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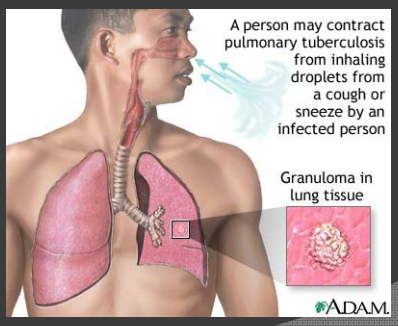
# TB AND CHRONIC MEDICAL CONDITIONS

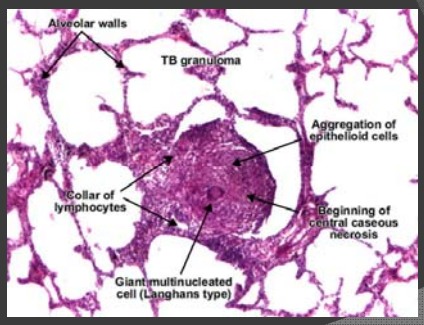
## Objectives

- Review Basic TB Pathophysiology and the role of the Immune system in TB disease
- Identify populations at higher risk for Tuberculosis due to medical conditions
- Overview of Chronic Medical conditions and how they may effect TB course or treatment

## Tuberculosis Infection in Healthy Person

- Tuberculosis exposure inhaled in droplets
- local inflammatory reaction often within a fibrotic, calcified lesion (Ghon focus).
- Latent TB is asymptomatic and is associated with both a positive TST and a chest radiograph that is either normal or shows only the self-contained infection.
- Of those patients with LTBI, about 90% will never develop an active infection



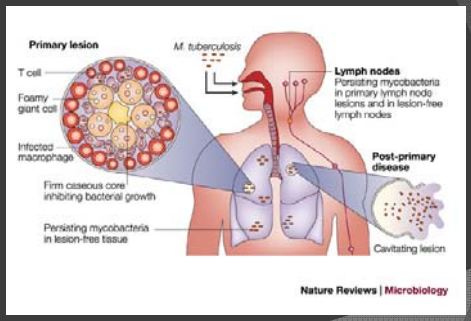




## Identifying Persons at Risk for Developing TB Disease

- HIV infection
- Injection drug use
- Radiographic evidence of prior healed TB
- Low body weight (10% below ideal)
- People from areas with high rates of Tuberculosis
- Diabetes?

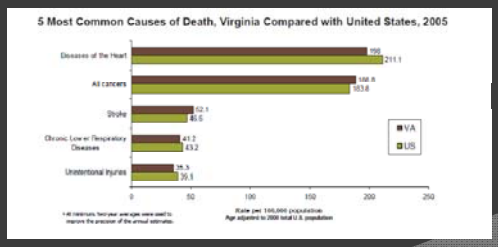
## Medical Conditions that increase risk of conversion from LTBI to TB

- Other medical conditions, such as:
  - silicosis
  - diabetes mellitus
  - chronic renal failure or on hemodialysis
  - gastrectomy
  - jejunoileal bypass
  - solid organ transplant
  - head and neck cancer
  - conditions that require prolonged use of corticosteroids or other immunosuppressive agents such as TNF-antagonists




## Chronic diseases

- In 2005, 133 million Americans—almost 1 out of every 2 adults-had at least one chronic illness
- 7 out of 10 deaths among Americans each year are from chronic diseases
- Heart disease, cancer and stroke account for more than 50% of all deaths each year



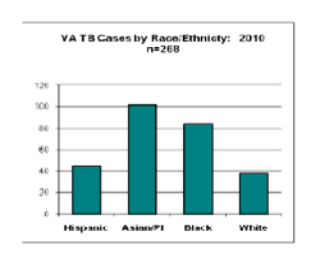

http://www.cdc.gov/nccdphp/publications/aag/pdf/virginia.pdf

## Common causes of chronic disease

- Lack of physical activity
  - -More than 1/3 of adults do not meet recommendations for aerobic physical activity
- Poor nutrition
  - -in 2007 only 24% of adults reported eating 5 or more servings of fruits/vegetables daily
- Tobacco use
  - -More than 43 million American adults smoke (~1 in 5)
- Excessive alcohol consumption

http://www.cdc.gov/chronicdisease/overview/index.htm

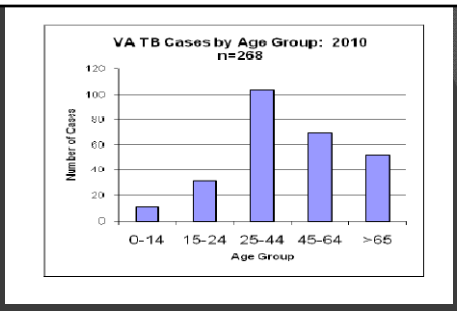
As of May 4, 2011, approximately 574,600 people have died from chronic disease this year. CDC.gov




- Virginia's TB case rate for 2010: 3.4/100,000
- Cases among US-born African Americans increased for the second year in a row from 48→52
- Cases among US-born Whites increased from 25→35

## Racial and ethnic health disparities

- **African Americans:**
  1.9 times more likely than white adults to have diabetes
  -Data from 2006 showed 70% more likely to die of viral hepatitis than whites
- **American Indians and Alaska Natives:**
  -2.3 times more likely than white adults to have diabetes
- **Hispanics/Latinos:**
  -In 2005, Hispanics were 1.6 times more likely to die of diabetes than non-Hispanic whites




- Almost 2/3 (65%) of TB cases in Virginia in 2010 were among people age 25-64

## Elderly TB patients

- Many elderly patients have multiple medical problems including:
  -Diabetes
  -Heart disease
  -Chronic lung disease
  -End-stage renal disease

## Heart disease (1)

- Cardiovascular disease:
  -heart attack, angina, stroke, high cholesterol, high blood pressure
- Arrhythmia:
  -atrial fibrillation
- Valvular disease
- Congestive heart failure

## Heart disease (2)

- In 2005, heart disease accounted for 25% of deaths in Virginia while stroke caused 6% of deaths
- In 2007, 27% of adult Virginians had high blood pressure and 37% had high cholesterol, which increases risk for heart disease and stroke

http://www.cdc.gov/chronicdisease/states/pdf/virginia.pdf

## Rifampin and heart medications

- Blood pressure:
  -verapamil, diltiazem, metoprolol, enalapril, losartan
- Heart failure:
  -coumadin, digoxin
- Cholesterol:
  -simvastatin
- Arrythmia:
  -propafenone, mexilitine

## Diabetes

- Diabetes- High Blood Sugar caused by insulin resistance or insulin shortage
- In 2005, sixth leading cause of death in US
- Leading cause of:
  1. Kidney failure
  2. Nontraumatic lower-extremity amputations
  3. Blindness among adults aged 20-74

## Links between DM and TB

- Diabetes increases the risk of developing active TB
  -diabetics are 3 times more likely to develop TB than non-diabetics
- TB is a disease of poverty and/or immunosuppression
- Diabetes also affects those in the lowest socio-economic strata
- 10-35% of patients with TB have diabetes
- Studies show longer time period to negative AFB and negative culture during initial treatment; however no significant difference in success of initial treatment

Jeon and Murray. PLOSmedicine. 2008;5:1091-1095

## Why are people with diabetes more likely to get TB?

- People with diabetes have an altered immune response due to chronic hyperglycemia
- Diabetics are more likely to become infected with bacterial and fungal pathogens
- Recent studies suggest that increased cytokine responses in patients with poor glucose control are associated with TB

Restrepo et al. Clin Infect Dis. 2008;47:634-41.

## Who is the typical TB/DM patient?

- *Restrepo et al.* found that they were more likely to be:
  - -older women (>40 yo)
  - -have no classic risk factors for TB (i.e. drug or alcohol abuse, history of imprisonment, homelessness)
  - -less likely to be HIV-positive

Restrepo BI et al. Am. J. Trop. Med. Hyg. 79;2008: 541-544.
Restrepo BI et al. Epidemiol. Infect. 135;2007:483-491.

## Kidney disease

- Kidneys remove waste and excess fluid from body
- 1 in 9 Americans has chronic kidney disease
- Major causes include: diabetes, hypertension
- Heart disease is the major cause of death in chronic kidney disease patients

www.kidney.org

## TB and kidney disease

- Ethambutol is 80% cleared by kidneys
- It may accumulate in  in patients with renal insufficiency and could cause toxicity
- To prevent this, it is dosed less frequently
- Ethambutol drug levels are often checked
- Pyrazinamide mostly metabolized by liver but some metabolites cleared by kidney so dosing also adjusted in renal insufficiency

## TB and dialysis

- All TB medications should be given after dialysis
- This is to prevent loss of drug during hemodialyisis
- This can also help facilitate DOT

**TABLE 15. Dosing recommendations for adult patients with reduced renal function and for adult patients receiving hemodialysis**

| Drug | Change in frequency? | Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis |
|---|---|---|
| Isoniazid | No change | 300 mg once daily, or 900 mg three times per week |
| Rifampin | No change | 600 mg once daily, or 600 mg three times per week |
| Pyrazinamide | Yes | 25–35 mg/kg per dose three times per week (not daily) |
| Ethambutol | Yes | 15–25 mg/kg per dose three times per week (not daily) |
| Levofloxacin | Yes | 750–1,000 mg per dose three times per week (not daily) |
| Cycloserine | Yes | 250 mg once daily, or 500 mg/dose three times per week* |
| Ethionamide | No change | 250-500 mg/dose daily |
| *p*-Aminosalicylic acid | No change | 4 g/dose, twice daily |
| Streptomycin | Yes | 12–15 mg/kg per dose two or three times per week (not daily) |
| Capreomycin | Yes | 12–15 mg/kg per dose two or three times per week (not daily) |
| Kanamycin | Yes | 12–15 mg/kg per dose two or three times per week (not daily) |
| Amikacin | Yes | 12–15 mg/kg per dose two or three times per week (not daily) |

Standard doses are given unless there is intolerance.
The medications should be given after hemodialysis on the day of hemodialysis.
Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.
Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing, using serum concentration monitoring.
* The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity (see Section 3).

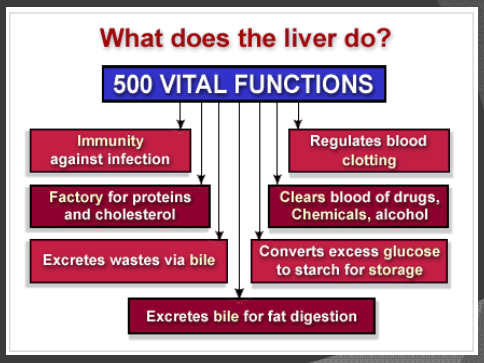
MMWR 2003;52: 64

## LIVER Disease-Hepatitis

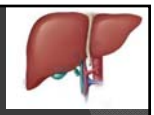
- Means “inflammation of the liver”
- Most commonly caused by viruses:
  -Hepatitis B
  -Hepatitis C
- Other causes:
  -NASH- Fatty Liver
  - Alcoholic
  -autoimmune

## Liver Disease- Hepatitis

- Fatty Liver Disease- Obesity and Diabetes
- Alcoholic Hepatitis- 10 -35% of long term heavy alcohol abusers
- Infectious Hepatitis A,B,C
  - Hepatitis A- Acute- food and water
  - Hepatitis B -Acute or Chronic – blood and sexual secretions
  - Hepatitis C – Chronic – blood




## TB and hepatitis



- Increased risk of drug-induced hepatitis in patients with preexisting liver disease
- Isoniazid, rifampin and pyrazinamide can all cause hepatitis
- Patients with liver disease may not receive some of these common TB medications to prevent hepatotoxicity
- Moxifloxacin often used instead

## TB and hepatitis

## TB and Cancer (1)

- Cancer treatment such as chemotherapy and steroids suppress the immune system and may increase the likelihood of TB reactivation

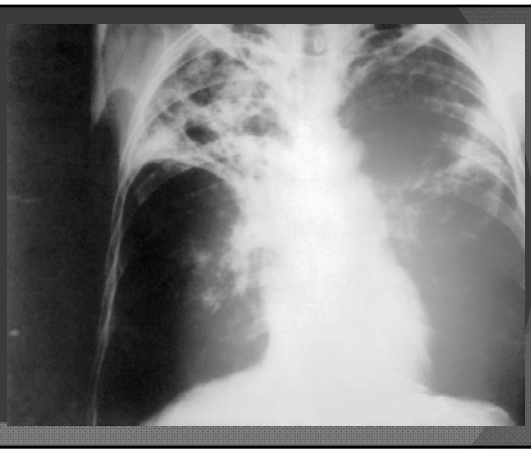
## TB and Cancer (2)

- Lung cancer is the leading cause of cancer death in the US
- Pulmonary tuberculosis is associated with an increased risk of lung cancer
- Initial diagnosis of both TB and Lung Cancer could be delayed due to occasionally similar appearance or large and obscuring tumors

Wu et al. Cancer 2011; 117:618-24

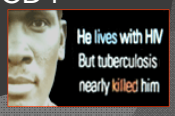
## Silicosis

- Lung damage caused by inhalation of silica dust
- Quartz, ceramics, stone workers, dental molds, glass making
- Can occur with Coal Workers Pneumoconiosis ( Black Lung ) if slica dust is present
- Increased rate of Tuberculosis in pts with silicosis

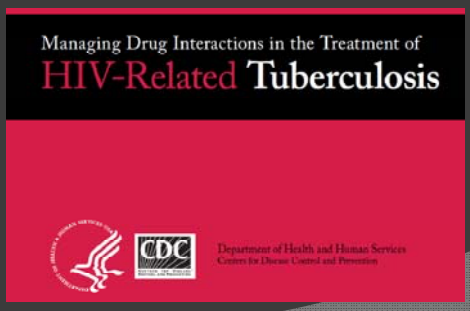



## HIV and Tuberculosis

- HIV increases the risk of TB reactivation enormously.
- PPD+, HIV- ⇒lifetime risk ~10%
- PPD+, HIV+⇒YEARLY risk ~10%
- TB may occur at higher CD4 Counts
- A deadly duo




## Drug interactions between TB medications and HAART




http://www.cdc.gov/tb/pubs/mmwr/Maj_guide/HIV_AIDS.htm

## TB – HIV Drug Interactions

- Rifampin should be avoided with nearly every Antiretroviral Regimen
- Rifabutin can be used safely at modified doses with Protease Inhibitors
- Doses of other ARVs may need to be adjusted as well
- Monitor closely for toxicities or treatment failure

## REACTIVATION TB - IRIS

- IRIS- Immune Reconstitution Inflammatory Syndrome- may occur with the initiation of HAART
- IRIS may worsen the course of Tuberculosis infection
- Starting treatment for HIV within the first 1-2 months of TB therapy confers a significant survival advantage

## TB and pregnancy

- Untreated TB presents a greater hazard to a woman and her child than treatment of TB
- Pyrazinamide is not routinely used to treat TB in pregnant women in the US because the effect is not known on the fetus
- As a result, therapy must be given daily for the first 8 weeks of therapy and the duration of treatment is extended to 9 months
- Streptomycin is also not used as it can cause congenital deafness
- Vitamin B6 should be given due to the risk of peripheral neuropathy in pregnancy

## TB and breast-feeding

- There are small concentrations of TB medications in breast milk but these do not produce toxicity in the nursing newborn
- Breast-feeding should not be discouraged

## Drugs that can cause Immune Suppression

- Long term Corticosteroid use
  - Used in many Auto Immune Diseases
- Cancer Chemotherapies
- Biologic drugs- TNF alpha inhibitors
  - Used in Arthritis treatments, Auto Immune diseases such as Crohn's Disease and Psoriasis