



PATIENT'S SYMPTOMS



Chills and Fever



Night sweats



Chronic productive cough



PATIENT'S SIGNS

- > Fever of 38.5°C
 - Fever: above 37.6°C (axillary or oral) and 38.1°C (in ear)

- Crackles in the right lung
 - o clicking, rattling, or crackling noises emitted during inhalation
 - caused by exudates dislodged by the cough
- Decreased breath sounds in the right lower lung
 - caused by fluid(secretions) in the lungs

[1][2][3][4]

ADDITIONAL COMMON SYMPTOMS

- Pleuritic chest pains
- Difficulty to sleep
- Unproductive coughs
- Loss of appetite
- Fatigue





ADDITIONAL COMMON SIGNS

• Tender or swollen lymph nodes



- Weight loss
- Hemoptysis due to erosion of blood vessels



HISTORY OF PRESENT ILLNESS (HPI)

DIAGNOSES

Generate different diagnoses

MEDICAL DECISION-MAKING

Guiding medical decision-making

Analyzing the patient's illness

ANALYSIS

INVESTIGATION

Investigating the

patient's condition

[6]

ROBERT'S CASE

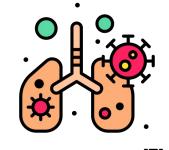
MIGRATED FROM INDIA

INCREASED LEVELS OF STRESS

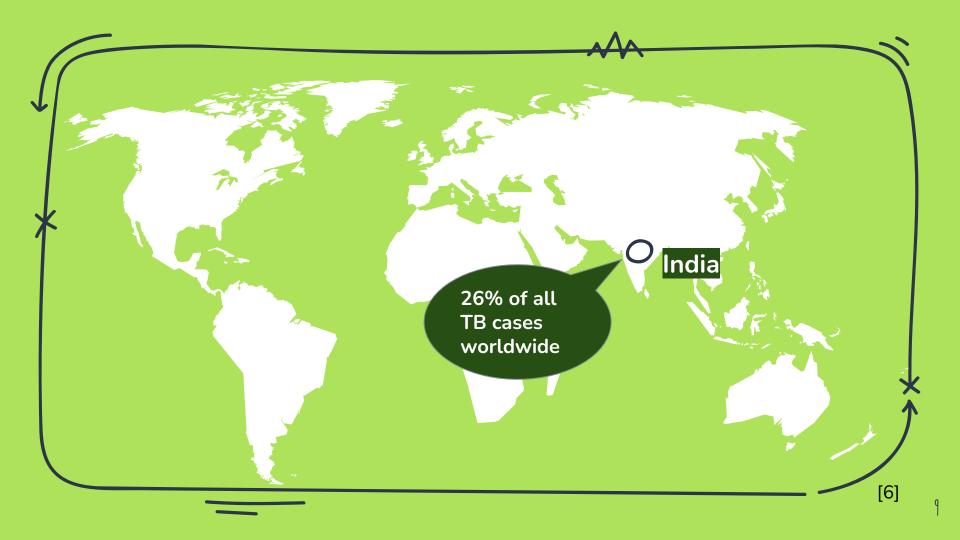
INCREASED
SUSCEPTIBILITY
TO TB













192 cases

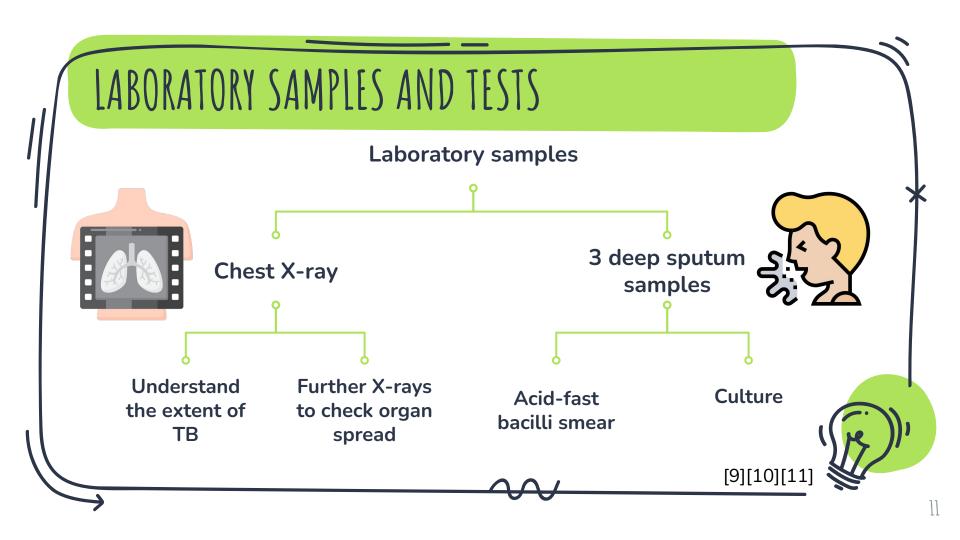
per 100,000 people

34%

Worldwide TB mortality among HIV- persons

38%

Overall number of TB deaths among HIV+ and HIV- people



ACID-FAST BACILLI SMEAR

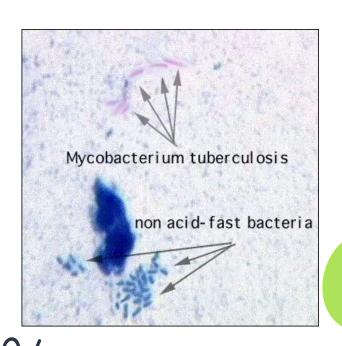
The sputum is smeared onto a glass slide



Use a specific dye to make Mtb visible under microscope



Count the acid-fast bacilli found in the smear



ACID-FAST BACILLI SMEAR (CONT.)

Smear Result (Number of AFB observed at 1000X magnification)	Smear Interpretation	Infectiousness of Patient
4 + (>9/field)	Strongly positive	Probably very infectious
3+ (1-9/field)	Strongly positive	Probably very infectious
2+ (1-9/10 fields)	Moderately positive	Probably infectious
1+ (1-9/100 fields)	Moderately positive	Probably infectious
+/- (1-2/300 fields)*	Weakly positive [†]	Probably infectious
No acid-fast bacilli seen	Negative	Probably not infectious**

System for reporting the number of acid-fast bacilli

^{*} There are variations on labeling for this result, and include listing the number of AFB counted.

[†] Laboratories may report these smear results as "doubtful" or "inconclusive" based on CDC guidelines.

ACID-FAST BACILLI SPUTUM CULTURE

Length of development

Drug susceptibility test

Expected results

Solid media

Positive: 4 weeks

Negative: no development

in 8 weeks

Employed

Positive: bacteria

exists

Negative: no bacteria

Liquid media Positive: 2 weeks

Employed

Positive: bacteria

exists

Negative: no bacteria

DEFINITIVE DIAGNOSIS







Mycobacteria stained with Fluorescent stain

Mantoux tuberculin skin test

Laboratory Diagnosis of Mycobacterium tuberculosis Infection





M. Tuberculosis colonies in LJ medium

GeneXpert MTB/RIF Assay

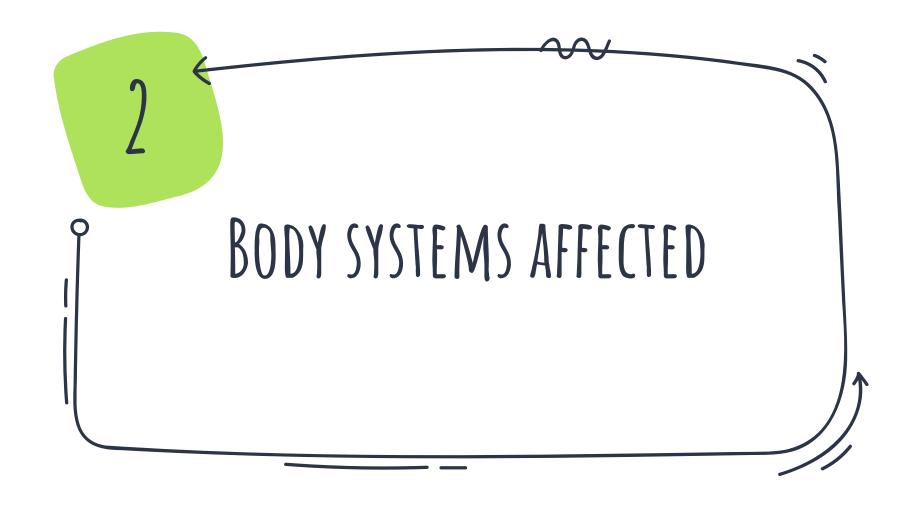
microbeonlin

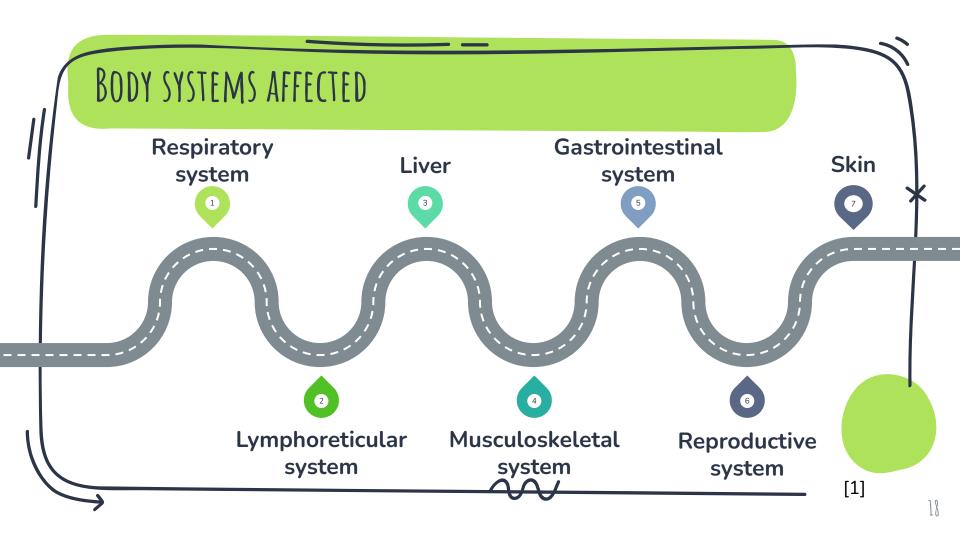
- Requires a positive
 mycobacterial culture or
 nucleic acid amplification test
 (NAAT)
- A single negative NAAT result does not rule out TB
- Sputum culture remains the gold standard

[12]

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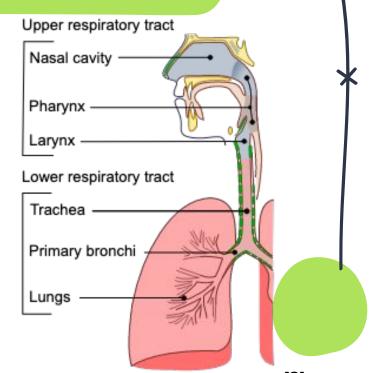




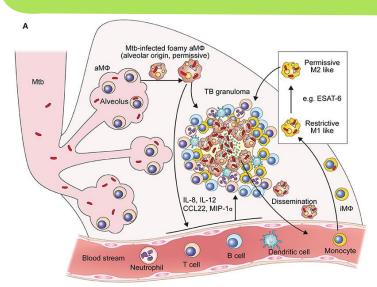
AFFECTED COMPARTMENTS OF THE RESPIRATORY SYSTEM

Lungs are mostly affected due to its gas exchange function

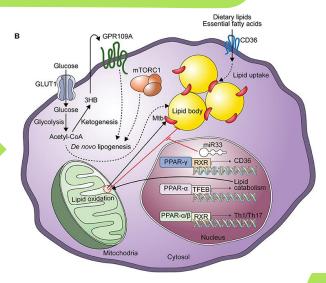
Mtb infection occurs due to airborne dried mucous droplets



EARLY STAGES OF TB INFECTIONS

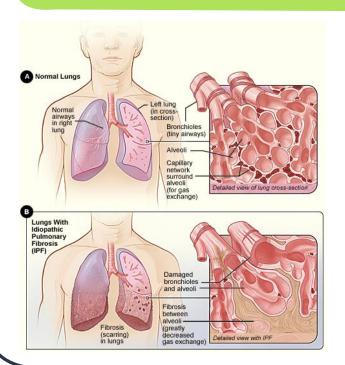


Alveolar macrophages initiate inflammatory response, leading to formation of granuloma.



Lipid pneumonia lesions lead to caseous necrosis formation, then coughed out by the patient, leaving a cavity

EARLY STAGES OF TB INFECTIONS (CONT.)



Extracellular matrix proteins deposit in lungs; normal lung tissue replaced with collagenous tissue

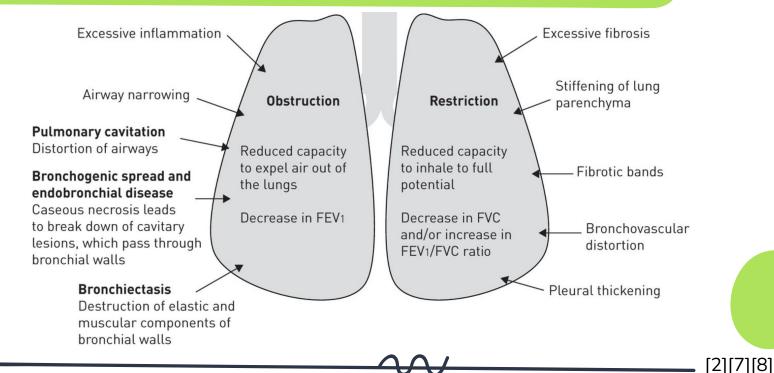


Lung walls become thick and stiff



Bronchiectasis may develop; bronchial walls lose elasticity and bronchi dilate

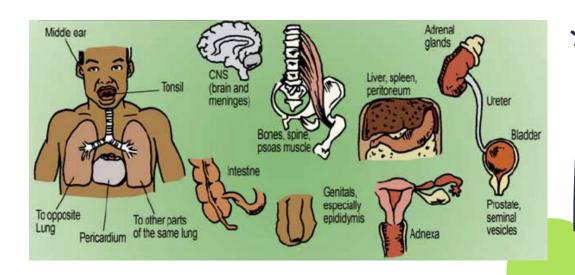
CONSEQUENCES OF TB INFECTIONS



WHAT IF LEFT UNTREATED?

May spread via:

- 1. Hematogenous route
- 2. Lymphatic route
- Descending direct spread
- 4. Sexual transmission



TB LYMPHADENITIS

in the NECK



Locations:

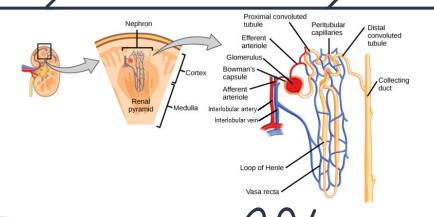
- Anterior and posterior triangles of the neck
- supraclavicular and axillary regions
- a sinus tract or ulceration of the surrounding skin (aka Scrofula)

EFFECTS ON THE KIDNEY

Granulomatous lesion in the glomeruli burst into renal tubule

Become caught up in the Loop of Henle

Cause Granulomatous progression, necrosis, cavitation



EFFECTS ON THE CENTRAL NERVOUS SYSTEM

TB can cross the blood-brain barrier and the blood-cerebrospinal fluid barrier

Can also enter by hijacking neutrophils and macrophages









TB stimulates an immune response, leading to inflammation and brain damage



Exudate forms and leads to edema and perivascular infiltration, resulting in encephalitis

[11][12][13][14][15]

BONE AND JOINT TB

Infection begins in the anterior-inferior portion of a vertebral body

Spreads beneath the anterior longitudinal ligament

Spreads to neighboring vertebral bodies, causing illness



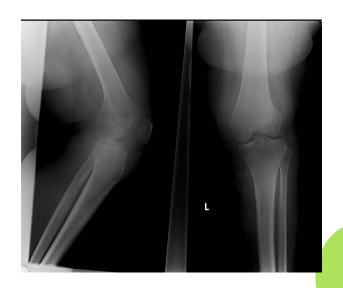
BONE AND JOINT TB (CONT.)

Tuberculous arthritis:

- Affects major, weight-bearing joints
- Symptoms: swelling, discomfort and loss of function

Advanced illness:

- Paraspinous fluid collections
- Compression of the spinal cord or peripheral nerves



GASTROINTESTINAL TB LOCATIONS

Ileocecal areas

Jejunoileal areas

anorectal areas

Most common

Hepatosplenic

biliary tract

pancreatic

Quite uncommon

Esophagus

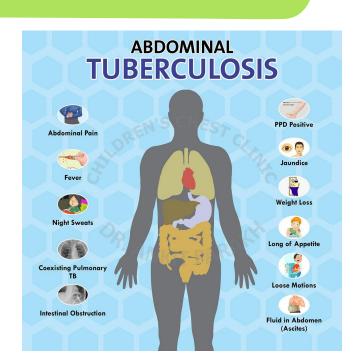
Stomach

Duodenum

Have been reported

GASTROINTESTINAL TB SYMPTOMS

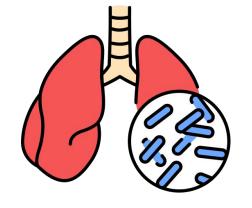
- Persistent abdominal pain
- Constitutional symptoms
- Right lower quadrant mass
- Ascites



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85%

Treatment success rate

60%

Mortality rate due to inappropriate treatment and multidrug resistant strains of TB

[1]

TREATMENT PERIOD FOR TB

Completely susceptible illness

Extrapulmonary TB

TB meningitis and TB pericarditis

Treatment duration

6 months for rifampin-based regimens

up to 9 months

corticosteroids administered for the first 1 to 2 months

[3][4][5]



STANDARD TREATMENT REGIMEN

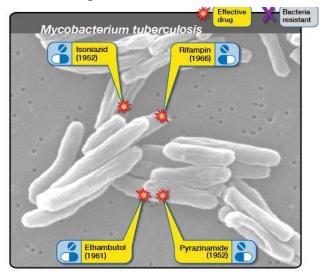
- 1. Isoniazid
- 2. Rifampin

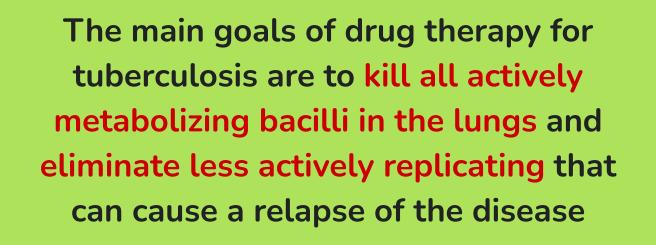
First 2 months

- 3. Pyrazinamide
- 4. Ethambutol

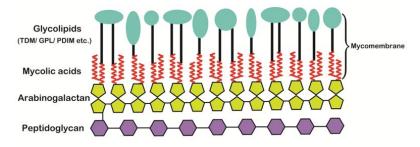
May be discontinued if bacteria are susceptible to the other 3 drugs

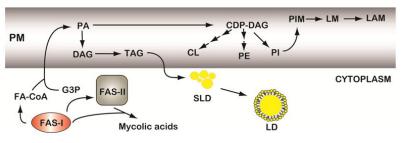
Following 4 months





MYCOLIC ACID - STRONG TARGET FOR DRUGS



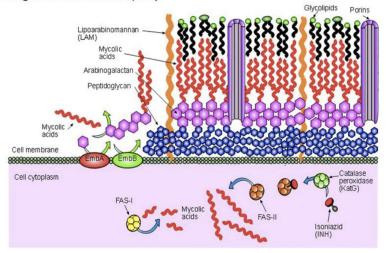


- X A component of Mtb cell wall
- Prevent chemical damage and dehydration of cell wall
- Prevent hydrophobic antibiotics from penetrating cell wall
- X Allow bacteria to grow within macrophages

[6][7]

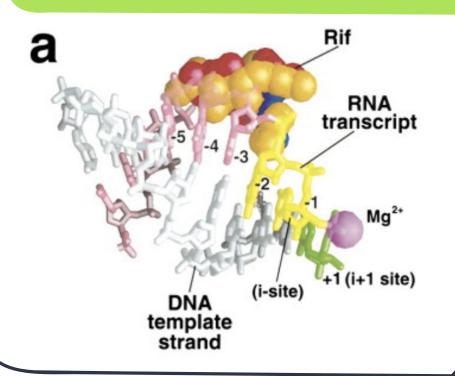
ISONIAZID MECHANISM OF ACTION

Drug action: Isoniazid (INH)



- Prodrug of isoniazid activated into its acyl radical form via catalase-peroxidase enzyme
- Catalyze the formation of the activated isoniazid intermediate from the prodrug and bind to the InhA protein
- Inhibit fatty acid synthesis by catalyzing the reduction of long-chain trans-2-enoyl-ACP in the type II fatty acid biosynthesis pathway of the bacteria
- 4. Inhibition of InhA disrupts the biosynthesis of the mycolic acid, leaving the bacterium vulnerable to destruction by the immune system

RIFAMPIN MECHANISM OF ACTION



Bind to the B subunit of the DNA-dependent RNA polymerase

➤ Block RNA transcription (RNA elongation at the 5' end)

Block bacterial RNA synthesis

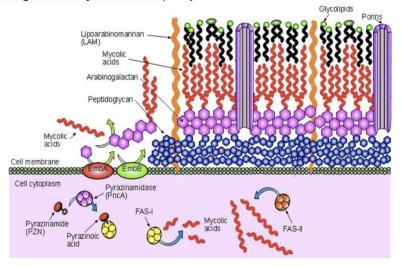
[9]

DOWNSIDES OF RIFAMPIN

- X Does not interfere with substrate binding/catalytic activity
- X If the RNA polymerase has already synthesized a transcript that has entered the elongation phase, it is completely resistant to the drug
- Must be used with isoniazid due to short-lived improvements and increased drug resistance

PYRAZINAMIDE MECHANISM OF ACTION

Drug action: Pyrazinamide (PZN)



- Targets non-growing bacilli
- converted to pyrazinoic acid via nicotinamidase encoded by the pncA gene
 - acidification of the bacteria leading to inhibition of crucial enzymes
 - inhibiting fatty acid synthesis and disrupting bacteria growth and replication
 - de-energize the membrane, inhibiting protein and RNA synthesis
 - inhibit ribosomal protein S1, preventing trans-translation

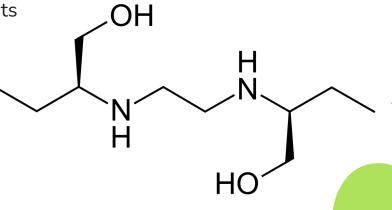
[11][12]

ETHAMBUTOL MECHANISM OF ACTION

Reducing the production of lipoarabinomannan and arabinogalactan which are cell wall components



Prevents bacterial replication as it needs cell walls to divide



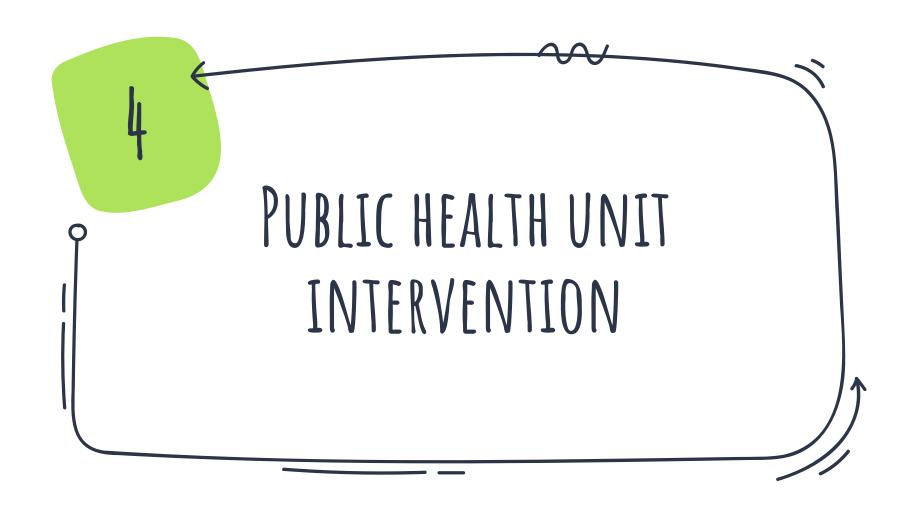
TREATMENT PRECAUTIONS

- Incorrect usage of medication could lead to:
 - ineffective treatment
 - o a higher chance for future complications
 - Resistant forms of TB
- Treatment of TB will take longer than other bacterial infections



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>3,000,000

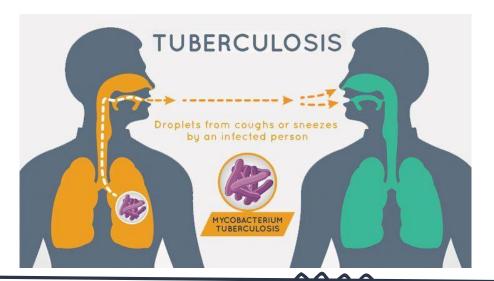
People get killed by TB each year

33%

World's population infected with latent TB

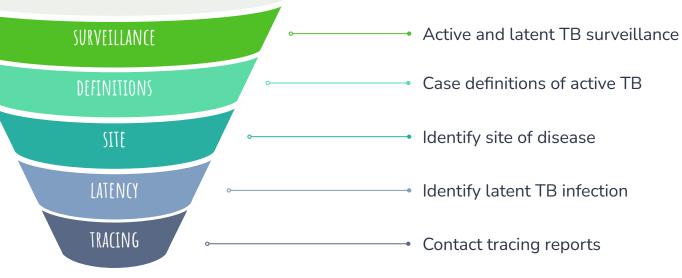
TRANSMISSIBILITY OF TB

- X Highly transmissible via spread in the air
- Public Health unit should be notified within 24 hours to prevent disease outbreaks





DETECTION OF POTENTIAL CASES



[4][5]

LABORATORIES

- Should report suspected or confirmed cases of TB, including:
 - Date
 - Results of tests
 - Name of physician
 - Address of physician
- Failure to submit reports will results in citations and fines



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THANKS!

