TUBERCULOSIS

EPIDEMIOLOGY
• One third of the world’s population is infected with the organism that causes tuberculosis
• Most of these individuals reside in underdeveloped countries
• Asia and Africa account for most of these infections

EPIDEMIOLOGY
• There are approximately 3 million deaths per year from tuberculosis
• There are approximately 8 to 10 million new cases every year
• The interactions between TB and HIV have caused active disease of both infections

Global Epidemiology
• Two-thirds of the cases in the world are not supervised by DOTS.
• This leads to more transmission and the development of new cases of TB in the world.
• There needs to be the ongoing treatment of TB and HIV/AIDS to stop the continued spread of tuberculosis and HIV/AIDS.

Global Epidemiology
• USA and Canada 17,000 cases estimated 5.6 cases per 100,000
• USA and Canada 18,0056 cases notified 5.8 per 100,000 notified

History of Tuberculosis
• There was a steady decline in the cases of tuberculosis from 1953 to 1985. There was a small bump in the number of cases in 1975 but this was related to an influx of people from Southeast Asia following an end to the war in Vietnam.
• There was a rise in the number of cases in the 80’s secondary to a number of issues chief of which was the lack of directly observed therapy, AIDS, homelessness, and lack of treatment for the mental health issues and the chemically dependent, and a lack of the public health infrastructure.

US Epidemiology

• The case rate has come done during the past decade.
• There are more cases of TB in the foreign-born than in US citizens.
• It is still a disease of the disenfranchised.
• Blacks and Hispanics are disproportionately affected

US Epidemiology

• The cases involved still largely affect young people between the ages of 15 and 50 years
• Men are more affected than women.
• Certain states are more affected than others; they include California, New York, Texas, Florida, Illinois

Number of Tuberculosis Cases by Place of Birth, Minnesota, 1996-2005

Clinical Symptoms of TB

• The typical symptoms that are described for TB include fever, chills, night sweats, anorexia, cough, sputum production, and weight loss.
• Extra-pulmonary sites determine the clinical symptoms that the patient may have at the time they seek help for their TB.

Foreign-Born Tuberculosis Cases by Region of Birth and Year of Diagnosis, Minnesota, 2001-2005

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Symptoms in HIV/AIDS

- Symptoms of TB in the HIV/AIDS can be quite varied. The diagnosis depends upon clinical suspicion and pursuing the site infected. Pulmonary infection needs to be eliminated along with the central nervous system.
- Patients may have false negative skin tests. Negative skin test are more likely in AIDS patients.

Anatomic Sites of Tuberculosis

- Pulmonary Only 82%
- Pleural 4.6%
- Lymphatic 5.1%
- Genitourinary 2.2%
- Bone and Joint 1.7%
- Miliary 1.4%
- Meningeal 0.9%
- Peritoneal 0.6%
- Other 1.5%

Diagnosis of Tuberculosis

- The definitive diagnosis is made by culture or identification of the genetic material by PCR.
- A diagnosis can be made by staining procedures that involve sputum, urine, gastric washings, CSF or tissue such as bone marrow biopsy or liver biopsy.

Diagnosis of Pulmonary Tuberculosis

- The diagnosis of pulmonary tuberculosis is first attempted by obtaining three early morning spuata and staining them for AFB. These are obtained three mornings in a row.
- They should be ordered to be induced by the respiratory therapist and delivered to the laboratory.
## Diagnosis of Pulmonary TB
- If the sputum samples are negative by staining and therapy needs to be initiated then it is possible to do a bronchoscopy to obtain a sputum specimen by BAL.
- A lung biopsy or pleural biopsy are other procedures that may be done to make a diagnosis of TB.

## Diagnosis of Extra-Pulmonary Tuberculosis
- Diagnosis is made by obtaining blood or tissue from the suspected organ site. This may involve obtaining CSF or meningeal tissue in the case of a central nervous system infection.
- Genito-urinary infection this may come from the urine itself or a biopsy of the bladder or the kidney.

## Diagnosis of Extra-Pulmonary Tuberculosis
- Bone and Joint TB are diagnosed by obtaining synovial fluid or tissue such as cartilage or bone for diagnosis.
- Peritoneal TB is diagnosed by obtaining a peritoneal biopsy.
- Pericardial Tb is made by doing a pericardial biopsy such as a pericardial window.

## Diagnosis of Extra-Pulmonary Tuberculosis
- The diagnosis of central nervous system TB is made by obtaining CSF from a lumbar puncture, a cisternal puncture, or a meningeal biopsy.
- The diagnosis of miliary TB is made by obtaining tissue from a biopsy such as the liver or bone marrow.

## Diagnosis of TB in HIV/AIDS
- The sites of TB in the HIV/AIDS include both pulmonary and extra-pulmonary.
- The HIV-infected were the first patients to grow TB and other mycobacterium directly from the blood.
- Both pulmonary and extra-pulmonary can occur in up to 75% of patients that are HIV infected.

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Diagnosis of TB

- The key to the diagnosis of TB is to make sure that one has adequate specimen to make the microbiologic diagnosis.
- It is always best to obtain more than one specimen in order to provide back up for the one specimen on which you are depending to do the susceptibility testing.

Diagnosis/Management

- After the culture or detection testing is positive then SUSCEPTIBILITY TESTING MUST BE DONE on ALL THE FIRST LINE AGENTS.
- The second specimen is for susceptibility testing should there be a problem with the first specimen.

Skin Testing in the HIV Positive

- It is important to skin test any HIV infected patient.
- Any positive reading may be important.
- The accepted rule of thumb is that 5mm of induration is considered positive.
- In the HIV negative patient 10mm of induration is considered positive.

RISK of Developing TB in the HIV-Infected

- The risk of developing TB in the HIV+ may be about 8% per year.
- The risk of developing TB may be higher as each year goes by if the CD4 count is dropping.
- The risk of developing TB in the HIV- is about 5% to10% over their lifetime.

Resistance

- Primary Resistance occurs prior to the start of therapy in the individual patient.
- Secondary Resistance develops while the patient is taking therapy.

Management of Tuberculosis

- The reason that there are at lest four drugs included in the regimen has to do with the underlying likelihood that the organism will develop resistance to the agents.

  - Isoniazide 1 in 1 million
  - Rifampin 1 in 10 million
  - Ethambutol 1 in 1 million
  - Streptomycin 1 in 100,000
Management of Tuberculosis

- All those patients who have active pulmonary tuberculosis need to have their therapy completed and documented. In some cases, this requires direct supervision.
- All the contacts of the active cases need to be identified and tested for their exposure to the active case of TB.

Management of Tuberculosis

- An assessment of the likelihood of compliance with the therapy needs to be done.
- An assessment of the likelihood of resistance to therapy that will help in the selection of a regimen for the patient.
- One has to be on the alert for the possibility of drug-resistance before starting therapy.

Management of Tuberculosis

- Monitoring of therapy needs to be done for drug levels if the patient is not responding to therapy and the patient is actually taking the therapy.
- Therapy needs to be monitored on the basis of the underlying disease such as diabetes, liver and renal disease.

Management of Tuberculosis

- The HIV epidemic brought to the forefront the problems of the management of tuberculosis in the United States.
- The lack of follow-up, directly observed therapy, homelessness, drug addiction all contributed to the problems of treating TB and led to an epidemic of TB in certain areas of the country.
Management of Tuberculosis

- There are four first line agents to treat tuberculosis; they include the following:
  - Isoniazide
  - Rifampin
  - Pyrazinamide
  - Ethambutol

Second-line Agents of Tuberculosis

- The agents include the following:
  - Clofazamine
  - Para-Aminosalicylic Acid
  - Quinolones
  - Ethionamide
  - Cycloserine

Second Line Agents Cont’d

- Aminoglycosides:
  - Kanamycin
  - Capreomycin
  - Amikacin
  - Streptomycin

Treatment of Tuberculosis

- The treatment of tuberculosis requires the following:
  1. An assessment of the host and any special considerations such as: HIV status, pregnancy, renal or liver disease, underlying immunosuppression such as diabetes, transplant, silicosis, gastrectomy, hepatitis B or C, mental illness, alcoholism

- Most of the patients who have TB are young and the major issues will involve taking their meds and keeping the drug regimen simple. This will require taking drugs for 6 months if they are compliant and they do not have drug resistance. This will as a general rule require taking 4 drugs for 2 months and then taking 2 drugs for 4 months. This will complete 6 months of therapy.

Treatment of Tuberculosis

- Monitoring for sterilization of the site of infection
- Monitoring for drug resistance to develop
- The successful regimens are known to have a specific number of doses of therapy that need to be completed in order to consider the patient finished with therapy
Regimens need 4 drugs initially and this usually includes INH, RIF, EMB, PZA. It is hard these days to get streptomycin from the CDC. Patient generally liked this medication because it meant one less pill for them to take.

**Treatment**

- Pick the regimen that will be the easiest to complete and that the patient will be able to tolerate.
- One needs to continually assess for the complications of worsening disease.
- One needs to assess for the complications of the therapy.

**Treatment of Tuberculosis**

- Assessment of the CXR for cavitation and the extent of disease.
- Assess the status of the sputum as to whether the sputum is positive or negative.
- Assessment of the likelihood that the patient will be compliant with the drug regimen.