ANTIMYCOBACTERIALS

Mycobacterium

- Rod like gram-positive aerobic bacteria.
- *M. tuberculosis* causes **Tuberculosis** & *M. leprae* causes **leprosy.**
- Mycobacterium **grow slowly**, lie **dormant**, has **thick cell wall and impermeable** & become **resistant to antibiotic therapies quickly.**

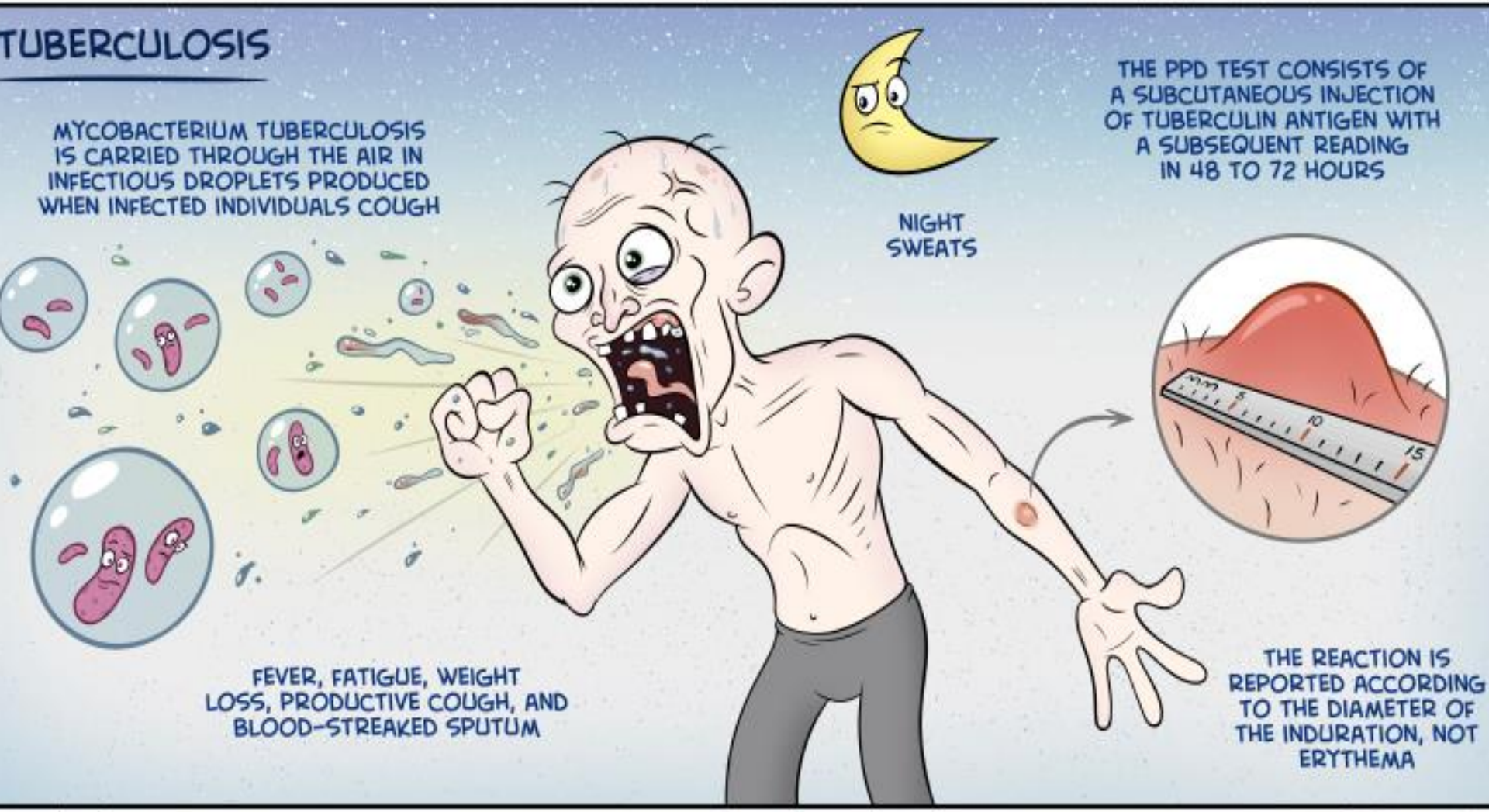
Therefore , long periods, with several different antibiotics simultaneously needed for eradication of ***Mycobacterium***

Tuberculosis

- **Infectious disease** Caused by ***Mycobacterium tuberculosis***

- ***Pulmonary TB (caseation)***
- ***Extrapulmonary TB (liver, bone ,spleen, skin)***

Miliary TB : ***tuberculosis c.c by a wide dissemination into the human body and by the tiny size of the lesions (1–5 mm)***


TUBERCULOSIS
MYCOBACTERIUM TUBERCULOSIS IS CARRIED THROUGH THE AIR IN INFECTIOUS DROPLETS PRODUCED WHEN INFECTED INDIVIDUALS COUGH
NIGHT SWEATS
THE PPD TEST CONSISTS OF A SUBCUTANEOUS INJECTION OF TUBERCULIN ANTIGEN WITH A SUBSEQUENT READING IN 48 TO 72 HOURS
FEVER, FATIGUE, WEIGHT LOSS, PRODUCTIVE COUGH, AND BLOOD-STREAKED SPUTUM
THE REACTION IS REPORTED ACCORDING TO THE DIAMETER OF THE INDURATION, NOT ERYTHEMA
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How pulmonary TB spreads

- **TB spread from person to person by**
  - **sharing food or drink**
  - **coughing**
  - **sneezing**
  - **Kissing**

Risk factors for pulmonary TB

- Older adults
- small children
- people who smoke
- people with an autoimmune disorder, such as lupus or rheumatoid arthritis
- people with lifelong conditions, such as diabetes or kidney disease
- people who are immunocompromised, such as those living with HIV, undergoing chemotherapy, or taking chronic steroids

Treatment of TB

- **<u>The objective therapy</u>**

  - to ***eliminate symptoms*** of active disease by killing multiplying bacilli (**phase 1**)

  - to ***prevent relapse, & emergence of drug resistance*** by eradication of problematic bacteria (**phase 2**).

Patient

Un Complicated

1st infection

[6m ttt]

First 2 months (Initial Phase)	Isoniazid (INH) + rifampicin + pyrazinamide + ethambutol or streptomycin (2HRPE)
4 months (Continuation Phase)	Isoniazid + rifampicin (4HR)

Complicated

Fail ttt or 2nd infection

[8 m ttt]

First 2 months (Initial Phase)	Isoniazid + rifampicin + pyrazinamide + ethambutol + streptomycin (2HRZES)
Further 1 or 2 Months	Isoniazid + rifampicin + pyrazinamide + ethambutol (1HRZE)
Five months (Continuation Phase)	Isoniazid + rifampicin + ethambutol (5HRE)

Anti TB

- *INH ; Rifampicine* **most active drugs for 9 months cure 90-95%.**
- Addition of *pyrazinamid* **decrease duration of ttt to 6 months** with same efficacy .
- *Ethambutol & streptomycin* will not decrease duration but provide **additional coverage of Isolate proves to be resistance to INH & Rifampicine**

INH (isoniazid H)

- ***Prodrug** activated by bacterial catalase-peroxidase.*
- *Sp. for Baciili inhibits the enzyme required for **mycolic acid synthesis**, an essential component of mycobacterium cell wall.*
- *Bactericidal against **rapidly multiplying organisms**.*
- Effective orally and metabolized by ***ACETYLATION which is genetically** controlled. Fast acetylators require high dose and slow acetylators are predisposed to* toxicity (particularly ***peripheral neuritis***) ,
- *other s/e **Sideroblastic anemia** due to B6 deficiency.*

Rifampicine

- *Broad spectrum antibiotic but restrict to TB to prevent resistance*
- *Secreted in bile, so does not require dose adjustment in renal failure.*
- Effective against ***intra- and extra-cellular bacilli.***
- ***Rifampicine is*** *Only bactericidal drug active* ***against dormant bacteria in solid caseous lesions****.*
- It is ***hepatotoxic*** *and may cause* ***skin rash, flu like syndrome and GI upset***

Pyrazinamide

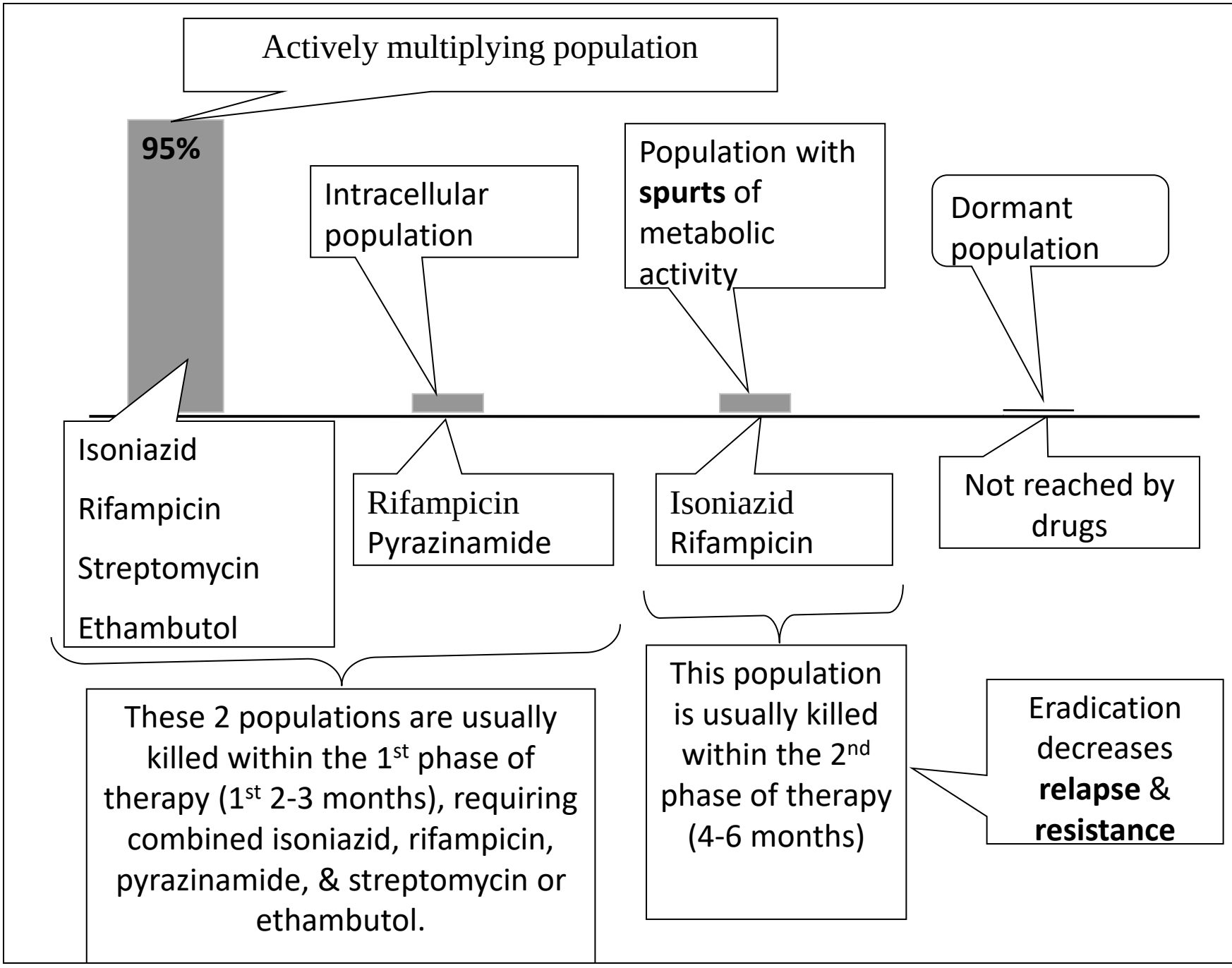
- ***Prodrug*** *converted to active form by intrabacterial* ***pyrazinamidase***
- *Effective in acidic media so benefit in* ***Acute inflammation & against quiscent bacilli within macrophage.***
- *in 40% of the patients it causes* ***non-gouty arthralgia.***

Ethambutol

- ***BACTERIOSTATIC agent, sp. for mycobacterium acts by inhibiting the synthesis of*** arabinogalactan (a component of cell wall) due to **inhibition of arabinosyl transferase**
- **used when *resistance to INH & rifampicine is suspected***
- **Causes *visual disturbances like optic neuritis***
- ***C****ontra-indicated in pregnancy & children.*

Streptomycin

- ***Tuberculocidal aminoglycoside.***
- **It is *not absorbed orally and must be administered by I.M injection.***
- It is active **only against extra-cellular bacteria.**
- **It is *NOT HEPATOTOXIC.***
- *Streptomycin is* ***contraindicated in PREGNANCY.***


Actively multiplying population
95%
Intracellular population
Population with spurts of metabolic activity
Dormant population
Isoniazid
Rifampicin
Streptomycin
Ethambutol
Rifampicin
Pyrazinamide
Isoniazid
Rifampicin
Not reached by drugs
These 2 populations are usually killed within the 1st phase of therapy (1st 2-3 months), requiring combined isoniazid, rifampicin, pyrazinamide, & streptomycin or ethambutol.
This population is usually killed within the 2nd phase of therapy (4-6 months)
Eradication decreases relapse & resistance

Leprosy

Infectious disease causes severe, disfiguring **skin** **sores** and **nerve damage** in the arms & legs, caused **by** **slow-growing** bacteria (**2-4 yrs** **incubation**) called ***Mycobacterium leprae.***

Treatment

- ***Dapson*** 1st choice
- other ***Rifampicine*** & ***Clofazimine***

Dapson

- **$t_{1/2}$ = 27hr , min duration is 2 years**
- *deposited in infected skin much more than normal skin.*

Rifampicine

- **600mg/monthly** *(not true for UTI)*

  *- Support dapson to **prevent infectivity***

Post antibiotic effect

continued suppression of bacterial growth following limited exposure of organisms to an antimicrobial agent e.g. **Rifampicine , amikacine , clarithromycin and ethambutol**

Clofazmine

- **$t_{1/2}$ = 70 days**
- *absorb in GIT & accumulate in tissues.*
- *used in dapson resistance*

NB: *Clofazmine activity depend on amount* ***accumulate in tissue*** *NOT on Plasma so we not depend on Css that is reach after (~ 350 days)*


Thank you