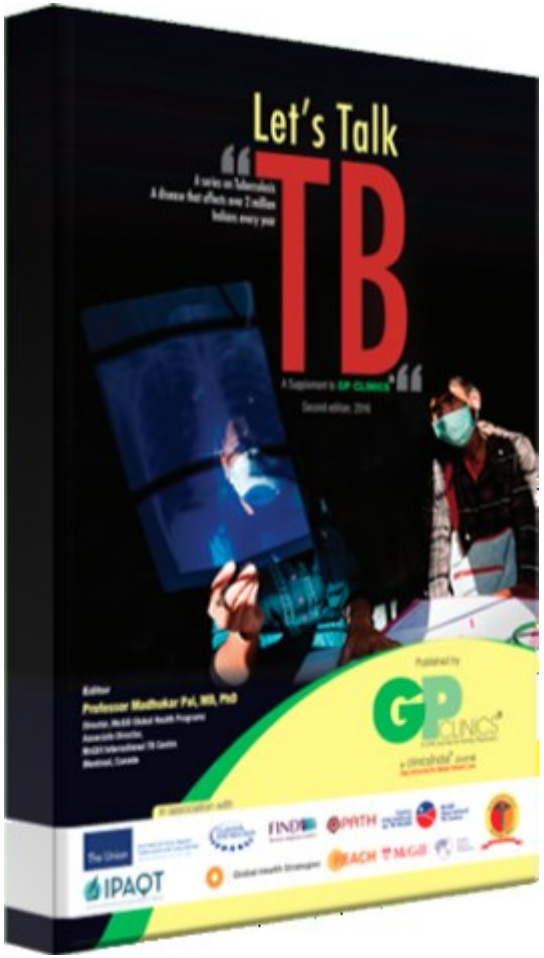

Let's Talk

TB:

A Supplement to GP CLINICS

Chapter 5:

Treatment of Pulmonary Tuberculosis

What Every GP Should Know

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Suspicion

- High incidence of TB in India
- Every GP in India must have a high index of suspicion for the disease in all patients with cough for more than two weeks
  - And in all patients with chest x-ray abnormalities.

If TB Is Suspected…

- Important to order sputum tests that can microbiologically confirm TB
  - Smear microscopy
  - Cultures
  - GeneXpert (Molecular tests)
- These tests are all endorsed by the World Health Organization (WHO) and available at more affordable prices in the private sector, via the IPAQT initiative (www.ipaqt.org)
  - 75 accredited private labs across India.

Blood Tests are NOT reliable for Pulmonary TB

- Pulmonary TB cannot be reliably detected by any blood test
- Sputum is the most important sample to collect
- Chest x-rays helpful, but they are not specific for TB
  - Must be followed by microbiological tests

Key Steps

- **Once TB is diagnosed, there are several key steps to ensure that patients have good outcomes**

Key Steps

- Assessment for multi drug-resistant TB (MDR-TB) risk factors
- Selection of correct first-line drug regimen, duration and dosage
- Ensuring treatment adherence
- Monitoring treatment success
- Management of adverse events
- Notification of TB cases
- Referral of patients with suspected MDR-TB

The Effective Treatment of TB has 3 aims

- 1. **The rapid reduction of bacillary load to ensure clinical improvement and to arrest transmission**
  - This is achieved through the use of potent bactericidal drugs such as isoniazid and rifampicin

The Effective Treatment of TB has 3 aims

- 2. **The prevention of the emergence of drug resistant strains.**
  - The emergence of such strains is dependent on bacillary load and spontaneous mutations occurring in multiplying bacilli within the lungs
  - The concurrent use of multiple anti-tuberculous drugs is aimed at suppressing the growth of such mutants, and is an important component of an adequate regimen for treatment

The Effective Treatment of TB has 3 aims

- 3. Prevention **of relapse**
  - This is achieved through prolonged treatment, especially with a regimen that includes rifampicin, and monitoring of adherence to ensure elimination of any residual, persistent organisms, which are known to responsible for relapse

Standards for Care

- Two important standards for TB care were released in March 2014:
  - 3rd edition of the International Standards for TB Care (ISTC)
  - 1st edition of Standards for TB Care in India (STCI)
- These standards establish the best practices for TB diagnosis, treatment and follow-up
  - Must be followed by all practitioners

Assessment for MDR-TB Risk Factors

- Before TB treatment is started, practitioners must assess the patient for MDR-TB risk

According to the ISTC…

- An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms, and the community prevalence of drug resistance (if known), should be under- taken for all patients
- Drug susceptibility testing should be performed at the start of therapy for all patients at a risk of drug resistance

According to the ISTC…

- Patients who remain sputum smear-positive at completion of 3 months of treatment, patients in whom treatment has failed, and patients who have been lost to follow-up, or relapsed following one or more courses of treatment should always be assessed for drug resistance

According to the ISTC…

- For patients in whom drug resistance is considered to be likely an Xpert MTB/RIF (GeneXpert) test should be the initial diagnostic test
- If rifampicin resistance is detected, liquid culture and testing for susceptibility to isoniazid, fluoroquinolones and second-line injectable drugs should be performed promptly

Selection of Correct First Line Drug Regimen

- In India, several studies have shown widespread use of incorrect and irrational TB drug prescriptions, especially in the private sector
- Incorrect prescriptions can lead to emergence of drug-resistance and result in poor patient outcomes
- This underscores the importance of clinician education and adherence to standards

WHO-approved first-line treatment regimen

- According to the ISTC, all patients who have not been treated previously and do not have other risk factors for drug resistance should receive a WHO-approved first-line treatment regimen using quality assured drugs

Initial Phase

- The **Initial phase** should consist of two months of isoniazid, rifampicin, pyrazinamide and ethambutol

Continuation Phase

- The **Continuation phase** should consist of isoniazid and rifampicin given for 4 months
- The doses of anti-tuberculosis drugs used should conform to WHO recommendations
- Fixed dose combination drugs may provide a more convenient form of drug administration
- The STCI recommends that the continuation phase should consist of three drugs (isoniazid, rifampicin and ethambutol) given for at least four months
  - This is because of the high levels of isoniazid resistance in India

- Evidence suggests that both daily and thrice-weekly intermittent drug regimens are acceptable for first-line TB therapy, provided mechanisms are put in place to ensure adherence

- Intermittent drug therapy makes it easier to implement directly observed therapy (DOT), while daily treatment provides a great margin of safety
- Dosages of drugs must be based on body weight and acceptable ranges are shown in **Table 1** (based on ISTC)

Drug Dosages

Table 1 – Doses of first-line antituberculosis drugs in adults and children

Drug	Recommended dose in mg/kg body weight (range)					
	Daily regimen			Three times weekly regimen		
Isoniazid	**Dose**	**Range**		**Dose**	**Range**	
Children	10	(7-15),	maximum 300 mg/day			
Adults	5	(4-6),	maximum 300 mg/day	10	(8-12),	maximum 900 mg/dose
Rifampicin						
Children	15	(10-20),	maximum 600 mg/day			
Adults	10	(8-12),	maximum 600 mg/day	10	(8-12),	maximum 600 mg/dose
Pyrazinamide						
Children	35	(30-40),	maximum 2000 mg/day			
Adults	25	(20-30),	maximum 2000 mg/day	35	(30-40),	maximum 3000 mg/dose
Ethambutol						
Children	20	(15-25),	maximum 1000 mg/day	30	(25-35),	maximum 2400 mg/dose
Adults	15	(15-20),	maximum 1600 mg/day			

Source: ISTC, 3rd edition (reference 6)

Fixed Dose Drug Combinations (FDC)

- Where possible, according to STCI and ISTC, fixed dose drug combinations (FDC) should be used
  - They reduce the number of pills taken daily
  - Increase patient convenience
  - Reduce the potential for medication errors

Duration

- With respect to duration of therapy, 6 months is the standard for first- line therapy
- The STCI recommends that the duration of the continuation phase can be extended by 3 – 6 months in special situations like bone and joint TB, spinal TB, and central nervous system involvement

Ensuring Treatment Adherence

- Since drug-sensitive TB requires at least 6 months of continuous therapy, ensuring adherence is a big challenge
- Providing support for, and making every effort to ensure adherence should be considered to be part of the prescription for the treatment of TB
- Important to develop an approach that is tailored to each patient and one that involves an agreement between the GP and the patient

- Every TB patient should receive counseling at the start of TB treatment
- They should be informed that they have a curable disease called TB, and that completion of the entire 6 month course is critically important to prevent poor outcomes

- Patients should also be informed about likely adverse drug events, and they should get a clear plan on when to come back for follow-up visits
- Mobile phone reminders may help with improving adherence and follow-up visits
- Patients also need to be advised about diet, return to work, smoking and alcohol cessation, and may need to be screened for co-morbid conditions like diabetes and HIV

- Doctors can also work with local community-based and non-governmental organizations, and enlist community health workers as 'treatment supporters' to supervise and support the patient with treatment completion
- To ensure treatment adherence, it is also important that doctors maintain some written record on what treatment was started, when, dosages, adverse reactions, results of follow-up lab tests, etc

Monitoring Treatment Success

- Weight of the patient should ideally be monitored on a monthly basis, and drug dosages adjusted to reflect the change in weight
- The STCI recommendation states that
  - 'Response to therapy in patients with pulmonary tuberculosis, new as well as retreatment cases, should be monitored by follow-up sputum microscopy (one specimen) at the time of completion of the intensive phase of treatment and at the end of treatment'

Management of Adverse Effects

- Drug-induced hepatitis is the most common major adverse reaction associated with ATT
- Severe nausea, jaundice or confusion should make the physician suspect the possibility of hepatitis
- Advancing age and pre-existing liver disease are known risk factors, and special monitoring and care needs to be exercised in these groups of patients

Hepatitis

- All TB drugs should be stopped when hepatitis is suspected
- The monitoring of the drug-induced hepatitis, and re-introduction of drugs is beyond the scope of this article and can be found elsewhere

Management of Adverse Effects

- Any reported visual impairment should warrant the stopping of ethambutol
- Severe skin rashes may have to be treated by stopping all drugs and re-introducing them one at a time under observation, to identify the offending agent
- Common minor side effects include nausea and anorexia
  - Can be minimized by taking the medications with small meals or just before bedtime

Management of Adverse Effects

- Joint pains caused by pyrazinamide can be treated with non-steroidal anti-inflammatory drugs
- Pyridoxine supplements may be used to alleviate the mild tingling and numbness in the hands and feet that may be caused by isoniazid

Notifications of TB Cases

- As per Government of India order and STCI recommendations:
  - "All health establishments must report all TB cases and their treatment outcomes to public health authorities (**District Nodal Officer for Notification**)"
- By notifying all TB cases to the local health authorities, private practitioners can seek help from the RNTCP to help follow-up patients who default

Referral of Patients with Suspected MDR-TB

- All patients with risk factors for drug-resistance (e.g. patients with a history of previous TB treatment) must be investigated for MDR-TB using drug-susceptibility testing
- Since MDR-TB requires long-term and specialized management, patients should be referred to chest specialists
  - Either in the private sector, or in the public sector where free treatment is available under the programmatic management of drug-resistant TB

Critical Role

- In conclusion, GPs have a critical role to play in the control of TB at a community level
  - Especially in India, where a majority of TB patients seek care in the private sector

Ensuring the Best Standards

- Ensuring the best standards of TB treatment comprises:
  - The prescription of the right drugs in the right regimens
  - Monitoring patients for signs of response to treatment and signs of adverse reactions to medications
  - Supporting the patient in maintaining adherence to treatment

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