

TREATMENT OF TUBERCULOSIS

I. Pre-antibiotic era

- A. Sanatorium movement
 - 1. Rest
 - 2. Fresh air
 - 3. Good food
 - 4. Sunlight
- B. Surgical approaches (removal of lung, collapse, ping-pong ball installation)
- C. Mortality rates of about 50% of cases in 5 years, for those who were smear-positive

II. Chemotherapy

- A. First drugs effective against tuberculosis (TB)
 - Streptomycin in 1944
 - P.A.S. in 1949
 - Isoniazid (INH) in 1952
- B. Very early it was learned that TB *must* be treated with more than one drug, and for a long time (many months)
- C. Current standard treatment (“first line drugs”)
 - 1. Initial regimen (first two months) of 4 drugs:

INH	300 mg daily
Rifampin	600 mg daily
Pyrazinamide	25 mg/kg daily
Ethambutol	15 mg/kg daily
 - 2. Continuation phase (for four months) of 2 drugs:

INH	300 mg daily or 900 mg bi-weekly
Rifampin	600 mg daily or 600 mg bi-weekly

This six-month regimen is called the “short course”

- D. Without PZA (pyrazinamide), INH and rifampin daily may be used to treat for 9 months, providing all organisms are fully susceptible (ethambutol or streptomycin should be added until susceptibility tests are completed)

- E. The treatment regimen must be changed if there is drug resistance, the patient is slow to improve, or does not convert to negative sputum cultures within 3 months
- F. General principles of treating TB
 - 1. Always treat with a multiple-drug regimen
 - 2. Never add a single drug to a failing regimen (why? to prevent drug resistance)
 - 3. Duration of treatment depends on the drugs used and the type of disease
 - 4. In persons with drug-resistant TB, treatment may extend to 18-24 months
 - 5. Serious side effects (such as drug-induced hepatitis) do arise in 10-20% of patients, requiring a change of medication regimen
- G. How do you know the treatment is effective?
 - 1. Symptoms improve, usually within weeks
 - 2. Sputum cultures, change to negative usually within 2-3 months
 - 3. At three months (sooner in children), chest x-ray improves

III. Directly-observed therapy

- A. The effectiveness of TB treatment rests on patient taking all the doses prescribed. After the first few weeks or months, the patient begins to feel better and enters a time when doses may be missed, leading to inadequate treatment
 - 1. Directly observed therapy (DOT) means a health worker *watches* the TB patient swallow each dose of the prescribed drugs
 - 2. DOT ensures the completion of an adequate course of medicine
 - 3. Failure to take all the doses prescribed has been found to be the *single most important factor* in treatment failure
 - 4. Many TB patients cannot complete the long course without the help provided through DOT
 - 5. DOT can occur either at a clinic or in the home or community

IV. Tuberculosis treatment during pregnancy and breastfeeding

- A. Untreated TB is a much greater threat to both mother and baby than treatment with appropriate drugs

- B. Initial drug regimen for a prenatal woman with TB
 - 1. INH – rifampin – ethambutol
 - 2. PZA is not used in the U.S., but is prescribed in other countries. Its effect on the unborn is not known
- C. The TB medicines cross the placenta but have no adverse effect on the fetus (streptomycin is the only TB drug known to be toxic to the developing fetus and can cause deafness)
- D. TB drugs in the breast milk are in such small concentrations that they are safe for infants. However, they do not protect the baby from TB if the mother is not taking adequate treatment!

V. Treatment in children with tuberculosis

- A. TB in children responds to the same treatment regimens as used for adults, but the doses differ (based on body weight)
- B. *Weights* in children receiving TB medications need to be carefully monitored over time and doses re-calculated as the child grows. Correct dosage for weight will avoid under-treatment and potentially toxic overdoses
- C. Adherence to treatment prescribed IS NOT better in children, and parents may not report missed doses, or be able to get the child to cooperate
- D. DOT is necessary for treating all children with TB

VI. Treatment of HIV-infected patients

- A. Rifampin interferes with protease inhibitors
- B. TB treatment must be coordinated with HIV treatment

VII. Adverse reactions to tuberculosis medications

- A. *Mycobacterium tuberculosis* grows slowly and is difficult to kill. Treatment includes powerful drugs, taken for many months
- B. Every health worker must be involved in monitoring the patient for signs of any drug toxicity

- C. Baseline tests when starting TB drugs
 - 1. Adults need liver function tests (not necessary for kids)
 - 2. If liver function is elevated, more frequent monitoring is needed by physician
 - 3. Ethambutol
 - a) everyone taking ethambutol needs monthly checks of visual acuity and red-green color perception
 - b) ethambutol is avoided in young children who cannot report vision changes
 - 4. All ages who are receiving streptomycin or other second line drugs need monitoring of hearing and balance
- D. All patients on TB medications, adults and children, need to be assessed *face-to-face* by a health worker at least monthly
- E. Dangerous adverse effects
 - 1. All patients and their families need education about dangerous adverse reactions, and should be instructed to stop treatment immediately and seek physician evaluation if they occur
 - 2. Health workers noting such reactions should remove all TB medications from the patient, as failure to stop taking the medications has been associated with fatalities. Immediate referral to the treating physician is necessary
- F. Symptoms associated with adverse TB medication reactions
 - 1. Skin rash and itching (most common side effect)
 - 2. Unexplained fever
 - 3. Joint pain or aching
 - 4. Blurred vision
 - 5. Tingling or burning sensation in hands or feet
- G. Signs of possible liver toxicity (hepatitis)
 - 1. Loss of appetite
 - 2. Nausea and vomiting
 - 3. Dark urine (coffee-colored)
 - 4. Yellowing of skin or eyeball (jaundice)
- H. Routine blood testing is not necessary unless the patient reports symptoms. Stopping the medications immediately upon noticing adverse reactions is most important

VIII. Expected drug interactions

- A. Isoniazid: when taken with dilantin, increases in blood concentration of both medicines. Dilantin doses should be reduced

- B. Rifampin
 - 1. The patient needs to be told that the urine, tears, and sweat will become orange in color as the medication is excreted
 - 2. The orange color may permanently stain soft contact lenses
 - 3. Decreases the effectiveness of birth control pills. Patient should be instructed to use another barrier method in addition to the oral contraceptive
 - 4. Interferes with methadone metabolism. Coordinate treatment with methadone maintenance programs