes
- The likelihood that a person with TB will die or relapse is significantly higher if the person also has diabetes.
- A large proportion of people with diabetes as well as TB are not diagnosed, or are diagnosed too late.

## THE DUAL EPIDEMIC OF TB AND DIABETES - Key actions

- Early detection can help improve care and treatment outcomes of both diseases. AM people with TB should be systematically screened for diabetes, Systematic screening for TB in people with diabetes should be considered in settings with high TB prevalence.
- WHO-recommended treatments should be rigorously implemented for people with TB/diabetes.
- It is important that proper care for diabetes is provided to minimize the risk of TB
- Diabetes prevention on population level also helps prevent TB
- A joint response is needed to ensure coordinated clinical management and address common health system bottlenecks and social determinants

## A strong association



- Smoking substantially increases the risk of tuberculosis (TB) and death from TB
- More than 20% of global TB incidence may be attributable to smoking

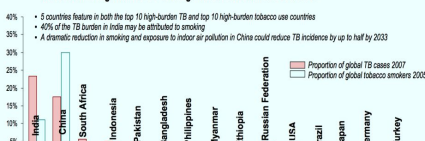


- Controlling the tobacco epidemic will help control the TB epidemic
- Smoking is a risk factor for TB, independent of alcohol use and other socioeconomic risk factors



- Smoking increases the risk of TB disease by more than two and a half times
- The WHO monograph on TB and tobacco describes other linkages and evidence

Correlation of high-burden TB and high-burden tobacco-use countries



### THE TUBERCULOSIS EPIDEMIC

- 2 billion people are infected with the TB bacilli
- TB is a disease of poverty with the vast majority of deaths occurring in low- and middle-income countries with more than half of all deaths occurring in Asia
- 9.27 million new TB cases in 2007
- 1.75 million people died from TB in 2007
- 5% of all TB cases have multidrug-resistant TB

### THE TOBACCO EPIDEMIC

- More than 1 billion people smoke with nearly 70% of them living in low- and middle-income countries
- Tobacco use is the leading preventable cause of death
- More than 5 million people die per year from tobacco use. Unchecked, the epidemic will kill more than 8 million people per year by 2030

1: It's a concern due to the high number of immigrants coming from countries with high TB prevalence.

The highest prevalence of TB in Saudi Arabia is in Jazan, Jeddah, Medina. Due to the low socioeconomic status, crowding and lots of immigrants.

# Practice Questions

**Q1:** Tuberculin skin test is considered +ve in which group of the following?

A. >5 Redness in patients with HIV

B. >5 Induration in patients with HIV

C. >5 in all patients

D. > 10 in all patients

**Q2:** Which of the following can result in a false +ve tuberculin skin test?

A. BCG vaccine

B. Recent infection

C. HIV +ve

D. Overwhelming TB

**Q3:** Which of the following is considered a risk factor for TB

A. Diabetes mellitus

B. Crowded places (e.g. prison)

C. Migration from countries with a high TB incidence

D. All are correct.

**Q4:** A patient is suspected to have TB, which of the following is the first step investigation?

A. Blood culture

B. Chest CT

C. Sputum collection

D. Chest X ray

**Q5:** A modern alternative to tuberculin skin test that is high sensitive and specific in diagnosing M. Tuberculosis infection

A. Smear examination

B. Blood culture

C. Quantiferon

D. Sputum collection

**Q6:** A person have got tuberculin test negative then after repetition of test the result showed positive what is the appropriate next step ?

A. Give chemoprophylaxis

B. Give vaccine

C. Repeat the test

D. Give both A and B

**Answer key:**

1 (B) , 2 (A) , 3 (D) , 4 (D) , 5 (C) , 6 (A)

# Team leaders

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