Treatment of TB and Leprosy

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TREATMENT OF TUBERCULOSIS

- The goals of antitubercular chemotherapy are:

1. Kill dividing bacilli

  - *with early* bactericidal action
  - rapidly reduce bacillary load in the patient and achieve quick sputum negativity
  - the patient is non-contagious to the community
  - transmission of TB is interrupted.
  - This also affords quick symptom relief.

2. Kill persisting bacilli

- *To effect cure and* prevent relapse.
- This depends on sterilizing capacity of the drug.

3. *Prevent emergence of resistance*

- the bacilli remain susceptible to the drugs.
- The relative activity of the first line drugs in achieving these goals differs,
- e.g. H and R are the most potent bactericidal drugs active against all populations of TB bacilli, while Z acts best on intracellular bacilli and those at inflamed

General principles

- Use of any single drug in tuberculosis -the emergence of resistant organisms and relapse in almost 3/4th patients.
- High number of organism do not respond to single drug and keep on multiplying
- massive infection (>1010 organisms) has to be treated by at least 3 drugs;
- and a single drug is sufficient for prophylaxis because the number of bacilli is small.

- H and R are the most efficacious drugs
- their combination is definitely synergistic
- So duration of therapy is shortened from > 12 months to 9 months.
- Addition of Z for the initial 2 months further reduces duration of treatment to 6 months

- A single daily dose of all first line antitubercular drugs is preferred.
- The ‘directly observed treatment short course’ (DOTS) was recommended by the WHO in 1995.

- Response is fast in the first few weeks as the fast dividing bacilli are eliminated rapidly.
- Symptomatic relief within 2–4 weeks.
- The rate of bacteriological, radiological and clinical improvement declines subsequently as the slow multiplying organisms respond gradually.
- Bacteriological cure -much longer.
- The adequacy of any regimen is decided by observing sputum conversion rates and 2–5 year relapse rates after completion of treatment.

- All anti TB regimens have an IP and CP
- IP- intensive phase with 4-6 drugs aimed to rapidly kill the bacilli
  - Bring about sputum conversion
  - Symptomatic relief

- Followed by Continuation Phase (CP)
  - 3 to 4 drugs
  - Remaining bacilli will be eliminated
  - To prevent relapse

- The dose of all first line drugs was standardized on body weight basis, applicable to both adults and children.

Dose

Drug	Daily dose (mg/kg)
Isoniazid	5
Rifampin	10
Pyrazinamide	25
Ethambutol	15
Streptomycin	15

Regimen- RNTCP guidelines 2016

Type of Patient	Intesive Phase	Continuation Phase	Total Duration
New	2 HRZE	4 HRE	6
Previously treated	2 HRZES + 1 HRZE	5 HRE	8

- **Multidrug-resistant (MDR) TB**
- MDR-TB is defined as resistance to both H and R, and may be any number of other (1st line) drug(s).
- multiple 2nd line drug regimens which are longer,
- more expensive and more toxic.

- The regimen should have at least 4 drugs
- Often 5–6 drugs are included, since efficacy of some may be uncertain.

- **Tuberculosis in pregnant women**
- H, R, E and Z to be safe to the foetus and recommend the standard 6 month (2HRZE + 4HRE) regimen for pregnant women with TB.
- S is contraindicated because it is ototoxic to the foetus.
- In, India current RNTCP 2016 considers Z to be safe
- Treatment of TB should not be withheld or delayed because of pregnancy.
- All pregnant women being treated with INH should receive pyridoxine 10–25 mg/day

- **Treatment of breastfeeding women All**
- anti-TB drugs are compatible with breastfeeding;
- full course should be given to the mother
- The infant should receive BCG vaccination and 6 month isoniazid preventive treatment after ruling out active TB.
- Breastfed infants, whose mothers taking INH should be supplemented pyridoxine 5 mg/day

TB with AIDS

- **Regimen for treatment of MAC infection**
- **Intensive phase**
- 1. Clarithromycin 500 mg BD *or* Azithromycin 500 mg OD
- 2. Ethambutol 1000 mg (15 mg/kg) per day
- 3. Rifabutin 300 mg per day

+/-

- Ciprofloxacin 500 mg BD/Levofloxacin 500 mg OD/ Moxifloxacin 400 mg OD
- **Maintenance phase***
- 1. Clarithromycin/Azithromycin
- 2. Ethambutol/Rifabutin/One fluoroquinolone

Leprosy

- Leprosy, caused by *Mycobacterium leprae*
- Considered as a social stigma.
- Due to availability of effective antileprotic drugs now, it is entirely curable, but deformities/defects already incurred may not reverse.

- CLASSIFICATION

1. *Sulfone- Dapsone (DDS)*
2. *Phenazine derivative -Clofazimine*
3. *Antitubercular drugs -Rifampin,* Ethionamide
4. *Other antibiotics Ofloxacin,*

   Moxifloxacin,

   Minocycline,

   Clarithromycin

Classification of Leprosy

- Paucibacillary
  - Noninfectious with few bacilli
  - Tuberculoid
  - <5 hypoaesthetic lesions, normal/partially deficient CMI, Bacilli are rarely found in biopsy
- Multibacillary
  - Infectious
  - Lepromatous leprosy
  - More than 5 hypoaesthetic lesion
  - CMI is largely deficient
  - Skin and Mucous membrane has numerous bacilli

- Dapsone
  - Closely related to sulfonamides
  - Inhibition of bacterial folic acid synthesis
  - Leprostatic
  - Well absorbed after oral administration
  - Well distributed in tissues and body fluids
  - Remains in skin, muscle, kidney and liver up to 3 weeks after stopping
  - Acetylated in liver and excreted in urine

- ADR
  - Well tolerated
  - Nonhemolytic anemia
  - Methhemoglobinemia in G6PD deficients
  - Dapsone to be avoided if Hb is less than 7 g%
  - Nausea, loss of Appetite, pruritus, drug fever, reversible neuropathy and hepatotoxicity

- During dapsone therapy for Lepromatous leprsoy, some reactive episodes may occur
- Lepra reactions
  - Two types
  - Type I Lepra reactions and Type II

- Type I Lepra reaction
  - Delayed hypersensitivity to M. Lepra antigens
  - Cutaneous ulceration, multiple nerve involvement
  - Corticosteroids

- Type II Lepra reaction
  - Erythema nodosum leprosum
  - Type III hypersensitivity
  - Humoral antibody response to dead bacteria
  - Abrupt onset, exisiting lesion enlarge, become red, inflammed and painful
  - corticosteroids

- Clofazimine
  - Binds with bacterial DNA and inhibits its growth
  - Leprostatic
  - Anti inflammatory property- advantage
  - Antileprotic effect- 6 to 7 weeks
  - ADR- red brown discolouration of skin
    - Abdominal pain with loose stools
    - Conjuctival pigmentation and phototoxicity

WHO Regimen

Drug	Paucibacillary (PB)	Multibacillary (MB)
Rifampicin	*600 mg once a month Supervised*	*600 mg once a month Supervised*
Dapsone	*100 mg daily self administered*	*100 mg daily self administered*
Clofazimine	-	*300 mg once a month Supervised 50 mg daily self administered*
Duration	**6 Months**	**12 Months**

Reference

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2	R S Satoskar	Cheotherapy of Tuberculosis	Pharmacology and Pharmacotherapeutics, 25th Edition	1