TUBERCULOSIS

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History of TB

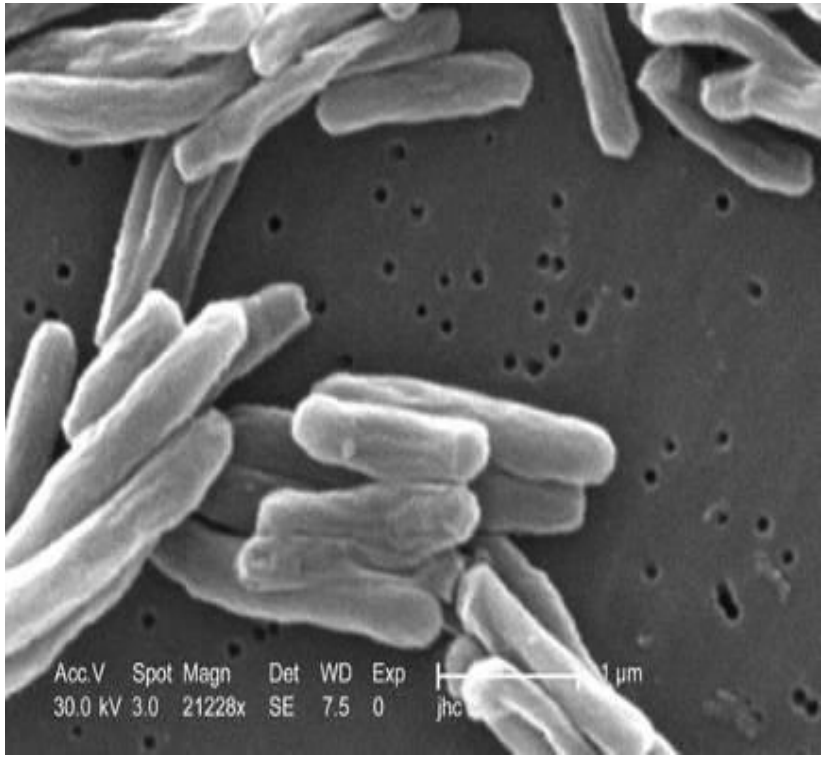
- TB has affected humans for millennia
- Historically known by a variety of names, including:
  - Consumption
  - Wasting disease
  - White plague
- TB was a death sentence for many

Vintage image circa 1919
Image credit: National Library of Medicine

History of TB

Scientific Discoveries in 1800s

- Until mid-1800s, many believed TB was hereditary
- 1865 Jean Antoine-Villemin proved TB was contagious
- 1882 Robert Koch discovered *M. tuberculosis*, the bacterium that causes TB

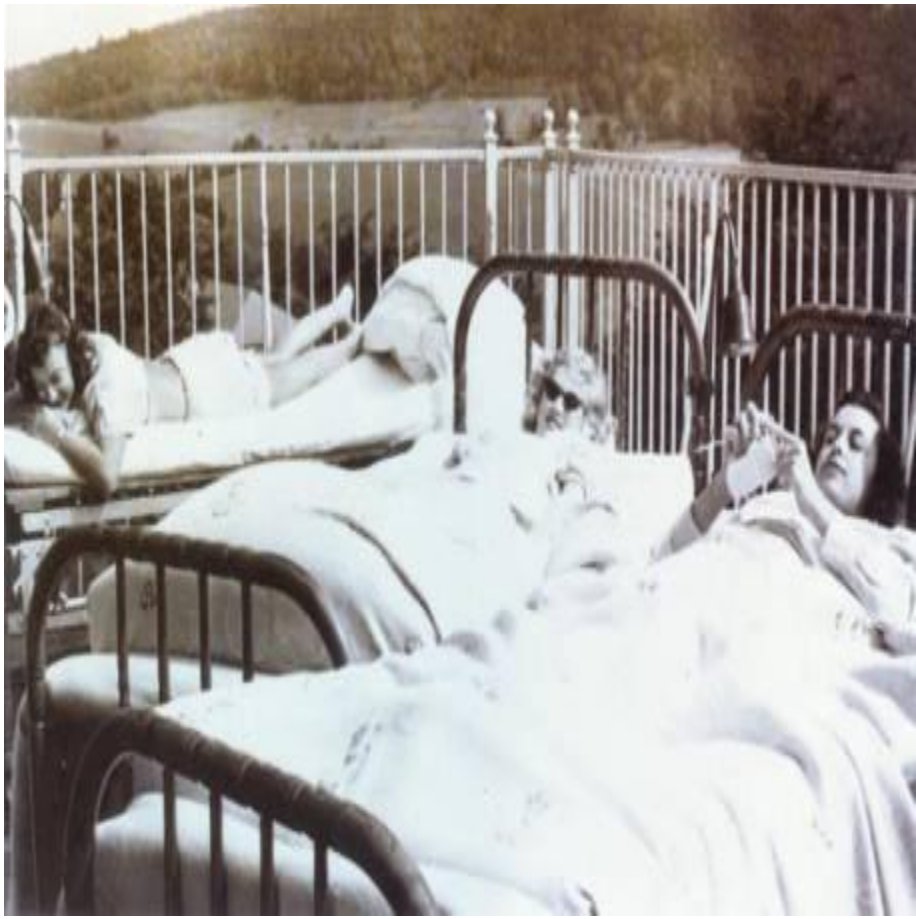


Mycobacterium tuberculosis
Image credit: Janice Haney Carr

History of TB

Sanatoriums

- Before TB antibiotics, many patients were sent to sanatoriums
- Patients followed a regimen of bed rest, open air and sunshine
- TB patients who could not afford sanatoriums often died at home

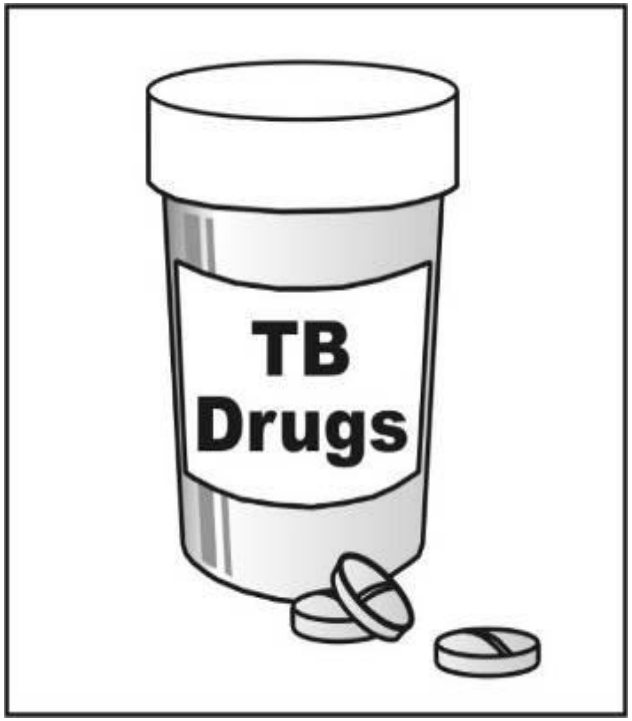


Sanatorium patients resting outside

Breakthrough in the Fight Against TB

Drugs that could kill TB bacteria were discovered in 1940s and 1950s

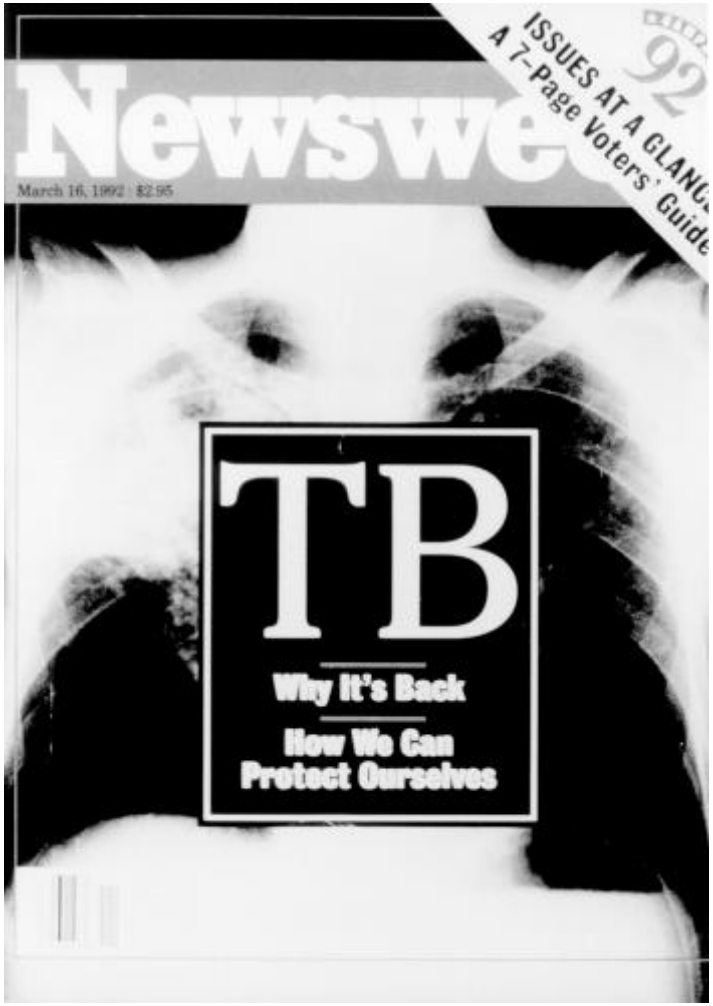
- Streptomycin (SM)-1943
- Isoniazid (INH) and *p*-aminosalicylic acid (PAS) - between 1943 and 1952



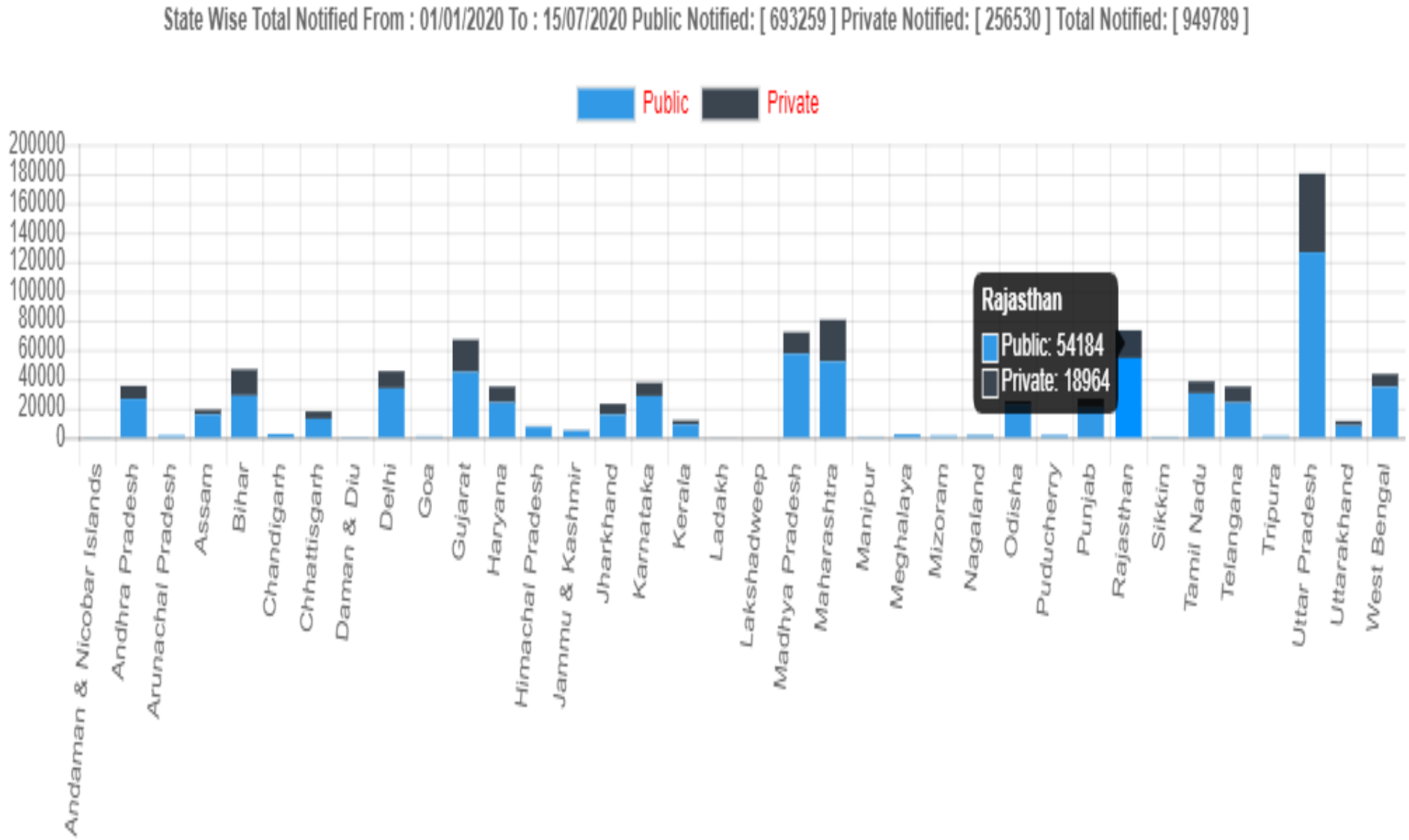
TB Resurgence

- Increase in TB in mid 1980s

- **Contributing factors:**
  - Inadequate funding
  - HIV epidemic
  - Increased immigration
  - Spread in homeless shelters and correctional facilities
  - Multidrug-resistant TB



March 16, 1992 Newsweek Magazine Cover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Rajasthan
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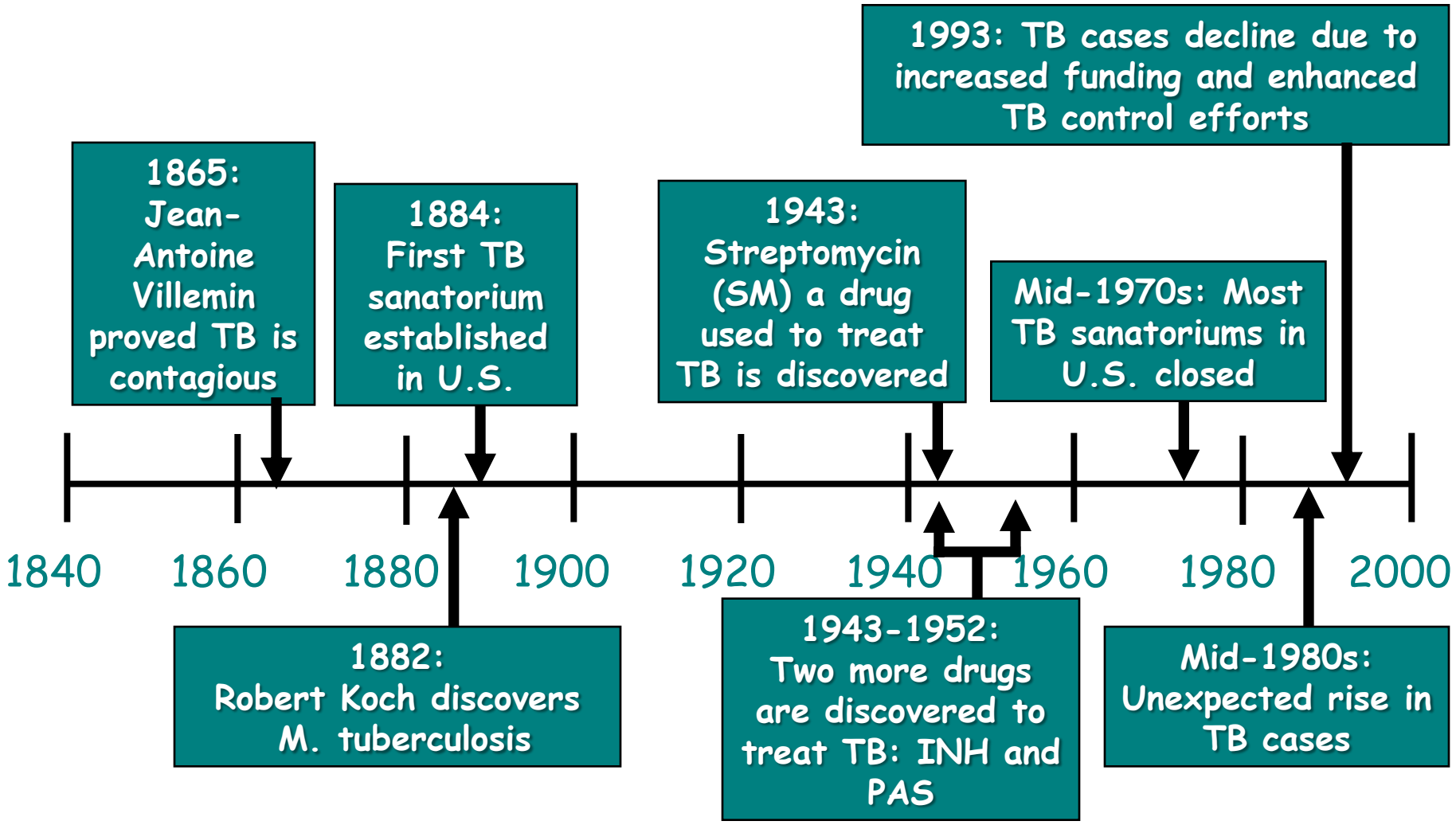
Private: 18964
Andaman & Nicobar Islands
Andhra Pradesh
Arunachal Pradesh
Assam
Bihar
Chandigarh
Chhattisgarh
Daman & Diu
Delhi
Goa
Gujarat
Haryana
Himachal Pradesh
Jammu & Kashmir
Jharkhand
Karnataka
Kerala
Ladakh
Lakshadweep
Madhya Pradesh
Maharashtra
Manipur
Meghalaya
Mizoram
Nagaland
Odisha
Puducherry
Punjab
Rajasthan
Sikkim
Tamil Nadu
Telangana
Tripura
Uttar Pradesh
Uttarakhand
West Bengal

TB History Timeline



TUBERCULOSIS

IS

PREVENTABLE AND CURABLE

WORLD TB DAY 2020

2020

It's time to End TB!

58,000,000

lives saved between 2000 and 2018 by global efforts to end TB

10,000,000

people fell ill with TB in 2018

1,500,000

people died of TB in 2018

484,000

people fell ill with drug-resistant TB in 2018

Source : https://www.cdc.gov/tb/worldtbday/default.htm

Tuberculosis is the world's top infectious disease killer.

Reaching people early with care can prevent death and suffering.

World Health Organization

It's time to Find.Treat.All.#EndTB

It's time

to ensure universal access to rapid molecular diagnostic tests

Affordable and rapid diagnostic tests are the first step towards timely tuberculosis care.

World Health Organization

END TB

1 in 3 people with tuberculosis (TB) miss out on access to quality care.

All people with TB deserve affordable and reliable health services wherever they access them.

World Health Organization

2018 — UN High-Level Meeting target: 40 million people with TB access care — 2022

END TB

It's time

for universal access to quality TB care

1 in 2 children with tuberculosis (TB) miss out on access to quality TB care, risking serious illness and death.

World Health Organization

2018 — UN High-Level Meeting target: 3.5 million children with TB access care — 2022

END TB

It's time

to ensure no child is left behind

It's time

to stand against stigma and discrimination

Health is a human right. Respect and dignity in healthcare settings and in communities ensures that this right is respected for people with TB.

World Health Organization

END TB

1 in 4 people have tuberculosis (TB) infection. People in close contact with TB patients and those living with HIV are at high risk of developing TB. TB preventive treatment can stop TB infection from turning into disease.

World Health Organization

2018 — UN High-Level Meeting target: >30 million people receive TB preventive treatment — 2022

END TB

It's time to prevent TB to end TB

GLOBAL SCENARIO

- It is the deadliest infectious killer in the world…but now its COVID-19 due to pandemic
- Each day..> 4,000 people lose their lives to TB
- And around 30,000 get TB infection daily
- In children 0-14 years :10 lakh (world) and 2.3 lakh died from TB

How many people have TB in India?

The World Health Organisation (WHO) TB statistics for India for 2018 give an estimated incidence figure of 2.69 million cases.

The TB incidence is the number of new cases of active TB disease during a certain time period (usually a year). The TB incidence figure for India is interim pending the results from the national TB prevalence survey planned for 2019/2020.

Estimates of TB Burden (WHO 2018)	Number	Rate per 100,000 Population
Incidence of TB cases (includes HIV + TB)	2.690 million	199
Incidence (HIV+TB only)	92,000	6.6
Incidence (MDR/RR-TB)	130,000	9.6
Mortality (deaths) (excludes HIV+TB)	440,000	32
Mortality (deaths) (HIV+TB only)	9,700	0.72

Some facts ….

- About one-quarter of the world's population has latent TB
- People infected with TB bacteria have a 5-15% lifetime risk getting TB disease.
- People with co morbidities are more prone.
- People with active TB can infect 5-15 other people through close contact over the course of a year
- Mortality among HIV +ve with TB is almost 100% and HIV –ve around 45%

INDIA

- India is the highest TB burden country in the world having an estimated incidence of 26.9 lakh cases in 2019 (WHO).
- In 2019,due to good surveillance 24 lakh notification was there… an increase of over 12% was observed as compared to 2018.
- Of the 24 lakh, 90% were incident cases of TB (N=21.6 lakhs) (New and Relapse/ Recurrent).
- And the incident notification rate of approx.159 cases/lakh against the estimated incidence rate of 199 cases lakh population.

Magnitude of Burden

Estimates of TB Burden (2018)	Global (Million)	India	% of Global
Incidence TB cases	10	2.69 Million	27%
Mortality of TB	1.2	440,000	31%
Incidence HIV TB	0.86	92,000	9%
Mortality of HIV-TB	0.25	9,700	4%
MDR-TB	0.5	130,000	24%
Children with TB	1.12	342,000	31%

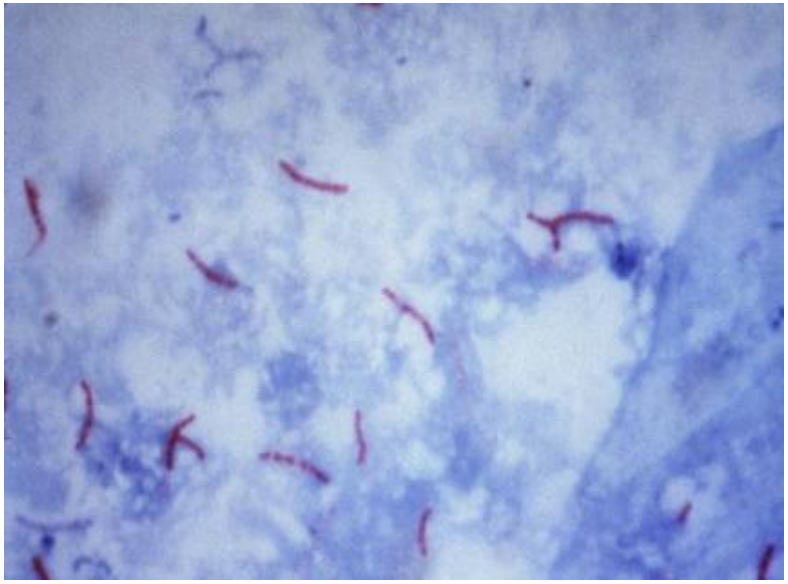
Source :NTEP Training module for MO ; 2020

AGENT

- Caused by Mycobacterium tuberculosis
- Small, acid fast , aerobic, non-motile, non-capsulated and non-sporing bacillus
- Facultative intracellular parasite
- Human and Bovine strain
- Indian strain is less virulent
- Atypical mycobacteria ..
- TB bacilli can not stand direct sunlight.
- Killed by heat (60^{o} for 15-20 minutes) and disinfectants like phenol & cresol
- Stand drying and remain viable in dried sputum for long periods.

Types of Mycobacteria

- *M. tuberculosis* causes most TB cases
- Mycobacteria that cause TB:
  - *M. tuberculosis*
  - *M. bovis*
  - *M. africanum*
  - *M. microti*
  - *M. canetti*
- Mycobacteria that do not cause TB
  - e.g., *M. avium complex*



M. tuberculosis

HOST

- Age : all ages
- Sex : Women : Men …1:2
- HIV
- Diabetes
- Under nutrition & Vitamin deficiencies
- Overcrowded living condition
- Smoking
- Indoor air pollution

HOST

- Silicosis
- Alcohol
- End stage renal failure
- Malignancy
- Genetic susceptibility
- Treatment therapy : TNF antagonist therapy, Cortisteroid , Tocilizumab…

Social factors contribute to occurrence and spread of TB

- Poor quality of life
- Poor housing & overcrowding
- Population explosion
- Under nutrition
- Lack of education
- Large families
- Lack of awareness about causes of illness etc.

TB is described as a "**BAROMETER of SOCIAL WELFARE**"

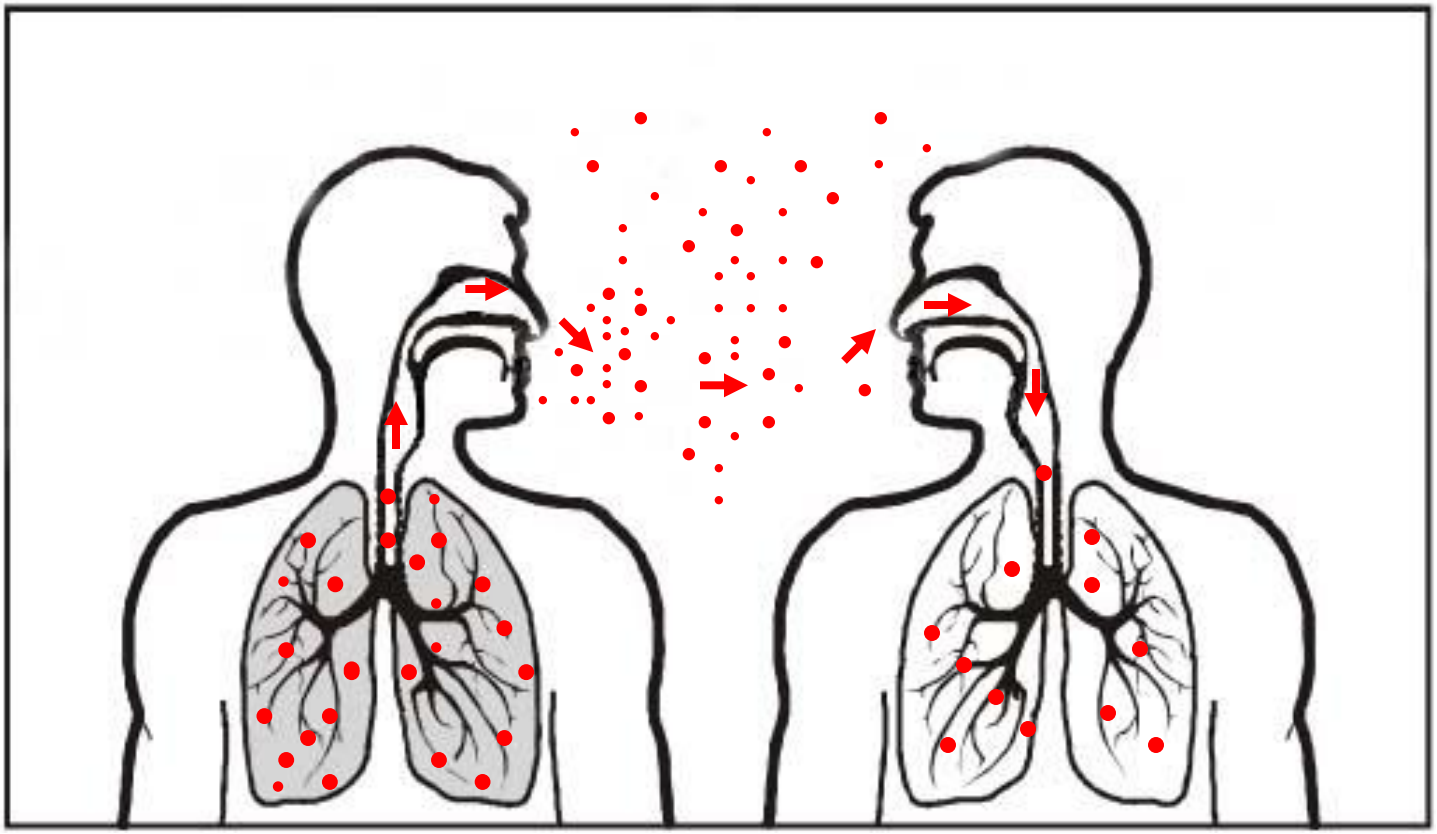
Risk of infection

A smear positive pulmonary TB case in the general population may infect **10-15** other persons in a year and remain infectious for **2 to 3 years** if **left untreated.**

MODE OF TRANSMISSION

- TB is spread person to person through the air via droplet nuclei
- *M. tuberculosis* may be expelled when an infectious person:
  - Coughs
  - Sneezes
  - Speaks
  - Sings
- Transmission occurs when another person inhales droplet nuclei

TB Transmission



Dots in air represent droplet nuclei containing *M. tuberculosis*

Incubation period

It usually takes **6-8 weeks** for the establishment and manifestation of infection.

Infection is indicated by detection of release of interferon gamma by a positive reaction to a tuberculin skin test (Mantoux test) or Direct IGRA.

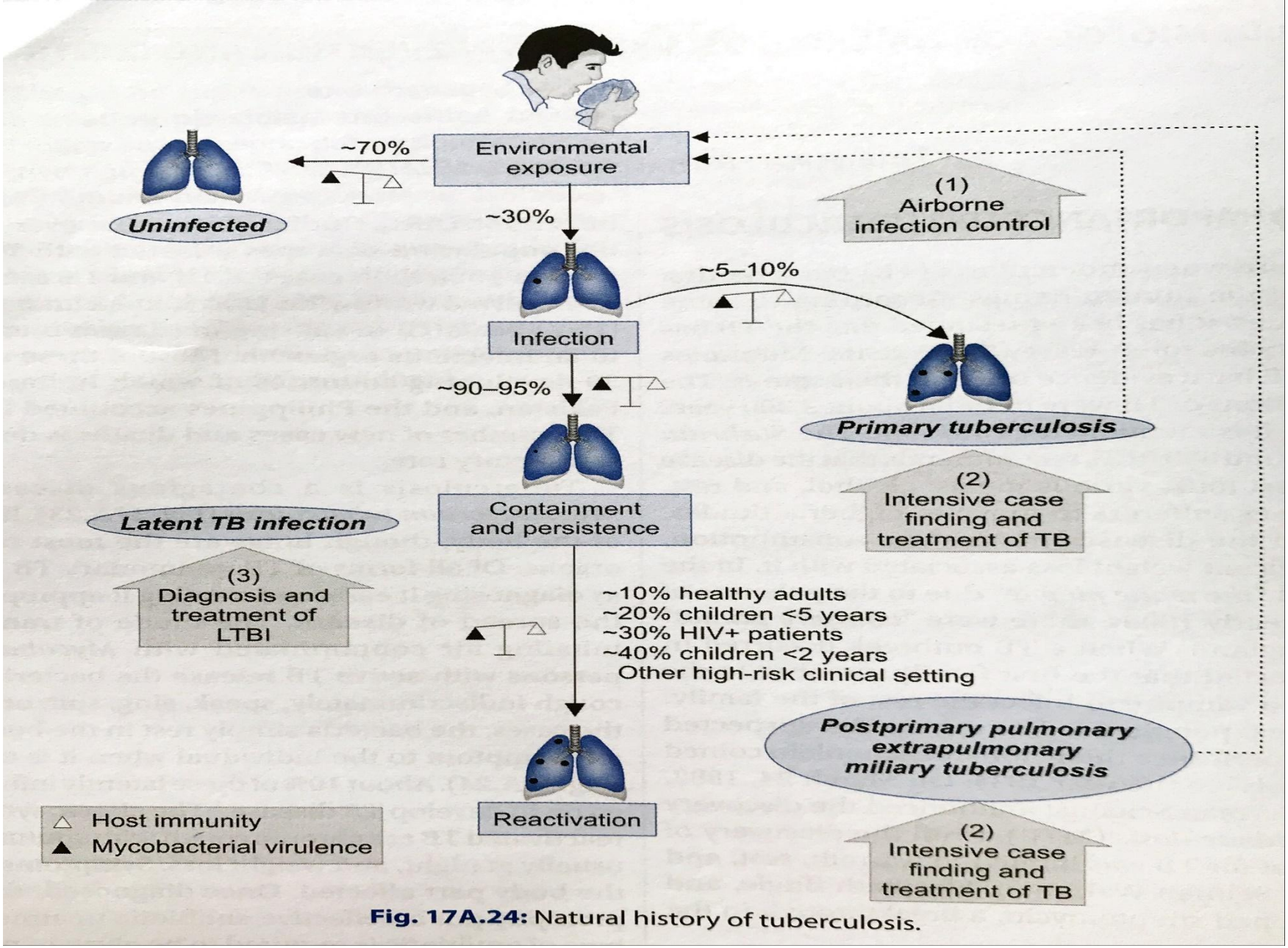
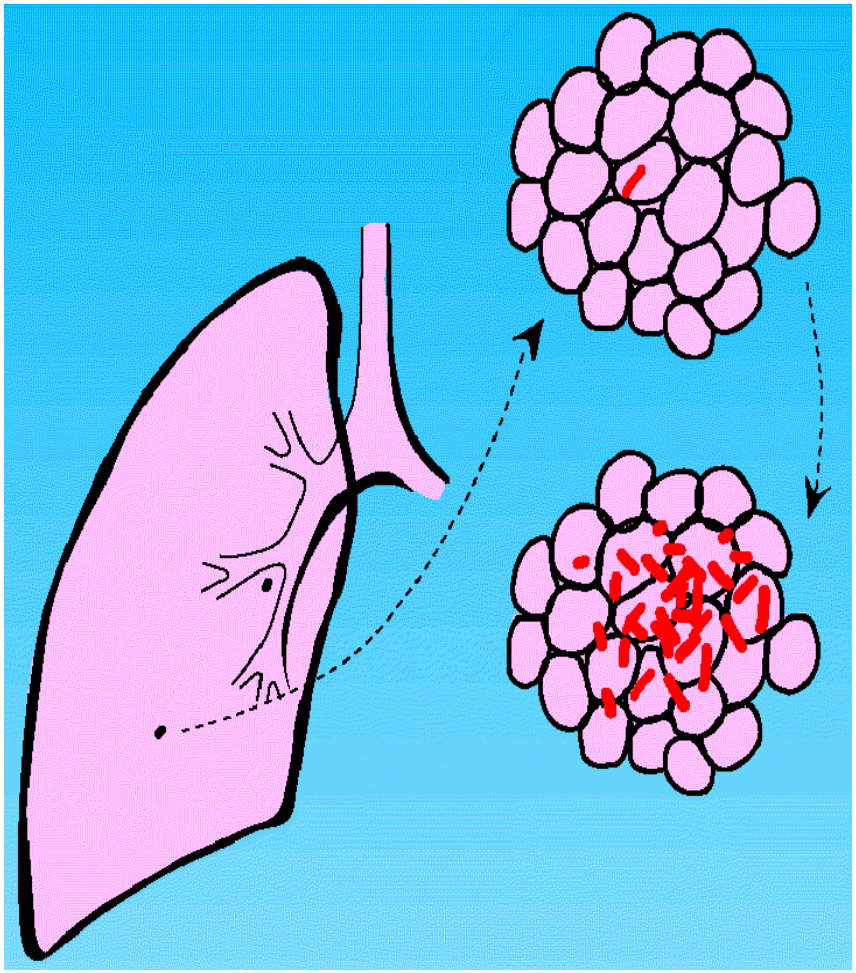
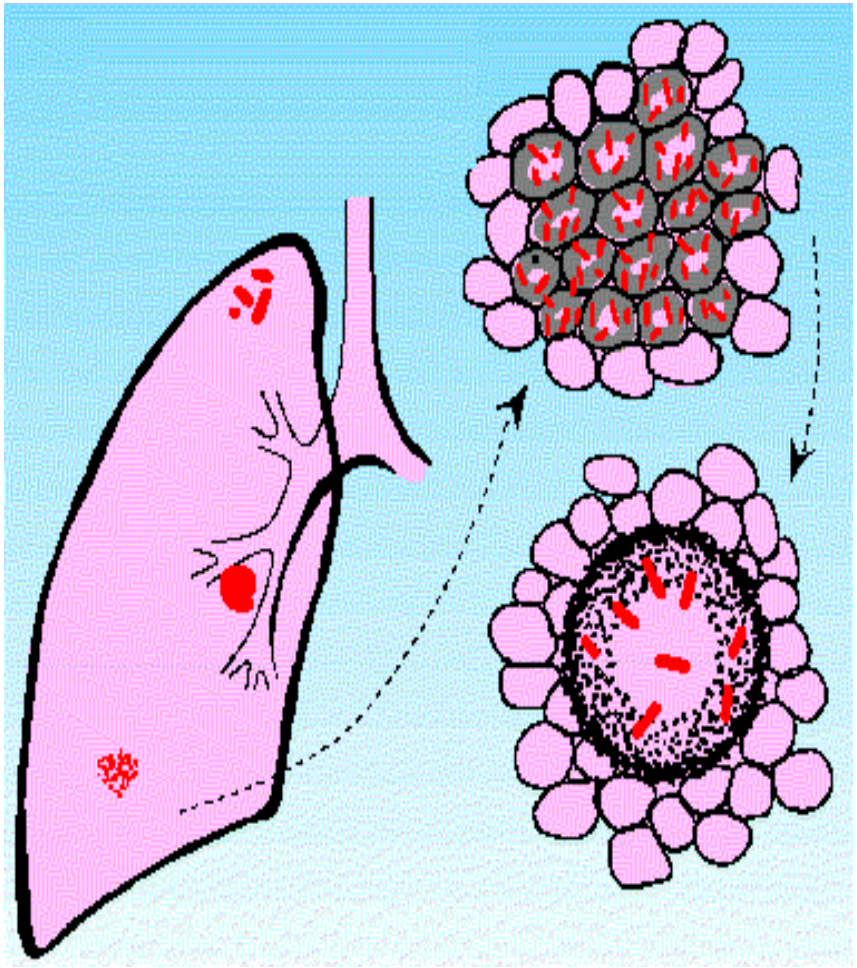


Fig. 17A.24: Natural history of tuberculosis.

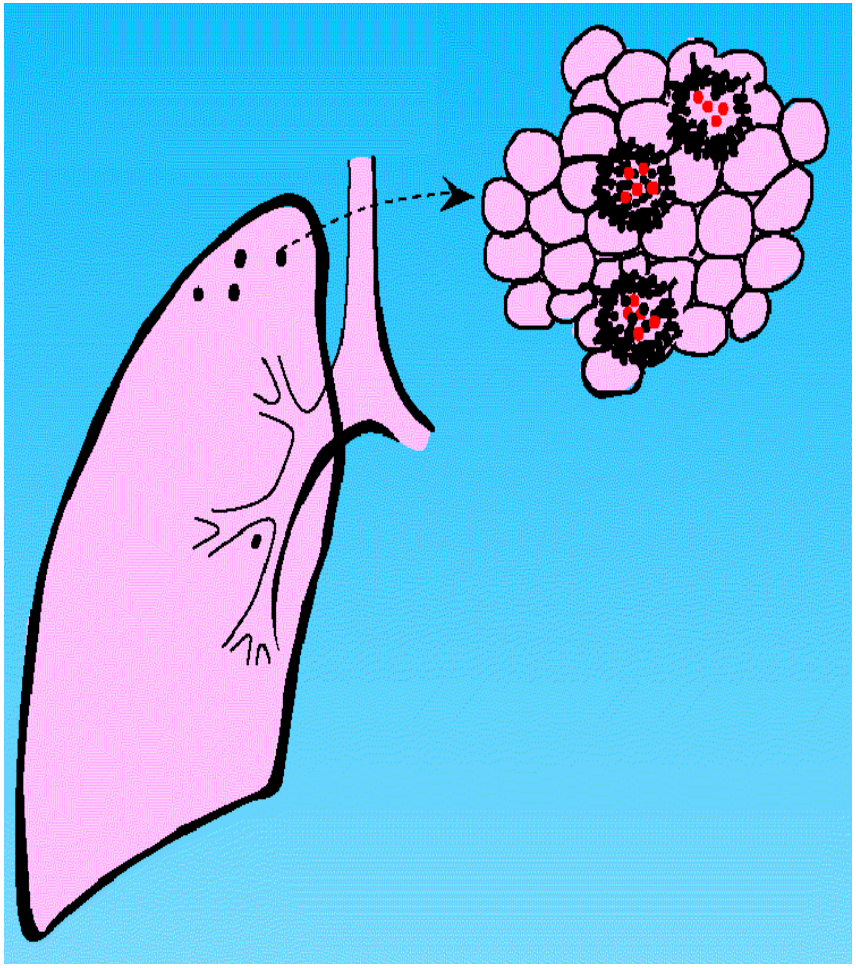
Source : IAPSM textbook of Community Medicine

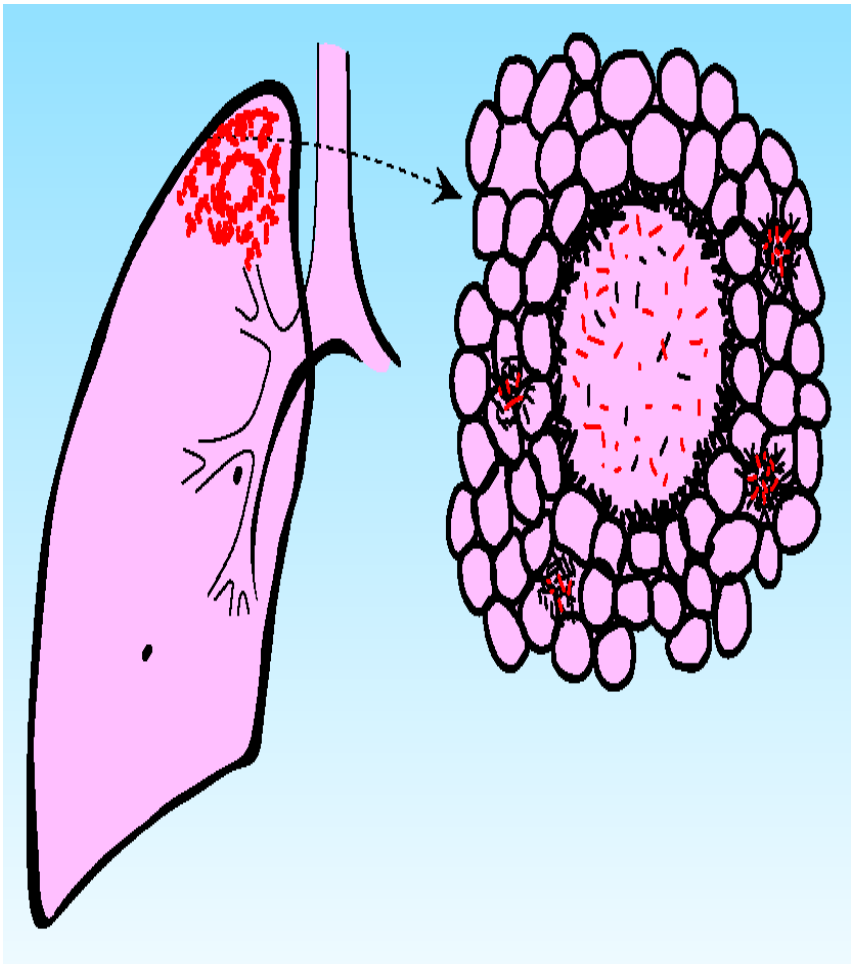
Infection begins…





Infection controlled…





CLINICAL FEATURES

- Productive prolonged cough*
- Chest pain*
- Hemoptysis*
- Fever and chills
- Night sweats
- Fatigue
- Loss of appetite
- Weight loss

*Commonly seen in cases of pulmonary TB

➢ **Some of the patients may have little or no symptoms with TB.**

Sites of TB Disease

- **Pulmonary TB** : lungs
  - 85% of all TB cases are pulmonary
- **Extrapulmonary TB** : places other than the lungs, including the:
  - Larynx
  - Lymph nodes
  - Pleura
  - Brain and spine
  - Kidneys
  - Bones and joints
- **Miliary TB** : when tubercle bacilli enter the bloodstream & are carried to all parts of the body

DIAGNOSIS (Microbiological confirmation)

1. **Sputum smear microscopy**
   - Zeihl- Neelson staining
   - Fluorescence staining
2. **Culture**
   - Solid (Lowenstein Jensen) media
   - Automated liquid culture systems (BACTEC MGIT 960, BactiAlert , Versatrek)
3. **Drug sensitivity test**
   - Modified DST for MGIT 960 system (for both 1st and 2nd line drugs)
4. **Rapid molecular diagnostic testing**
   - Line probe assay for MTB complex & detection of RIF & INH resistance
   - Nucleic Acid Amplification test **(NAAT)** : Xpert MTB/RIF testing using the GeneXpert system

Advantages of Sputum smear microscopy

- Simple, inexpensive, requires minimum training
- High specificity
- High reliability with low inter-reader variation
- Can be used for diagnosis, monitoring and defining cure
- Results are available quickly
- Feasible at peripheral health institutions
- Correlates with infectivity in pulmonary TB

DIAGNOSIS

- **Radiography**
  - More sensitive
  - Less specific
  - Higher intra reader variation
  - Useful for extrapulmonary TB

- **Tuberculin test**

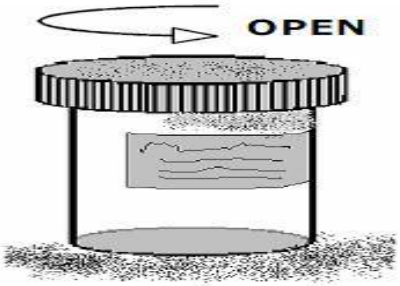
Sputum Collection

- Sputum specimens : essential to confirm TB
- **Mucus from within lung, not saliva**
- Collect 2 different specimens
  - Sample 1 : on the spot
  - Sample 2 : early morning

  (Spontaneous morning sputum more desirable than induced specimens)
- Collect sputum before treatment is initiated

Appendix Section 3-E
Sputum Collection Procedure – Information for clients

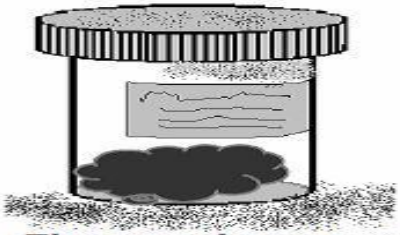
1. Gargle or rinse and then spit out the water you are given.



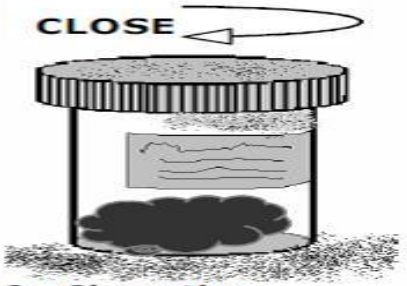
2. Open the sample container.

3. Hold the container to your mouth with your lips inside it.

4. Take as deep a breath as you can and cough then spit into the container (do NOT just spit saliva).

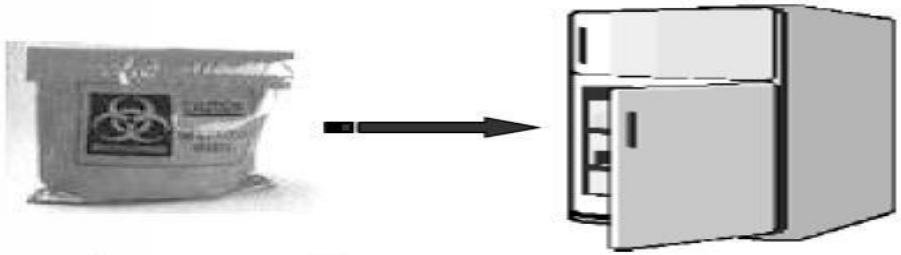


5. The sample you cough should look thick and yellow or green. More than a tablespoon of sample is needed.



6. Close the container lid tightly and seal with parafilm.

7. Give the sample to your caregiver right away

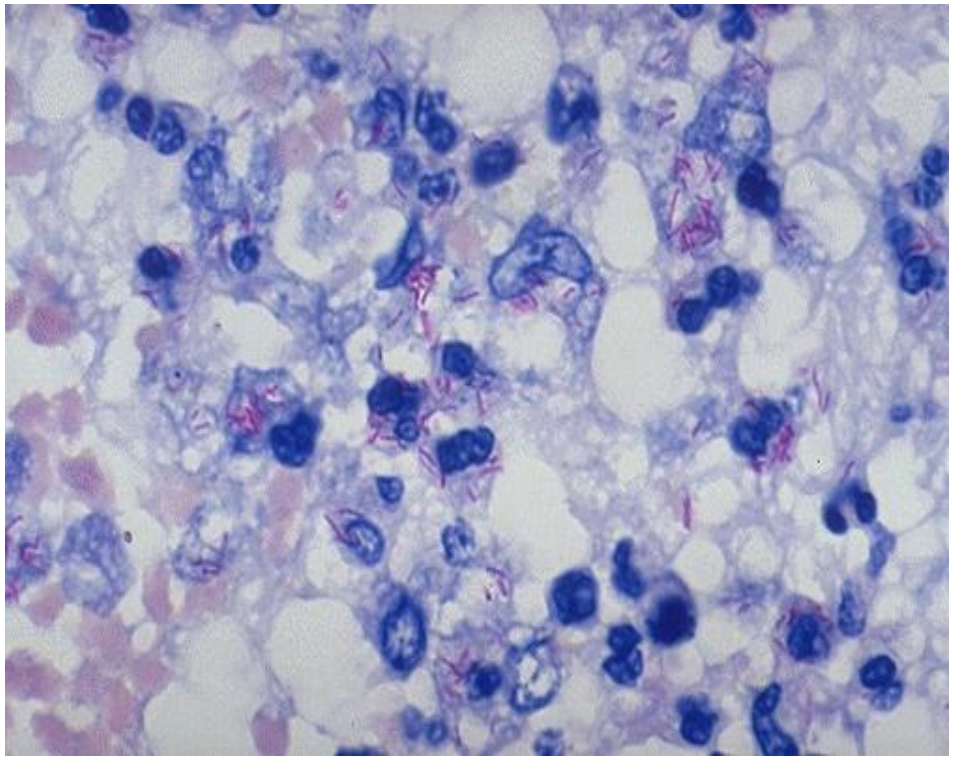


8. If you are at home:
   - Put your sample in the plastic bag you were given.
   - Close the bag and put it in the fridge right away.
   - Return your sample to your caregiver within 24 hours.

Sputum collection

Ziehl-Neelsen stain

The no of bacilli seen in a smear reflects disease severity & patient infectivity, So.. it is important to record the number of bacilli seen on each smear.



Grading of smears

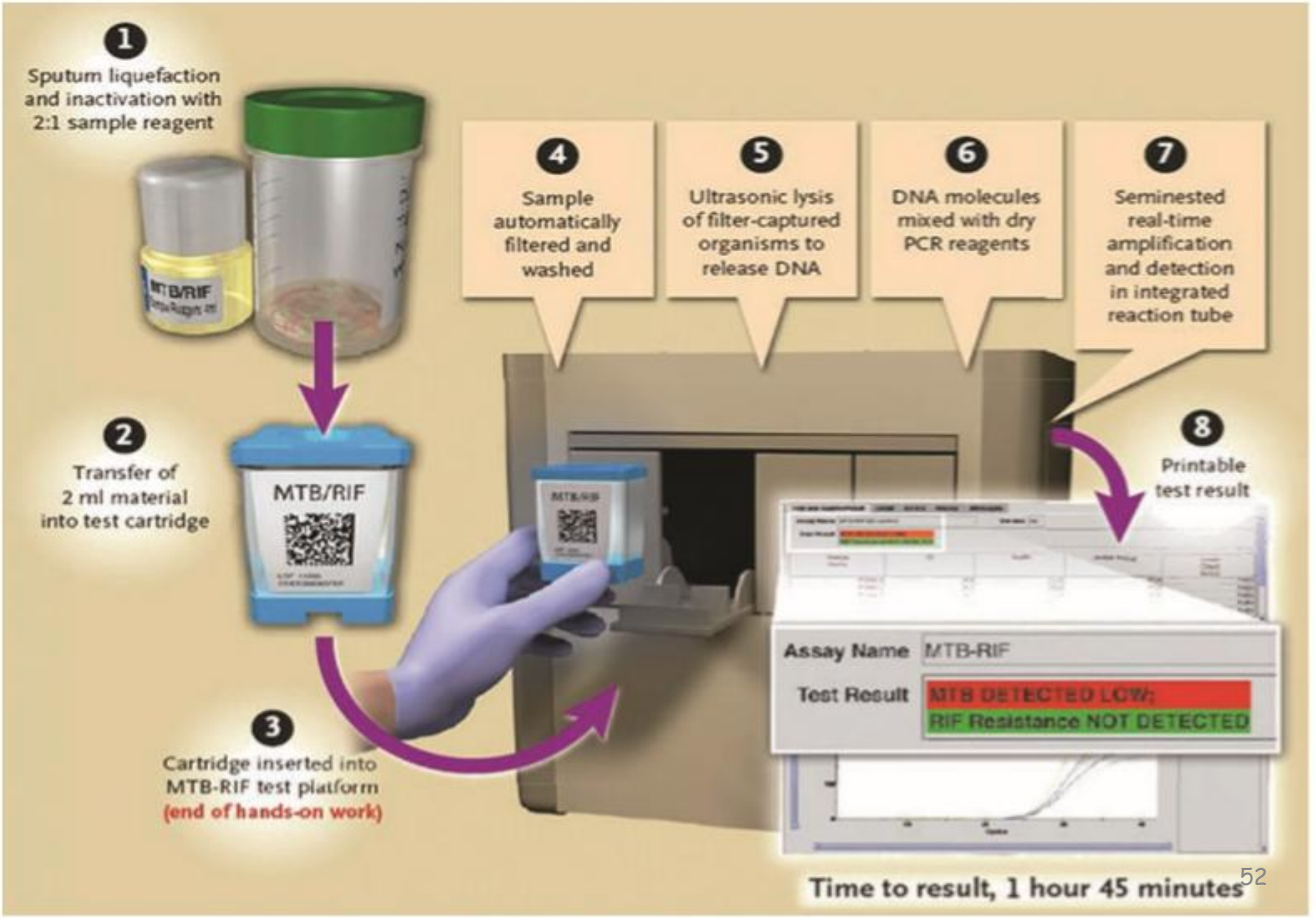
Examination	Result	Grading	No. of fields to be examined
No AFB in 100 fields	Negative	0	100
1-9 AFB/100 fields	Scanty	Record exact no.	200
10-99 AFB/100 fields	Positive	1+	100
1-10 AFB/ fields	Positive	2+	50
>10 AFB/field	Positive	3+	20

CBNAAT

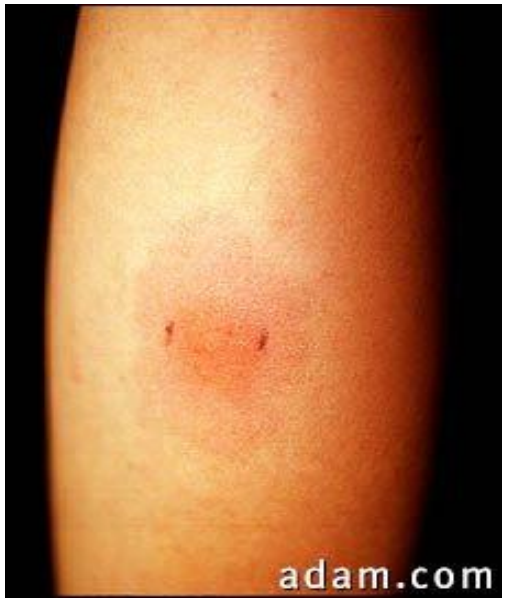
Cartridge Based Nucleic Acid Amplification Test

- Second generation NAAT
- very high sensitivity (approaching that of liquid culture – the current gold standard for TB diagnosis)
- Some versions of NAAT also provide information on drug susceptibility to rifampicin..

CBNAAT


1
Sputum liquefaction and inactivation with 2:1 sample reagent
2
Transfer of 2 ml material into test cartridge
MTB/RIF
3
Cartridge inserted into MTB-RIF test platform
(end of hands-on work)
4
Sample automatically filtered and washed
5
Ultrasonic lysis of filter-captured organisms to release DNA
6
DNA molecules mixed with dry PCR reagents
7
Seminested real-time amplification and detection in integrated reaction tube
8
Printable test result
Assay Name
MTB-RIF
Test Result
MTB DETECTED LOW;
RIF Resistance NOT DETECTED
Time to result, 1 hour 45 minutes

Tuberculin Test



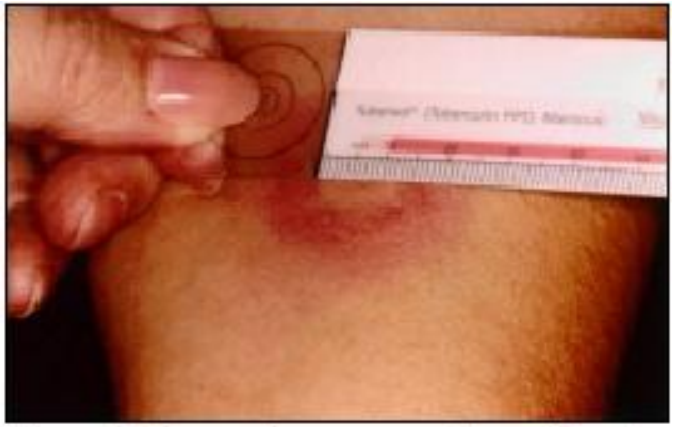
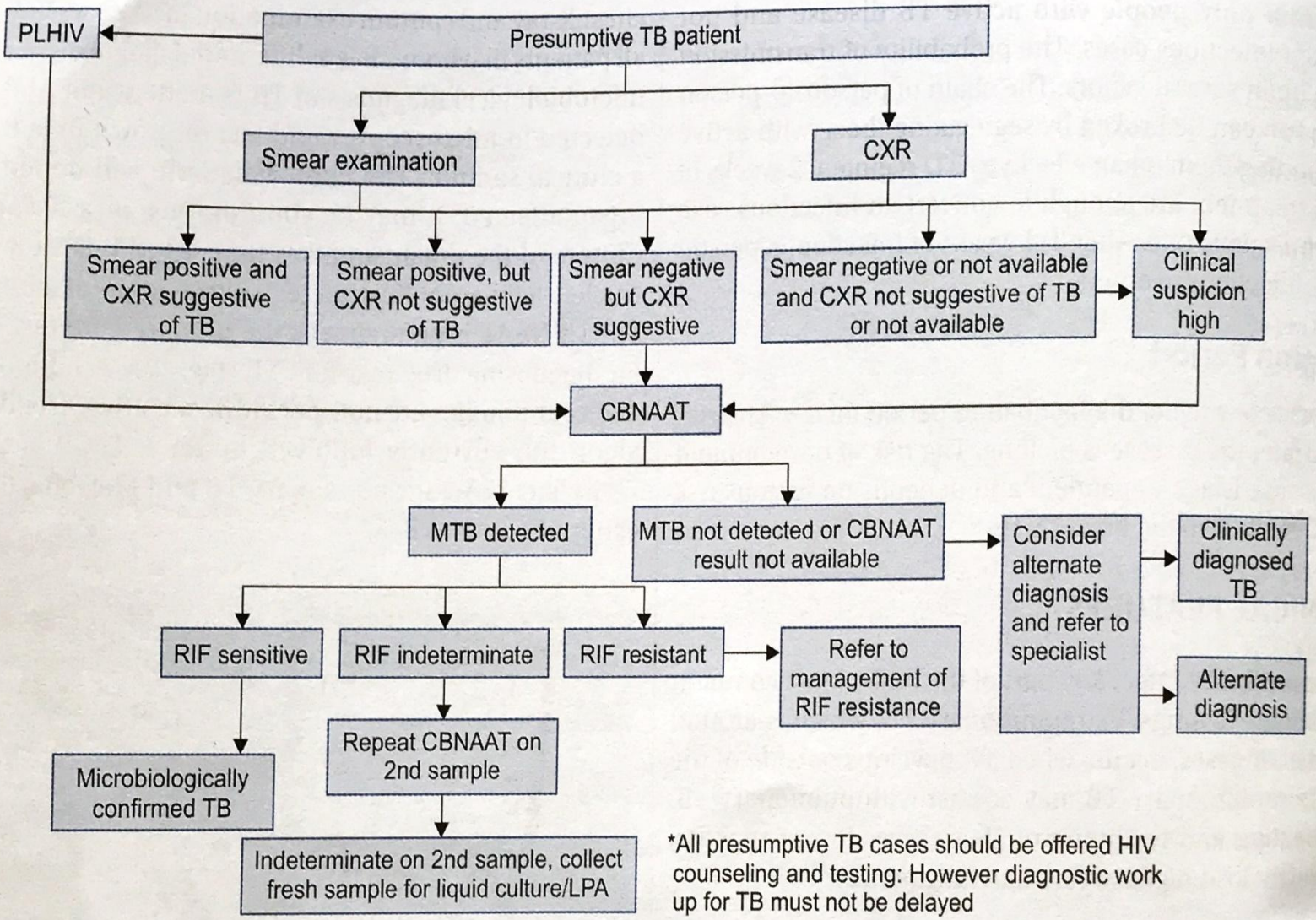


Figure 2. Correct measure of reaction to the tuberculin skin test.

- Mantoux test
- Purified protein derivative (P.P.D.).
- 5-T.U.
- 48 - 72 hours.
- Induration / Erythema.
- Positive: >15 mm.
- Converter/associated risk :10mm.
- Contacts/H.I.V./ fibrotic lesions/drug users : 5mm.
- **useful as an additional** tool for diagnosing paediatric TB,

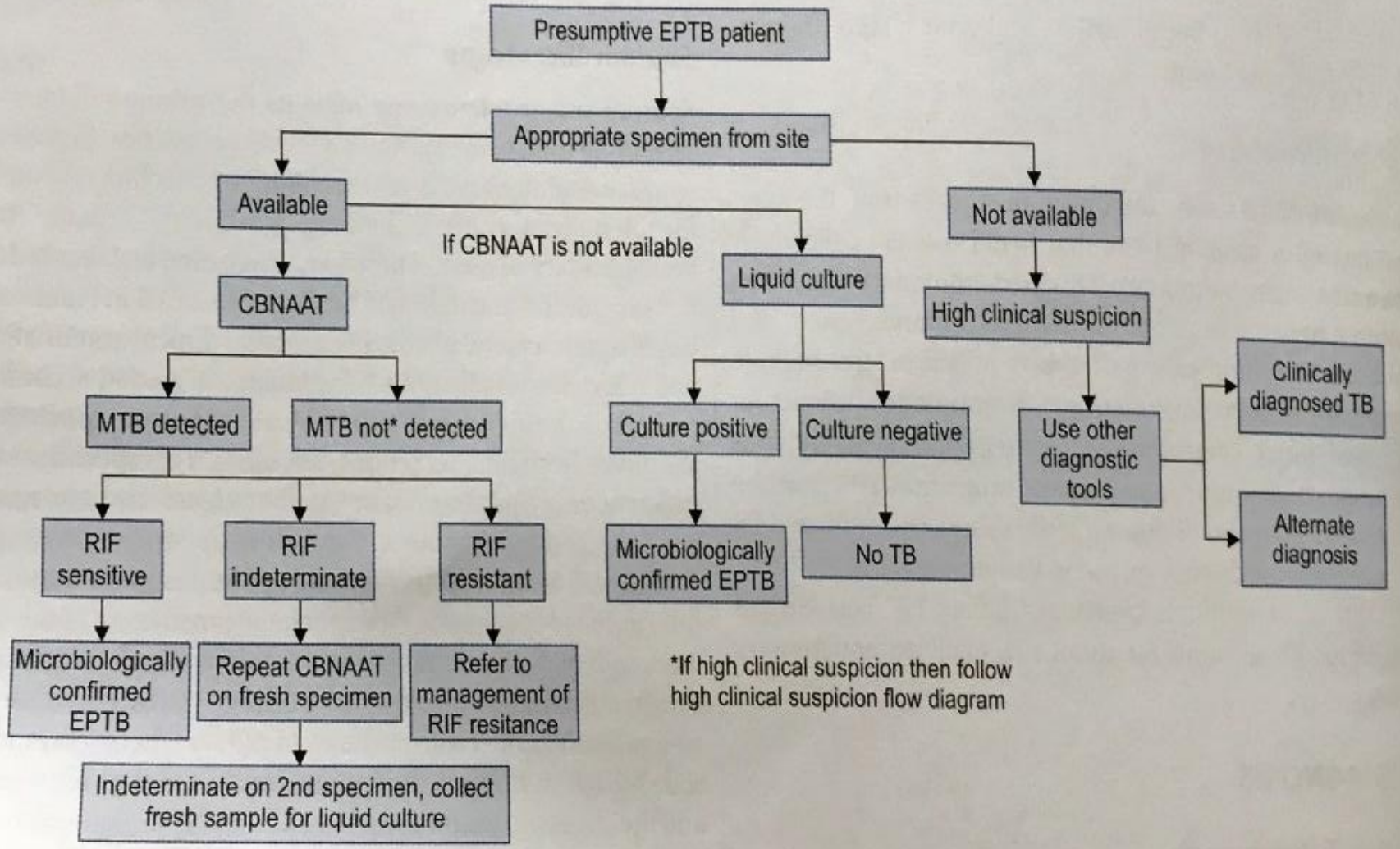
Flowchart 17A.2: Diagnostic algorithm of pulmonary tuberculosis.



(CBNAAT: Cartridge-based nucleic acid amplification test; CXR: chest X-ray; MDR multidrug resistant; MTB: *Mycobacterium tuberculosis*; LPA: line probe assay; PLHIV: people living with HIV, PMDT: Programmatic management of drug resistant tuberculosis)

Source : IAPSM textbook of Community Medicine

Flowchart 17A.3: Diagnostic algorithm of extrapulmonary tuberculosis.



(CBNAAT: cartridge-based nucleic acid amplification test; EPTB: extrapulmonary tuberculosis; MTB: *Mycobacterium tuberculosis*)

Source : IAPSM textbook of Community Medicine

Epidemiological indices

1. **Incidence** : no. of new and recurrent (relapse) episodes of TB (all forms) occurring in a given year.

2. **Prevalence** : no. of TB cases (all forms) at a given point in time.

3. **Mortality (TB):** no. of deaths caused by TB in HIV-negative people, according to the latest revision of the ICD-10. TB deaths among HIV-positive people are classified as HIV deaths in ICD-10.

Epidemiological indices

4. **Case fatality rate** : is the risk of death from TB among people with active TB disease.
5. **Case notification rate** : refers to new and recurrent episodes of TB notified to WHO for a given year, expressed per 100,000 population.
6. **Case detection rate** : calculated as the number of notification of new and relapse cases in a year divided by the estimated incidence of such *cases in the same year.*

Epidemiological indices

7. **Prevalence of drug-resistant cases** :prevalence of patient excreting tubercle bacilli resistant to anti-tuberculosis drugs.

8. **Prevalence of infection** *: percentage of* individuals who show a positive reaction to the standard tuberculin test.

CASE DEFINITIONS

- Presumptive Pulmonary TB
- Presumptive Extra Pulmonary TB
- Presumptive DR-TB
- Microbiologically confirmed TB
- Clinically diagnosed TB
- Pulmonary TB
- Extrapulmonary TB
- New cases of TB
- Retreatment case of TB

DEFINITIONS

- **Presumptive Pulmonary TB :**
  a person with any of the S/S suggestive of TB, including : cough for 2 weeks or more, fever for 2 weeks or more, significant weight loss, haemoptysis, any abnormality in chest radiograph.

- **Presumptive Extra Pulmonary TB :**
  Presence of organ specific S/S like swelling of lymphnode, pain & swelling in joints, neck stiffness, disorientation, &/or constitutional symptoms like significant weight loss, persistent fever for > 2 weeks, night sweats

DEFINITIONS

- **Presumptive DR TB** : patient who is eligible for RIF resistant screening at the time of diagnosis or/& during the course of treatment for DS TB or H mono/poly.

This includes following patients:

- All Notified TB patients (Public and private)
- F/up +ve on microscopy including treatment failures on standard first line treatment & all oral H mono/poly regimen;
- Any clinical non-responder including paediatric (if specimen available)

DEFINITIONS

- **Presumptive Paediatric TB :**

  children with persistent fever and/ or cough for 2 weeks or more, loss of weight*/ no weight gain &/ or h/o contact with infectious TB cases**.

* H/o of unexplained weight loss or no weight gain in past 3 months; loss of weight is defined as loss of > 5% body wt. as compared to highest wt. recorded in last 3 months

** In a symptomatic child, contact with a person with any form of active TB within last 2 years may be significant

Definitions

- **Microbiologically confirmed TB**
  - a presumptive TB case from whom a biological specimen is positive for acid fast bacilli, or positive for Mycobacterium tuberculosis on culture, or positive for tuberculosis through Rapid Diagnostic molecular test

- **Clinically Diagnosed TB**
  - a presumptive TB case who is not microbiologically confirmed, but has been diagnosed with active TB by a clinician on the basis of X-ray abnormalities, histopathology or clinical signs with a decision to treat the patient with a full course of Anti-TB treatment.

Definitions

- **Classification based on anatomical site of disease**
- a) **Pulmonary tuberculosis (PTB) :**

  any microbiologically confirmed or clinically diagnosed TB involving the lung parenchyma or the trachea bronchial tree

- b) **Extra Pulmonary tuberculosis (EPTB) :**

  any microbiologically confirmed or clinically diagnosed TB involving organs other than the lungs such as pleura, lymph nodes, intestine, genitourinary tract, joint & bones, meninges of the brain etc.

- **Miliary TB :** classified as PTB because there are lesions in the lungs
- A patient with **both pulmonary and extra-pulmonary TB :** classified as a case of Pulmonary TB.

Classification based on drug resistance

- **Mono-resistant (MR):** A TB patient, whose biological specimen is resistant to one 1st line anti-TB drug only.
-
- **Poly-Drug Resistant (PDR):** A TB patient, whose biological specimen is resistant to more than one first-line anti-TB drug, other than both INH and Rifampicin.

- **Multi Drug Resistant (MDR):** A TB patient, whose biological specimen is resistant to both isoniazid and rifampicin with or without resistance to other first-line drugs, based on the results from a quality assured laboratory.

Classification based on drug resistance

- **Rifampicin Resistant (RR):** resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs excluding INH. Patients, who have any Rifampicin resistance, should also be managed as if they are an MDR TB case.

- **Extensively Drug Resistant (XDR):** A MDR TB case whose biological specimen is additionally resistant to a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable anti TB drug (kanamycin, amikacin, or capreomycin) from a quality assured laboratory.

PREVENTION AND CONTROL

When we can say TB
is under
CONTROL ??

PREVENTION AND CONTROL

1. Elimination of reservoirs

2. Breaking the chain of transmission

3. Protection of susceptible

Elimination of reservoirs

- Early detection of cases and prompt treatment
  - Early diagnosis…..
  - Treatment …chemotherapy..

Breaking the chain of transmission

- Disinfection of sputum mainly and belongings of patient (linen, utensils etc)
- Sputum in sputum cup, ½ filled with **disinfectant** (5% cresol or 8% bleaching powder
- Sputum in **paper handkerchief** disposed off by burning
- **Patient** – avoid indiscriminate spitting of sputum

Protection of susceptible

- **General measures**
  - Health promotion
  - Health education

- **Specific measures**
  - BCG vaccine

BCG

- **Aim** : induce benign, artificial 1° infection …stimulate acquired resistance to possible subsequent infection with virulent tubercle bacilli ⇩ … morbidity..mortality

- **Vaccine** : Live attenuated, "Danish 1331"

- **Type** : Freeze dried and liquid

- **Dosage** : 0.05ml (<4weeks) , 0.1ml (upto 1 year)

- **Administration** : ID

THANK YOU….