Proceedings S.Z.P.G.M.I vol: 12(3-4) 1998, pp. 98-101.

Current Guidelines for Management of Tuberculosis

Syed Nazim Hussain Bokhari
Department of Pulmonary Medicine, Shaikh Zayed Postgraduate Medical Institute, Lahore

SUMMARY

Tuberculosis represents the single biggest killer of all the infectious diseases, accounting for 26% of all the diseases in developing countries. About 1/3 of the world's population (1.7 billion people) is latently infected with Mycobacterium. tuberculosis. Five million new cases are being added to the existing pool world-wide. In Pakistan 1.5-2% of the population is suffering from active disease, whereas, over 80% of the adult population has been exposed to mycobacterium tuberculosis. According to the Population Commission report, Tuberculosis is the fourth major cause of death in Pakistan. Major obstacles to the control of Tuberculosis have been identified and include; inadequate prescription, improper or late diagnosis, irregular intake of drugs by the patients and poor follow-up.
Under the prevailing circumstances the best way of controlling Tuberculosis in this country is to make early diagnosis of active pulmonary cases, who are particularly infectious and treat them under strict supervision to achieve at least 85% cure and 70% detection rate, which is the target set by the WHO.

DIAGNOSIS

There is no better diagnostic test than isolation of Mycobacterium (AFB) through smear or culture. Sputum should be examined repeatedly. If cough is non-productive than sputum may be induced through nebulizing (hypertonic) saline or bronchial lavage may be requested. AFB can also be isolated from pleural fluid, ascitic fluid, CSF, pus, urine and even stools.

There is no radiological finding which is diagnostic of Tuberculosis. In endemic areas over diagnosis is common. Only when repeated sputum samples are smear negative and clinical suspicion very high that a presumptive diagnosis of tuberculosis be made based on chest radiograph. However, once the diagnosis is made, even on clinical grounds, an appropriate full course of ATT may be given irrespective of the clinical course of the disease.

Tuberculin Test or ESR may not be used as diagnostic criteria no matter what the degree of induration. In a community where > 85% of the adult population is infected and where BCG vaccination is mandatory for every new-born, tuberculin test is likely to be positive in most of the cases.

Pathological specimens may be obtained either by excisional biopsy or needle aspirates through ultrasound or CT guidance and must be checked by ZN (Ziehl-Neclson) staining besides looking for granulomas.

Serological and other antigen based tests (like PCR) neither have high specificity nor sensitivity in our setup and should not be relied upon for making a diagnosis.

DEFINITIONS

- A **Case of Tuberculosis** is an individual who is discharging mycobacteria and transmitting the disease in the community.

- **Smear Positive** patient, should have at least two sputum specifimens positive for AFB; or

one culture positive; or one smear positive and highly suggestive radiograph.

- **Smear Negative** patient, should have two smears negative but culture may be positive, with chest radiograph highly suggestive of active disease. Tuberculosis is spread almost exclusively through droplets or aerosol from lungs, skin, dry dressings or lab specimens. When patient has no cough, AFB can be transmitted through sneezing, laughing or talking loudly.

- **Cavitary tuberculosis** is most infectious as their sputum contains 1-100 million bacilli/mL. Such cases should be given high priority for early treatment.

- **Extrapulmonary Tuberculosis** is practically not transmitted to another person; this includes pleural and glandular tuberculosis.

- **New Case**: A newly diagnosed patient who has never taken ATT for more than 4 weeks.

- **Chronic Case**: Patient who remains AFB positive even after completion of full course of supervised treatment; should be referred to a specialized chest unit.

- **Drug Resistance** or **Treatment Failure**: When sputum remains AFB positive after 5 months of chemotherapy; or a patient who has interrupted ATT for more than 2 months. upto 5 months after the start of chemotherapy, and is smear positive.

- **Relapse**: Patient once declared cured with appropriate ATT, presents again with sputum positive for AFB.
(If Rifampicin (R) containing regimen was used same drugs may be given, if non-R containing regimen was used patient is likely to be resistant to same ATT).

- **DOTS (Directly observed Tuberculosis)**: Short courses of ATT may be prescribed and directly observed to be swallowed by the patients by health workers or volunteers who visit homes. Cure rate of > 90% have been achieved with DOTS.

CATEGORIES OF TUBERCULOSIS AND TREATMENT

Abbreviations: Isoniazid (H), Rifampicin (R), Ethambutol (E), Pyrazinamide (Z), Streptomycin (S), Thiacetazone (T), Antituberculous Chemotherapy (ATT).

Category-I (High Priority Class)

Newly diagnosed cases with sputum positive for AFB, not treated with ATT before for >4 weeks, seriously ill patients with disseminated disease like, meningitis, polyserositis, spinal tuberculosis, or extensive pulmonary parenchymal disease (but sputum -ve for AFB).

Treatment

- 2 x RHZE (S) + 6 x HT (E)
  or + 4 x HR
- If sputum is AFB + at 2 months continue 4 drugs till 3 months.
- If sputum is + at 3 months, send for AFB/C&S and start continuation phase.
- If sputum is AFB + at 5 months, this is treatment failure.
- If overall drug resistance is high add 3rd drug (R or E) in continuation phase (sputum may be checked for AFB C&S).
- If overall drug resistance is low (non-endemic areas) E may not be added.
- In case of meningeal disease continuation phase may be prolonged by 3 months.

Category-II (Highest Priority Class)

Patients with relapses and treatment failure (Smear +) after short course chemotherapy.

Treatment

- 2 x HRZE(S) + 6x HRE(T)
- If sputum is AFB + at 2 months or culture facility not available continue 4 drugs (omit S) till 3 months.
- If sputum is AFB + at 3 months send sputum for AFB/C&S, continue 4 drugs till 4 months supervise treatment till smear -ve.
- If sputum is AFB + at 5 months (or C & S) shows MDR) treat as category-IV; refer to a specialist unit; achieving cure is remote.

Category-III (Limited Disease)

Sputum negative pulmonary, pleural, glandular

or localized extrapulmonary disease. Pulmonary cases have higher priroity than non-pulmonary.

Treatment

- 2 x HRZ + 6 x HT (T)
  or + 4 x HR
- If sputum found + for AFB treat as category-I.
- If a child cannot complain about visual disturbance, avoid ethambutol.

Category-IV (Low Priority Class)

MDR (resistant to at least R & J), and chronic tuberculosis.

Treatment

- If non affording may be put on R+H for rest of life.
- If affording may be referred to specialized unit for treatment after C&S/or second line drugs.

Note: In continuation phase RIFAMPICIN (R) may not be used for national programmes (for countries with limited resources) to avoid emergence of drug resistance; however, for an individual case R may be prescribed, when good compliance is predicted.

Pregnancy

In human beings no teratogenic effect of ATT has been observed so there is no absolute contraindication to the use of these drugs at any stage of pregnancy. Streptomycin may be avoided because of toxicity to the fetus. Breast-feeding may be continued during ATT.

Hepatic Dysfunction

If a patient has deranged liver function, stop ATT if liver enzymes are 3 times normal. When enzymes become normal restart ATT, if it gets abnormal again stop all drugs and refer him to a chest unit. Tuberculosis itself may result in deranged LFT particularly high Alk. Phosphatase, which become normal after ATT. Streptomycin, Ethambutol and PAS are safe in liver disease or jaundice.

Renal Dysfunction

Avoid ethambutol, PAS and cycloserine, while dosages of streptomycin, INII and PZA may be adjusted in renal insufficiency. Cases with acute renal failure, post-transplant or on dialysis may be referred to a chest unit.

Dosage Adjustment

Serum Creatinine	Ethambutol	INH	Streptomycin
2 mg%	give 2/3 of dose	Normal	0.5 Gm/D
2-3 mg%	reduce by 50%	Normal	0.25 Gm/D
> 3 mg%	give 1/3 of dose	Reduce by 1/3	0.25 Gm/ alt day

Chemoprophylaxis

In general there is no place for chemoprophylaxis in endemic areas like Pakistan: if clinical sunpicion is high for active disease full course of ATT may be given. For infants born to recently diagnosed tuberculous mothers, chemoprophylaxis may be given, i.e., H+R x 3 months. During this period mother is treated and hopefully gets converted and become non-infectious. At 3 months. check baby with tuberculin test; if negative give BCG vaccine, if positive keep under observation till appearance of clinical signs of active disease and then treat with full ATT.

Drugs	Dose (Adult)	Max	Dose (Paeds)
INH	5mg/kg	(300mg)	10-20 mg/kg
ETH	15-25 mg/kg	(1500mg)	15-25 mg/kg
RIF	10mg/kg	(600 mg)	10-20 mg/kg
PZA	15-30 mg/kg	(2000 mg)	15-30 mg/kg
STREP	15 mg/kg	(0.75-1 Gm)	20-40 mg/kg
THIA	2-5 mg/kg	(150 mg)	2.5 mg/kg

Ethambutol

Dosage during initial phase in 25mg/kg and in continuation phase is 15mg/kg. Visual acuity may be checked periodically as dose dependant visual loss may occur.

Isoniazid

Pyriodoxine supplement of 10mg may be given to prevent peripheral neuropathy. Can also produce irreversible acute optic neuritis.

Rifampicin

On reintroduction after a long gap may result in acute renal failure and severe hemolysis.

Thiacetazone

May not be used when HIV is positive.

Streptomycin

May be avoided during pregnancy. Wear protective gloves when giving injections. Can produce sterile abscess at injection site.

Pyrazinamide

May not be used in gout and epilepsy. Can change blood glucose levels.

Fixed Drug Combinations

In endemic but developing countries fixed drug combinations are far superior as compliance is better, cost is reduced and chances of acquired drug resistance is lower in case of missed dosages. Dosages may be prescribed according to body weight, rather than flat doses and altered with gain or loss in weight.

Dosage

- 4 drug combination containing REIZ
  = one tab for 12 kg (maximum = 5 tab)
- 3 drug combination containing RIE
  = one tab for 15Kg (maximum 4 tab.)
- 3 drug combination containing RIZ
  = one tab. for 10Kg (maximum = 6 tab.)

Monitoring During Therapy

At the start of treatment chest radiograph, sputum for AFB/C&F if facilities available (besides smear), baseline liver enzymes, renal functions (serum uric acid, urea, creatinine) and complete blood count are mandatory. During treatment periodic neurological evaluation is needed (which includes, visual acuity, colour vision, hearing, proprioception), as well as serum biochemistry in high risk patients.

REFERENCES

1. Dolin PJ, Ravinglione MC, Koch A. Global tuberculosis incidence and mortality during 1990-2000, Bull WHO 1994; 72: 213-20.
2. Schluger NW. Multidrug resistance tuberculosis: Pulmonary Perspective. American College of Chest Physicians. June 1996. Vol 13.
3. Aziz A. Tuberculosis control programme in West Pakistan. In: Nadi PL, Cam WK (eds) Proceeding of the 7th Asia Pacific Congress on Disease of the Chest Hongkong, 1981.
4. WHO. Model prescribing information; drugs used in mycobacterial disease. WHO Geneva, 1991.
5. WHO. Drug information, Geneva 1993.
6. American Thoracic Society. Treatment of tuberculosis and tuberculous infection in adults and children. Am Rev Resp Dis 1986; 134: 355-63.
7. Joint tuberculosis committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom. Recommendations 1998.

The Author:

Syed Nazim Hussain Bokhari
Associate Professor
Department of Pulmonary Medicine,
Shaikh Zayed Postgraduate Medical Institute,
Lahore

Address for Correspondence:

Syed Nazim Hussain Bokhari
Associate Professor
Department of Pulmonary Medicine,
Shaikh Zayed Postgraduate Medical Institute,
Lahore