Basic Principles of TB

Satellite Conference and Live Webcast
Thursday, December 11, 2014
10:00 a.m. – 12:00 p.m. Central Time

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Faculty

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Objectives

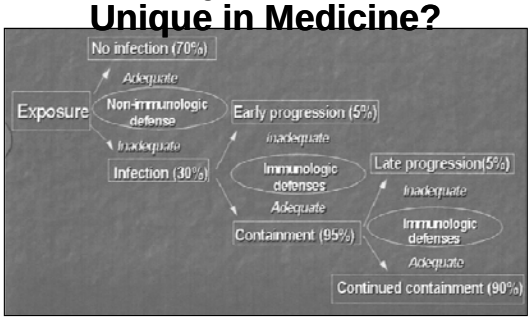
- **Basic information about tuberculosis**
- **Transmission and pathogenesis of tuberculosis**
- **Describe how humans contract tuberculosis and the effects of TB on different organ systems**
- **Differentiate between "TB infection" and "TB disease"**

What Makes TB Unique in Medicine?

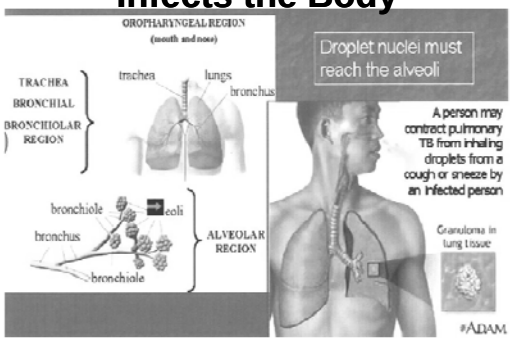
- **TB is a social disease with medical aspects**

  − Sir William Osler

Transmission and Pathogenesis of TB Unique in Medicine?



How TB Enters and Infects the Body



One Little Droplet!

- Droplet nuclei are infectious particles one to five microns in size which can remain suspended in air for several hours
- One droplet nuclei can contain one to three mycobacterial organisms (Starke)

Macrophages are "Big Eaters"

- When the droplet nuclei are inhaled and encounter alveolar macrophages
  - The mycobacterium can be killed
  - The mycobacterium can be contained
  - The mycobacterium can progress to active disease

ajrcmb v.32, 2005

We are all about those "T's"

- T lymphocytes are vital to the host's ability to contain mycobacterial infection

Oh the Places You Will Go!

- Lungs
- Lymph nodes
- Kidneys
- Bones
- Meninges
- And all the wrong places!

Who Gets TB and Who Doesn't?

- Number and viability of bacilli (One bacillus can initiate infection)
- Susceptible host

Hanging Out With the TB Germ!

- Good environments
  - Small space
  - Closed in space with less air circulation
  - Institutions - SHARED AIR
- Time
  - Length of exposure
  - Frequency of exposure

My Germ is Stronger Than Your Germ!

- Cough
- Sneeze
- Singing
- Shouting
- Duration of symptoms
- Cavitary
- Smear positive

My Germ is Better Than Your Germ!

- One cough can spread 500 droplets
- Average patient may produce 75,000 droplets / day prior to therapy
- Droplet nuclei may remain suspended in air

Well, My Germ is the Biggest Germ on the Block!

- Number of organisms dispersed in the environment
- Virulence of the organism
  - Genetics can play a role in the susceptibility of the host
  - Genetics can also determine the hosts ability to respond to pharmacologic agents

TB: A Contact Sport

- Shared air
- Length of exposure - distance from case
- Ventilation of area
- Recirculation of air

OK, So Back to Who Has the Best Germ!

- Pulmonary or laryngeal disease
- Cough
- Failure to cover cough
- Positive smear for AFB
- Cavitation
- Noncompliance
- Poor clinical response

What Else Can Go Wrong?

- Age of patient
- Immune Status
- Underlying disease

Age and Risks

- Puberty to 19 years of age 23% risk of cavitary disease in one study
- Elderly increased risk due to decline in immunity

Progress / Progress / Progress

- About 10% of adults with LTBI will develop tuberculosis
  - In the United States, about 5% will develop TB within the first two years after infection
  - Additional 5% risk over lifetime
  - The remaining 90% will always be infected but will not develop disease

Medical Conditions That are Problematic With TB

- HIV infection
- Organ transplant
- Silicosis
- Diabetes mellitus
- TNF antagonists / High dose steroids

Medical Conditions That are Problematic With TB

- Renal disease
- Some cancers
- Gastrectomy
- Abnormal CXR
- Low body weight

What Was That Again About a Social Disease?

- Social
  - Substance abuse
  - Foreign born
  - Homeless
  - Poor social support

A Little Detective Work: Infection Versus Disease

- Medical History
- Skin Test or IGRA
- CXR
- Physical examination (as clinically indicated)
- Sputums

Positive Skin Test or IGRA

- 2 - 10 weeks after exposure
- Correlates with development of cellular hypersensitivity

Differences in LTBI and Disease

- LTBI
  - No symptoms or physical findings
  - TST or IGRA - usually positive
  - CXR - normal
  - Sputums (if indicated) negative

Differences in LTBI and Disease

- TB Disease
  - Symptoms may include fever, cough, weigh loss, night sweats, productive sputum, chills, hemoptysis, chest pain, fatigue, anorexia
  - TST or IGRA - usually positive
  - CXR usually abnormal
  - Sputums usually smear and or culture positive

Infectious Versus Not Infectious

- LTBI
  - Cannot spread TB bacteria to others
  - Consider preventive therapy to reduce risk of development of TB disease

Infectious Versus Not Infectious

- TB Disease
  - May spread TB bacteria to others
  - Needs treatment with proper protocol to render noninfectious and cure disease

HIV and TB lead to DOUBLE TROUBLE

- Person with LTBI becomes infected with HIV / develops TB as immune system weakens
- Person with HIV infection becomes infected with M.TB and rapidly develops TB disease
- Risk of developing tuberculosis 7% to 10% per year

TB Disease – A Potpourri of Clinical Factors

- May have positive or negative PPD or Interferon Gamma Release Assay
- Abnormal CXR or other radiographic study (Depending on nidus of infection)

TB Disease – A Potpourri of Clinical Factors

- May have smear positive for AFB
- May have culture positive for Mycobacterium tuberculosis
- Clinical improvement on antituberculosis regimen

That NAAT!

- Nucleic Acid Amplification Test has become a very useful tool for clinical management
  - Smear Positive and positive NAAT = Tuberculosis
  - Smear Positive and negative NAAT = Unlikely to be Tuberculosis

Tuberculosis Disease

- Lungs
- Extra pulmonary

And Those Places You Will Go?

- Extrapulmonary is not generally considered contagious unless
  - The site is laryngeal
  - There is risk of aerosolization such as in autopsy or surgical procedure

If All Goes Well… Treatment of TB

- Standard Four Drug Therapy
  - Isoniazid, Rifampin, PZA and EMB
  - Four drugs for two month (Can drop EMB if drug sensitive)
  - Then Isoniazid and Rifampin for six months

So When is the Person Not Contagious?

- Adequate regimen with appropriate drugs AND
- Good clinical response AND
- Three negative sputum smears on different days

Sometimes We Don't Like Those "Regular"Medicines! Multidrug Resistance and All That Jazz!

- Resistance to at least Isoniazid and Rifampin
- Requires additional considerations for treatment

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And Sometimes, We Don't Like Anything Very Much! Extensively Drug Resistant Tuberculosis

- Multi Drug Resistant tuberculosis plus
  - Resistance to a fluroquinolone AND
  - At least one of three injectables
    - Amikacin
    - Kanamycin
    - Capreomycin

Schecter 2008 Francis J. Curry

And Sometimes, We Don't Like Anything Very Much! Extensively Drug Resistant Tuberculosis

- Very challenging treatment regimen for extended length of time

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Concerns About Multi Drug Resistant Tuberculosis

- Previous therapy for TB, especially if recent, increases risk for MDR
- Foreign born persons from countries or ethnicities with increased MDR are at risk
- Persons with poor response to standard four drug therapy could be MDR

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Concerns About Multi Drug Resistant Tuberculosis

- Persons with known exposure to MDR patients are at risk for MDR
- Persons who are HIV positive can respond poorly to standard therapy and acquire MDR

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Concerns about Extensively Drug Resistant Tuberculosis (XDR)

- Multiple factors increase the risk for XDR
  - Introduction of second line TB drugs into low and middle income countries
  - Suboptimal TB control practices

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Concerns about Extensively Drug Resistant Tuberculosis (XDR)

- Multiple factors increase the risk for XDR
  - High HIV prevalence
  - High burden of tuberculosis

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TB Management is a Journey

- TB is treatable
- Treatment varies with length of symptoms prior to diagnosis
- Compliance with therapeutic regimen and close monitoring by health department is essential to maximizing therapy