Tuberculosis Medications
MW, a 36 y/o woman, is admitted to the hospital with a 2 month history of cough, which has recently become productive. She also is experiencing fatigue, night sweats, and has lost 10 pounds. Other medical problems include diabetes mellitus, which is controlled with 10 units of NPH daily, and poor nutritional status secondary to frequent dieting.
MW works as a volunteer in a nursing home several days a week. Recently two patients that she had been caring for were diagnosed with TB.

MW’s physical exam was normal but MW’s chest X-ray revealed bibasilar infiltrates. A PPD skin test and sputum collection for cultures and sensitivity and a smear for AFB were ordered as part of MW’s diagnostic workup.

Initial lab tests were within normal limit.
The result of MW’s PPD skin test, read at 48 hours was palpable induration of 14mm. Her sputum smear was positive for AFB, and additional sputum cultures for M. tuberculosis were ordered to confirm a diagnosis of active disease.
Question:

What subjective and objective findings does MW have that are consistent with TB?
Subjective Findings:

- History of cough
- Fatigue/general malaise
- Night Sweats
- Anorexia
- Pleuritic pain
Objective Findings:

- Fever
- Bibasilar infiltrates
- Positive sputum for AFB
- Positive PPD
- Risk factor of diabetes
Question:

- Should MW be tested for HIV infection?
- Why or why not?
Yes! TB may be the first manifestation of HIV infection.

Approximately 37% of HIV-infected patients develop TB within five months compared with 5% of exposed persons with intact immune defenses.
Question:

- MW’s HIV test was negative. How should treatment be initiated in MW pending the results of the sputum C & S?
The goal of tuberculosis treatment is to interrupt tuberculosis transmission, prevent acquisition of medication resistance and cure the patient.
Treatment of Tuberculosis – General Principals

- Four medications must be included in the initial treatment regimen
  - INH (isoniazid)
  - RIF (rifampin)
  - PZA (pyrazinamide)
  - EMB (ethambutol)

- Exceptions
  - Very young children – exclude EMB
  - Pregnant women – exclude PZA

- The purpose of a 4 medication regimen is to prevent acquisition of medication resistance.
Directly observed therapy (DOT)

- Standard of care for treatment of active TB
- Direct observation by a trained health care worker of every anti-tuberculosis medication dose administered
- DOT should be used with both pulmonary and extrapulmonary TB patients
Never add a single medication to a failing regimen – Doing so can lead to acquired medication resistance.
Manage TB patients in the least restrictive manner possible.

Identify strategies tailored to the individual patient which will lead to treatment adherence and avoid the need to invoke more restrictive measures to assure treatment completion.
Treatment Guidelines:

- The standard treatment regimen for Maryland consists of two phases
  - Initiation Phase
  - Continuation Phase
Treatment Guidelines:

- **Initiation Phase**
  - INH, RIF, PZA and EMB for a total of 8 weeks
  - Daily therapy is provided initially followed by twice weekly treatment for the remainder of therapy
  - The first weeks of therapy can be handled by giving every dose directly observed for either 7 days per week for 2 weeks, or 5 days per week for 3 weeks.
  - Providing medication in weekend and holiday packets is not recommended for the first 2 weeks of therapy.
Treatment Guidelines:

- Continuation Phase
  - After completion of the daily therapy portion, the preferred medication regimen for pan-sensitive TB is twice weekly DOT for the remainder of treatment.
  - The medication regimen should be changed at this point to:
    - INH and RIF twice weekly – DOT for 18 wks, or
    - INH and RPT (rifapentine) twice weekly – DOT for 18 wks
Medication Interactions:

- Medication-medication interactions can result in changes in the concentrations of one or both of the medications involved.
- There are relatively few interactions that substantially change the concentrations of anti-tuberculosis medications.
- Most medication interactions are associated with rifampin.
Medication Interactions:

- Methadone
  - TB patients on methadone may require up to a 50% increase in methadone while on treatment for TB.

- Oral contraceptives
  - Rifampin reduces the contraceptive effect of oral contraceptives. TB patients taking both rifampin and oral contraceptives should be instructed to use a barrier method of birth control.
Medication Interactions:

Other medication interactions with Rifampin

- Antiretrovirals
- Coumadin
- Anticonvulsants
- Cardiovascular agents
- Bronchodilators
- Oral hypoglycemics
- Immunosuppressants
- Antifungals
- Psychotropic medications
Back
To the
CASE STUDY
Question:

MW, now on treatment for TB....

- Can she transmit infection during treatment?
Answer:

- She should cease to be infectious about two to four weeks after therapy has been started, at which time the number of organisms in her sputum should be reduced.
Question:

Six weeks later MW’s sputum cultures were positive for M. tuberculosis. Sensitivity tests showed that the organism was sensitive to both INH and rifampin.

- What medication regimen should be used for continued therapy of MW?
- How long should treatment be maintained?
After completion of the daily therapy portion, the preferred medication regimen for pan-sensitive TB is twice weekly DOT for the remainder of treatment.

The medication regimen should be changed at this point to:

- INH and RIF twice weekly – DOT for 18 wks, or
- INH and RPT (rifapentine) twice weekly – DOT for 18 wks
Question:

- Why is multiple medication therapy indicated for the treatment of active TB disease?
Answer:

- To prevent the development of medication resistance.
- To sterilize the sputum as quickly as possible.
Question:

- If MW does not respond to her current therapy should one more medication be added to her regimen?

- Why or why not?
Answer:

- NO!
- Adding a single medication to a failing regimen is the most common and devastating mistake in TB therapy. This is essentially the same as monotherapy because one can assume that the organisms are resistant to the medications currently being used. Resistance to the new medication will eventually develop, further reducing the patient’s chance of cure. New susceptibilities should be obtained and treatment adjusted accordingly.
Adverse Medication Effects

- INH
  - Hepatitis
  - Peripheral neuropathy
  - Allergic reactions
  - Medication interactions e.g. phenytoin (Dilantin), carbamazapine (Tegretol), diazepam (Valium)
Adverse Medication Effects

- Rifampin
  - Flu-like syndrome
  - Hepatotoxicity
  - Thrombocytopenia
  - Nausea and vomiting
  - Discoloration of bodily fluids
  - Medication interactions
Adverse Medication Effects

- INH-rifampin
  - Hepatotoxicity
- Ethambutol
  - Optic neuritis