
WEL
COME

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Historical Permutation

- 17th centuries TB took 1 in 5 adult lives
- 1850 – 1950 one billion people died of TB
- Current decade 2000 – 2010
  - 300 million new infections
  - 90 million new cases
- More people died from TB last year than any year in history

Tuberculosis in the w  rld

- 1/3rd of the world's population infected
  - 95% in developing countries
  - 75% in the age group 15 – 50 yrs
- 9 million new cases per year
- 3 million deaths per year
- 98% of TB deaths in developing countries

---- WHO

Tuberculosis in the w  rld

- 18.5% of all deaths in adults age 15 – 59
- 50% ever get any treatment
- 25% ever get effective treatment

TB could be eliminated Because we understand it

- We know it's
  - Cause
  - Transmission
  - Treatment
  - Prevention

Problems of TB Control in Developing Countries

- Shortage of resources
- Limited availability of diagnostic facilities
- Costly drugs in treatment schedule
- Lack of sound healthcare infrastructure
- Poor transport system

What is tuberculosis 

- Chronic, specific infection
- Systemic communicable disease
- Caused by M. tuberculosis complex

Tuberculosis: Infection VS Disease

- Once infected
  - TB develops in 10%
    - 5% within a year
    - 5% later

Types of mycobacterium

- Mycobacterium complex
  - *Mycobacterium tuberculosis*
    - Classical type
    - South Indian type/Asian type
  - *Mycobacterium bovis*
- Opportunistic mycobacterial infections
  - *Mycobacterium kansasii*
  - *Mycobacterium xenopi*
- MAIs Complex

Mycobacterium

Discovered by Robert Koch in 1882

- Slightly curved rod
- Non-sporing, non-flagellated, non-motile
- Acid and alcohol fast
- Strictly parasitic
- Generally found in
  - Sputum , faeces, urine, CSF

Types of tuberculosis

- Pulmonary tuberculosis
  - Most common form
  - Occurs in 80% of cases
- Extra pulmonary tuberculosis
  - Occurs in organs other than lungs
  - Lymph nodes, spinal joints, GIT, CNS

What are the sources of infection?

Human source

Bovine Source

How does it enter into the body 

- Nasal
- Oral
- Percutaneous
- Direct inoculation

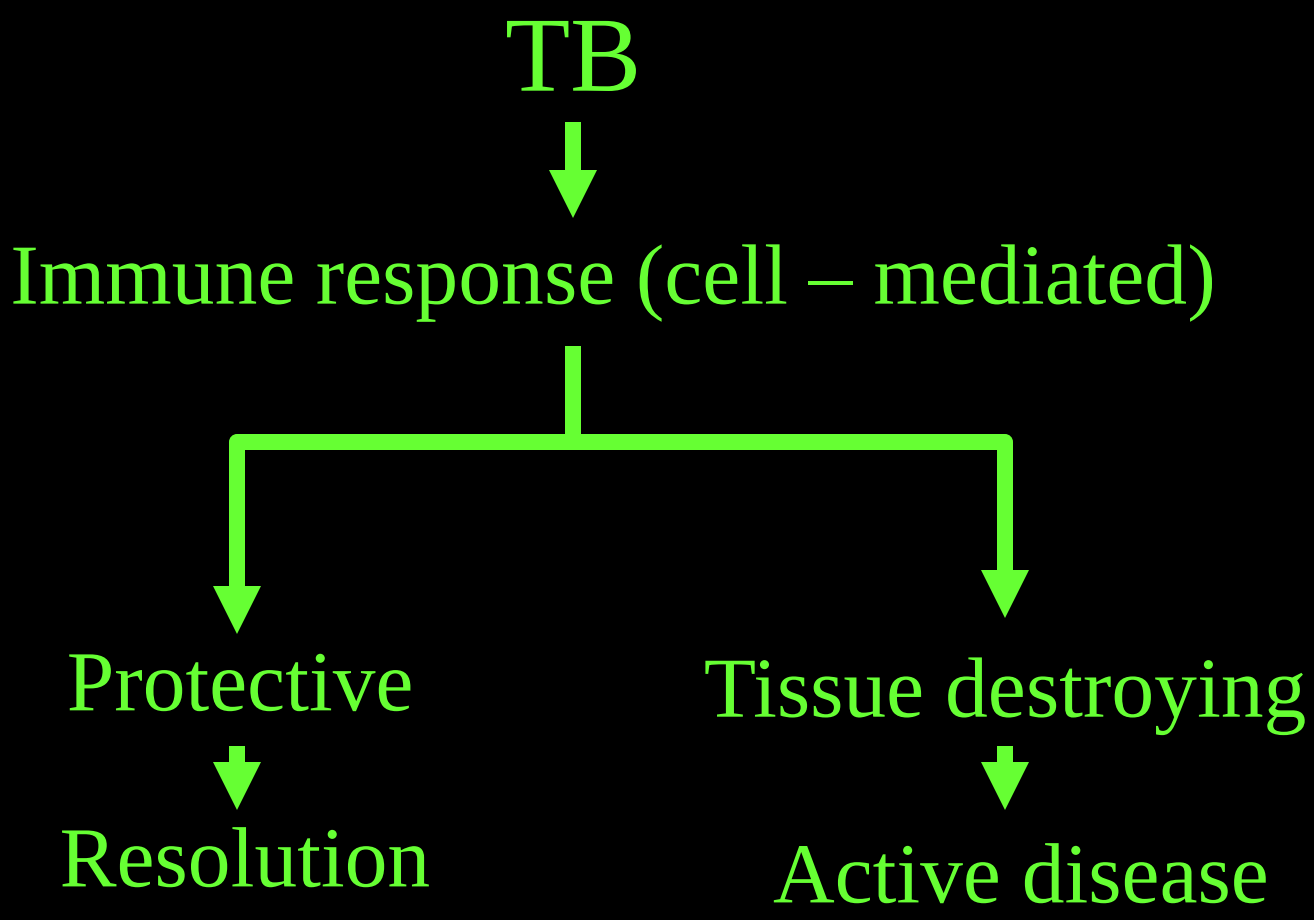
How does it spread

- Inhalation
- Ingestion
- Inoculation
- Transplacental

Who are at risk of developing TB 

- Close contact with sputum smear +ve case
- Immunosuppression
- HIV infection
- Renal failure
- Family history
- IV drug abuser

Immunology of TB



Pathology

- Characteristic histological lesion
  - Granuloma
    - Epithelioid cell
    - Multinucleate giant cells
- Primary complex of Ranke
  - Ghon’s focus
  - Plus hilar lymphadenopathy

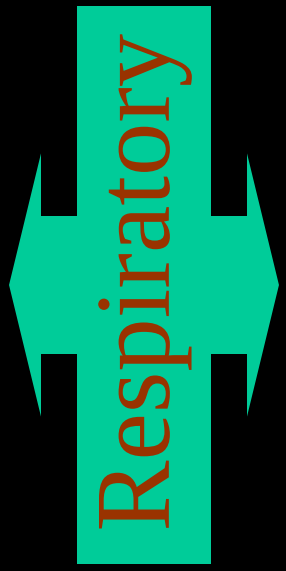
Clinical features

- Asymptomatic
- Symptomatic
  - Respiratory symptoms
  - General symptoms

Clinical features

Symptoms

- Cough > 3 weeks
- Sputum production
- Blood spitting
- Chest wall pain



- Breathlessness
- Localize wheeze
- Frequent cold

Clinical features

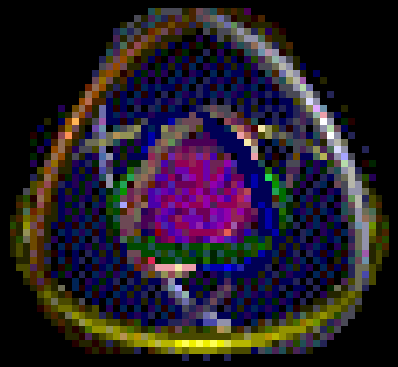
Symptoms

- General
  - Low grade fever with sweating
  - Loss of weight
  - Tiredness
  - Loss of appetite

Clinical features

Signs

- No physical sign
- Signs of
  - Fibrosis
  - Collapse
  - Pleural effusion
  - Pneumothorax
  - Cavitary lesion



Primary Pulmonary Disease

- Exogenous infection
- Mostly in children
- Ultimate residuum is Gohn's complex
- Localizes to middle & lower zones

Primary Pulmonary Disease

- Regional lymphadenopathy
- Majority heals spontaneously
- May form small calcified nodule
- May contains viable org. – Simon foci

Primary Pulmonary TB : Outcome

- No clinical disease
- Hypersensitivity Reactions
  - Erythema nodosum
  - Phlyctenular conjunctivitis
- Pulmonary and pleural complications
  - Tuberculous pneumonia
  - Lobar collapse
  - Pleural effusion

Primary Pulmonary TB : Outcome...

- Disseminated disease
  - Miliary disease
  - Lymphadenopathy
  - Meningitis,
  - Pericarditis

Post primary pulmonary TB

- Occurs mainly in adults
- Arises in one of the 3 ways
  - Direct Progression of primary lesion
  - Reactivation of a quiescent lesion
  - Exogenous re infection

Post primary pulmonary TB…

- Usually localized to
  - apical & post. segments of UL
  - Superior segments of LL
- Extensive caseous necrosis

Complications: primary PTB

- IMMEDIATE
  - Pleural effusion
  - Bronchopneumonia
  - Disseminated tuberculosis

Complications: primary PTB

- INTERMEDIATE
  - Non pulmonary TB
- LATE
  - Bronchiectasis
  - Post primary TB

Complications: post primary PTB

- DIRECT
  - Pleural effusion
  - Empyema
  - Laryngeal TB
  - More distant spread

Complications: post primary PTB

- INDIRECT
  - Air flow obstruction/COPD
  - Corpulmonale
  - Aspergilloma
  - Amyloidosis
  - Haemoptysis

Investigations of TB

- Blood
  - ESR – increase
- Bacteriological examination
  - Sputum
    - Microscopy for AFB
    - Culture
    - PCR

Investigations of TB …

Bacteriological examination…

- Other samples
  - Gastric aspirates
  - Laryngeal swab
  - Bronchoscopic specimens
  - Transtracheal aspirates

Investigations of TB …

Radiological: CXR findings

- Classical
  - Opacity mainly in the upper zones
  - Patchy or nodular opacities
  - Cavity(s)
  - Calcification
  - Opacities that persist after several weeks

Investigations of TB …

Radiological: CXR findings

- Atypical
  - Interstitial infiltrates
  - No cavitation
  - No abnormalities

Investigations of TB …

Tuberculin Skin Test (TST)

- Mantoux tests
  - <5 mm – negative
  - 5 – 10 mm – doubtful
  - >10 mm - positive

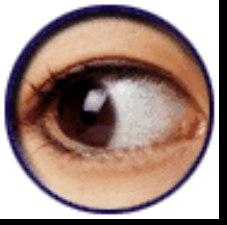
Investigations of TB …

Newer diagnostic procedure

- Serological diagnosis
  - ELISA
  - Immunobloting technique
  - Agglutination based test

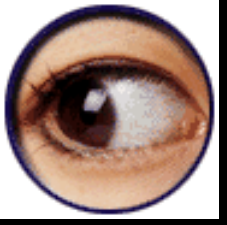
Investigations of TB …

- PCR
  - Require 10 CFU in specimen to be +ve
  - Sensitivity 81.3%
  - Specificity 94.2%
- RFLP



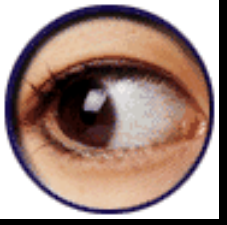
PTB: Assessment of Activity

- Bacteriological positivity
- Symptoms
  - Cough
  - Haemoptysis
  - Tiredness
  - Loss of weight



PTB: Assessment of Activity…

- Signs
  - Crepitation
  - Pleural effusion
  - Pneumothorax



PTB: Assessment of Activity…

- Certain radiological appearance
  - Cavity
  - Soft shadows, esp. if wide spread
  - Pleural effusion
  - Pneumothorax

Therapy over the century

1885 ▼ 1947

- 1885 : Surgery (Collapse therapy), Rest, nutrition, air
- 1912 : INH invented, Anti-TB action unknown
- 1940 : Dapsone for mice TB
- 1943 – 1944 : Streptomycin 2 gm/day (monotherapy)
- 1946 – 1947 : PAS invented Thiacetazone introduced but abandoned

Therapy over the century

1950 ▼ 1972

- 1950 - 1952 : Anti-TB action of INH discovered, combined chemotherapy, resectional surgery
- 1956 : Pyrazinamide introduced
- 1961 : Ethambutol invented Thiacetazone were valued
- 1964 : Two phases chemotherpy intermittent chemotherapy
- 1966 – 1968 : Rifampicin introduced
- 1972 : Short course chemotherapy

Aims of anti-TB drug treatment

- Cure the patient
- Prevention of death
- Prevention of TB relapse
- Decrease dissemination to others

Scientific basis of combination chemotherapy

- Action of drugs on
  - different phases of bacterial population
- Prevention of emergence of
  - acquired resistance

Scientific basis of combination chemotherapy …

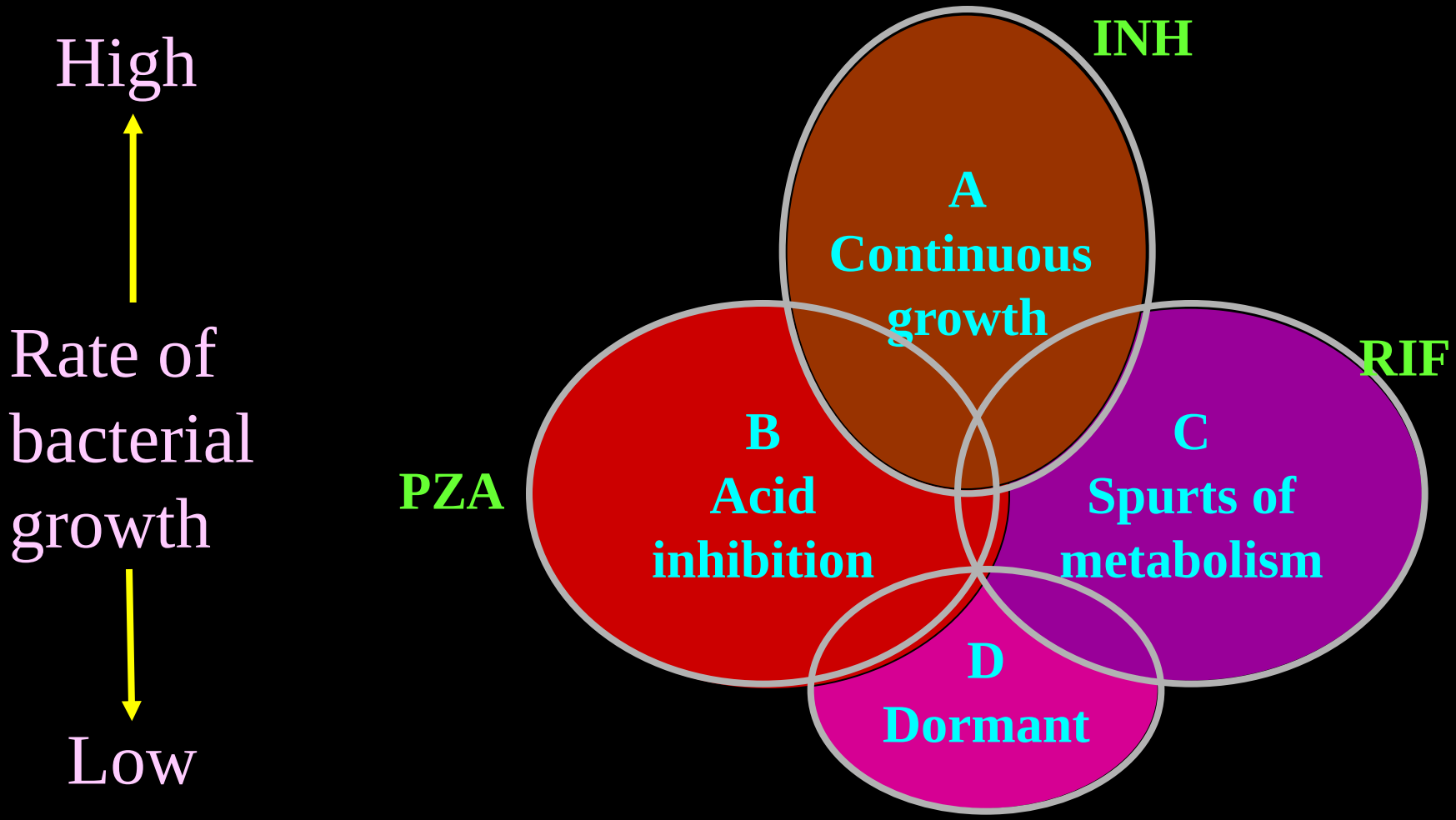


Fig: Action of drugs on the components of bacterial population

Scientific basis of combination chemotherapy …

Prevention of emergence of acquired resistance

- Resistance due to spontaneous mutation
  - INH 10^{-6}, Ethambutol 10^{-6}
  - Streptomycin 10^{-5}, Rifampicin 10^{-8}
  - Resistance to INH + RIF = $10^{-6} \times 10^{-8} = 10^{-14}$
  - Organism in a cavitary lesion 10^{8-9}

Criteria of good chemotherapy

1. Effective combinations
2. Right dose
3. Uninterrupted administration
4. Optimal duration

Chemotherapy : 1st line drugs

- Isoniazid
- Rifampicin
- Pyrizinamide
- Streptomycin
- Ethambutol
- Thiacetazone

Chemotherapy : 2nd line drugs

- Aminoglycosides: *kanamicin, amikcin*
- Thioamides: *Ethionamide, proethionamide*
- Fluoroquinolones: *ofloxacin, ciprofloxacin*

Chemotherapy : 2nd line drugs…

- Cycloserine or terizidone
- Para-amino salicyclic acid
- Others: rifabutin, clofazemine

Standardized Treatment Dosage

Recommended dose

Anti-TB drugs	*Mode of action*	*Daily dose (mg/kg)*
Isoniazid (INH)	Bactericidal	5 (4 – 6)
Rifampicin (R)	Bactericidal	10(8 – 12)
Pyrazinamide (Z)	Bactericidal	25(20 – 30)
Ethambutol (E)	Bacteriostatic	15 (15 – 20)
Streptomycin (S)	Bactericidal	15 (12 – 18)

Chemotherapy standardazied treatment regimen

TB Rx Category	TB treatment	TB treatment regimens	
		Initial phase	Continuation phase
1	New smear +ve PTB & seriously ill extra pulmonary or smear -ve pulmonary	2SHRZ(EHRZ) 2 HRZ(EHRZ) 2 HRZ(EHRZ) 2 $E_3H_3R_3Z_3$	6HE 4HR 4H_3R_3 4H_3R_3
2	Sputum smear +ve relapse, treatment failure and return after default	2HRZE/1HRZE 2SHRZE/1HRZE 2 $S_3H_3R_3Z_3E_3$/ 1 $H_3R_3Z_3E_3$	5 $H_3R_3E_3$ 5 HRE 5 $H_3R_3E_3$
3	Smear-negative PTB and extra pulmonary TB	2 HRZ or 2 $H_3R_3Z_3$ 2 HRZ or 2 $H_3R_3Z_3$ 2 HRZ or 2 $H_3R_3Z_3$ 2 $H_3R_3Z_3$	6 HE 2HR/4H 2H_3R_3/4H 4H_3R_3
4	Chronic case	NOT APPLICABLE(Refer to special center if second-line drugs available)	

National tuberculosis control program

Management of PTB

Category I

- New patients smear +ve PTB
- New patients smear - ve PTB with extensive parenchymal involvement
- New cases of severe forms of extra pulmonary TB
  - Regimen: 2 HRZE/6HT (Total 8 months)

National tuberculosis control program

Management of PTB

Category II

- Previously treated smear +ve PTB
- Relapse
- Default
- Treatment failure
- Regimen: 2 SHRZE/1HRZE/ 5HRE (total 8 months)

National tuberculosis control program

Management of PTB

Category III

- New patients smear -ve PTB
- New less severe extra pulmonary TB
  - Regimen: 2 HZE/10 HT (Total 12 m)

National tuberculosis control program

Management of PTB

Category IV

- Chronic case still sputum- +ve after supervised retreatment)
  - Regimen: Refer to WHO guidelines for use of 2nd line drugs in specialized centres

Common side effects of anti-TB drugs

- Isoniazid
  - Peripheral neuropathy
  - Hepatitis: 1-2%
  - Anorexia, nausea, vomiting, abdominal pain
- Rifampicin
  - Hepatitis: mild
  - Reduced effectiveness of OCP

Common side effects of anti-TB drugs

- Pyrazinamide
  - Hepatitis: most hepatotoxic
  - Hyperuraecemia and arthralgia
- Streptomycin
  - VIIIth nerve damage
  - Renal damage

Common side effects of anti-TB drugs…

- Ethambutol
  - Optic neuritis
- Thiacetazone
  - Skin rash
  - Steven-Johnson's syndrome

Hypersensitivity reactions to anti-TB drugs

- Commonly occurs in 2nd to 4th wks
- Rare in 1st wk
- Common in streptomycin and thiacetazone
  - Thiacetazone reaction is dangerous in HIV pt.
- Less common with rifampicin and INH

Hypersensitivity reactions to anti-TB drugs

Clinical features

- Mild: itching
- Moderate: fever and rash
- Severe
  - Steven – Johnson's syndrome
  - Generalized lymphadenopathy
  - Hepatosplenomegaly

Monitoring of TB patient during treatment

- ESR, HB%
- Sputum – smear microscopy
  - At the time of Dx
  - At the end of initial phase
  - In continuation phase at 5 months
  - On completion of treatment

Monitoring of TB patient during treatment…

- CXR
- Monitoring for adverse reactions
  - Liver function test
  - Visual acquity
  - Uric acid

Treatment response

- By second week
  - Smear negative
- After 4 weeks
  - Feeling well, weight gain
  - Afebrile, no cough and sputum

Treatment response…

- By 2 months
  - 80% culture negative
- By 3 months
  - 100% culture negative
- Chest radiographic changes
  - Should have improvement
  - May take several months

Prevention of TB

- General health promotion
- Effective treatment of sputum +ve cases
- Specific Protection
  - Active immunization
- Chemoprophylaxis

BCG Vaccination

- Protection up to 7 years
- Protection in young adult 0 - 70%
- Minimize the risk of disseminated TB

Conclusion

- Tuberculosis is a
  - Major human killer
  - Multisystem involvement
  - Preventable disease
  - Curable disease
  - Mortality and morbidity can be prevented
  - Combination drugs are mainstay of treatment