# Tuberculosis

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# Tuberculosis

- Mycobacterium Tuberculosis (TB) = #1 Cause of Death Worldwide from a Single Infectious Agent

- 1993 World Health Organization: Declared TB **Global Health Emergency**

# TB: History

- Earliest Archeological Evidence of Spinal TB is from Egyptian Mummies, 4000 BCE.
- Earliest Evidence of Pulmonary TB 1000 BCE in a 5 Year old Boy

# TB: History

- Earliest Written Description 668-626 BCE:

*The Patient Coughs Frequently, His sputum is Thick and Sometimes Contains Blood. His Breathing is Like a Flute, His Skin is Cold but His Feet are Hot. He Sweats Greatly and his Heart is Much Disturbed.*

# TB: Ancient Names

- Hindus = **Sosha** = Cough

  **Rayakshma** = Waisting

Greeks = **Phtisis** = To Waste

English Term From Latin = **Consumption**

# TB: History

- TB Peak = Industrial Revolution 17th- 18th Century
  Resulting in 25-30% of all Adult Deaths in Europe

# TB: Epidemiology

Estimates for 1990

- World Wide # Infected = 1.7 Billion
- World Wide # Deaths = 3 Million
- SE Asia # Infected = 426 Million
- SE Asia # New Cases = 2.47 Million
- SE Asia # Deaths = 900 Thousand

# TB: Transmition

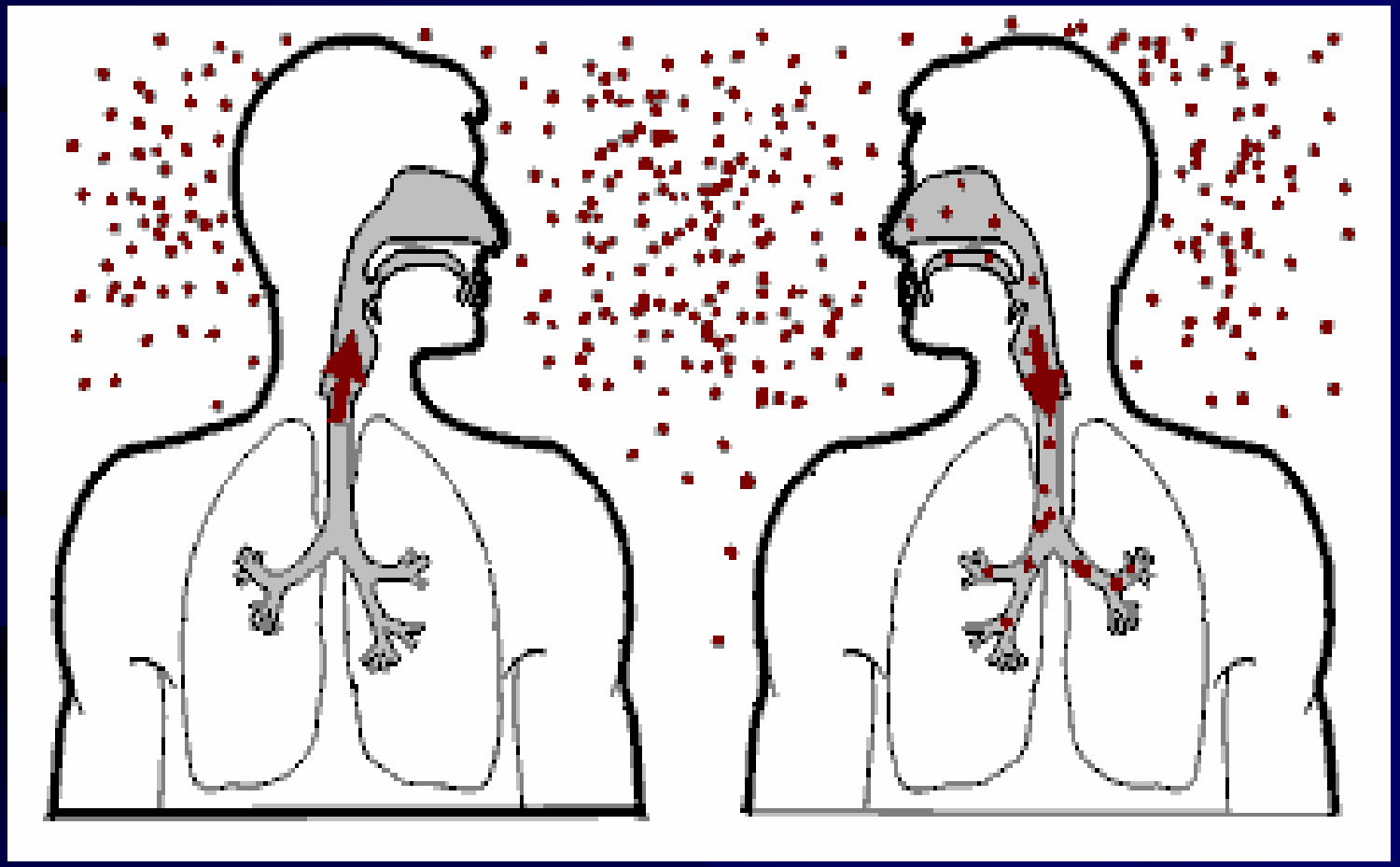
- Infection = Person to Person via Airborne Infectious Aerosol:

Coughing

Sneezing

Talking

# Transmission and Pathogenesis



# TB: Transmition

- Aerosolized Droplets 5 Micrometers = 1-400 Bacilli
- Estimated 5-200 Organisms Required for Infection

# TB: Transmition

- Influences on Becoming Infected:

  Infected Contact

  Duration of Exposure*

  Ventilation in Infected Environment

*Suspended Airborne Particles are Infectious after Source Leaves the Room

# TB: Natural History

Inhaled Particle

*

Dissemination

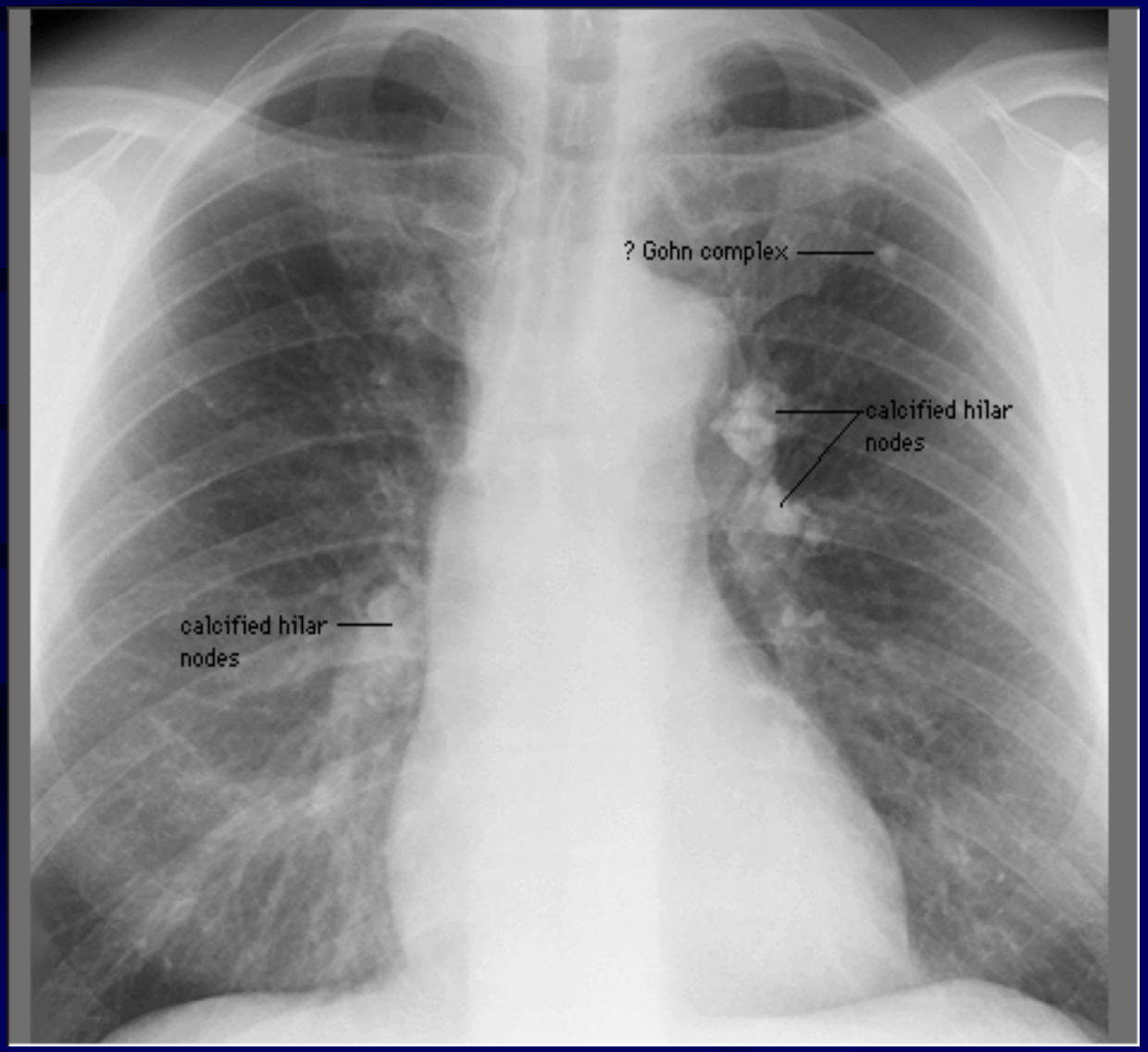
*

Immune System Activation

*

Granuloma Formation

# CXR with evidence of TB infection



# TB: Disease

- Estimated Only 10% of Immunocompitent People Infected With TB (PPD+) Will Develop Clinically Significant Disease

- 50% in First 2-3 years Following Exposure
- 50% in Remote Future

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# TB: Determinants of Disease

- Defects in Cell Mediated Immunity
  - Advanced Age
  - Malnutrition
  - Genetic Factors
  - Immunosuppressive Meds
  - Co-existing Disease: Diabetes
    - Malignancy
    - HIV
    - Renal Failure

# TB: Disease Pattern

- Primary Tuberculosis
- Reactivation Tuberculosis

# TB: Primary

- Associated With New TB Exposure
- Symptoms in Series of 517 New Converters:

Fever 70% (Duration 2-10 Weeks)

Chest Pain 25%

Pleuritic Chest Pain

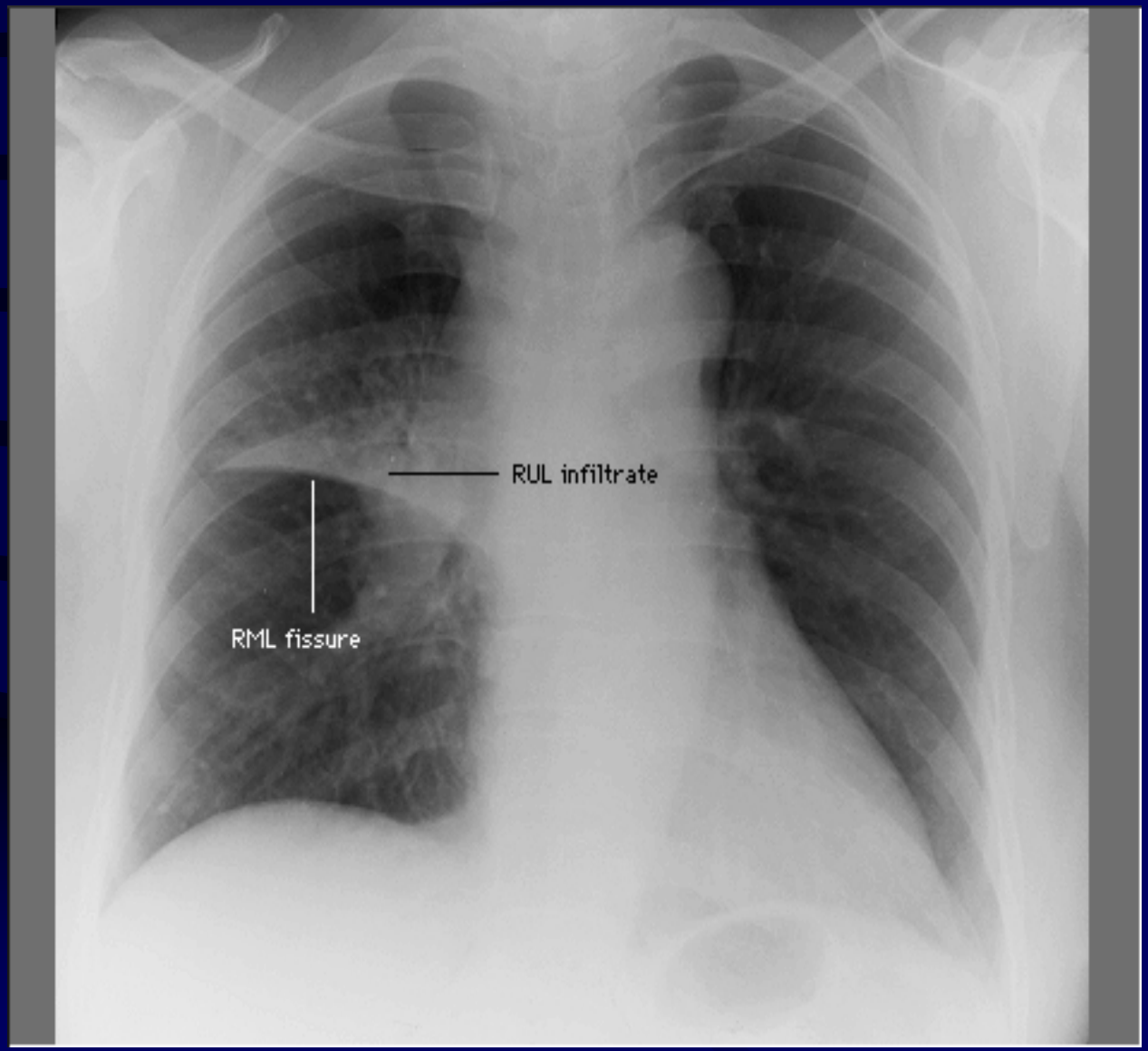
Erethema Nodusum Lower Extremities

(Women > Men)

# TB: Primary Chest X-Ray

- Hilar Adenopathy 64% (Children > Adults)
- Hilar Changes Right > Left
- Pleural Effusion 29% (Adults > Children)
- Unilateral Infiltrate/Ipsolateral Hilar Nodes 27%

# Possible primary tuberculous pneumonia



# TB: Reactivation

- Accounts For 90% of Adult non HIV TB
- Reactivation = Result of a Previously Dormant Organism Implanted Years Before by a Primary Infection
- Most Common Location = Apical Post Segment of Lung

# TB Reactivation: Symptoms

- Nonspecific
- Cough 78%
- Weight Loss 74%
- Fatigue 68%
- Temperature 60%
- Night Sweats 55%
- Hemoptosis 37%

# TB Reactivation: Physical Exam

- Non Specific

# Apical Cavitary Disease

# TB: Diagnosis

- PPD
- Sputum Examination
- Chest X-Ray
- Culture

# TB: PPD

- PPD = Purified Protein Derivative
- The Tuberculin Skin Test Identifies Individuals Who Have Been Infected With Mycobacterium Tuberculosis, it Does not Differentiate Between Old and New Infection

# TB: PPD

- Dose of Tuberculin = 5TU
- Injection Site = Intradermally  Dorsal Side of Forearm
- Inflammatory Reaction = 24-72 Hours
- Result Test in 48-72 Hours (If Positive at 6 Days = true Positive)

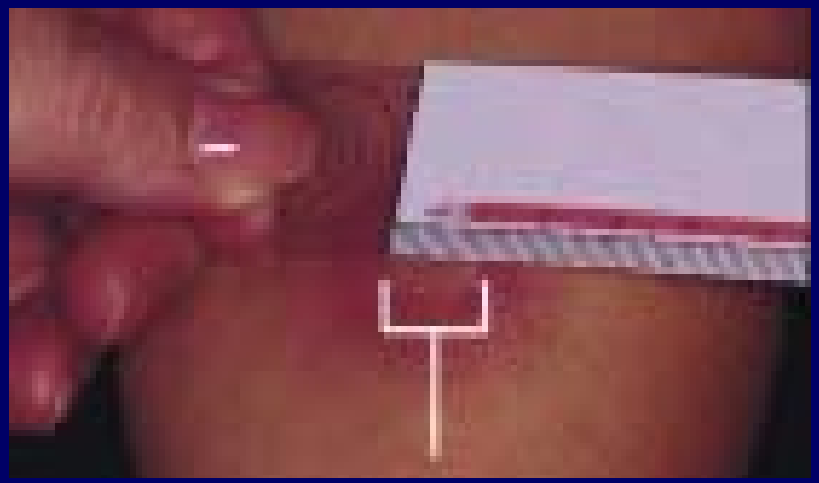
# Testing for TB Disease and Infection

# TB: PPD Resulting

- Diameter of Induration = Determinant of Disease
- Technique: Use Ball Point Pen Start 1-2 cm Away from Margin of Test When Ball Point Pen Reaches the Margin Resistance is Felt. Repeat From Opposite Side. Distance between Lines = Diameter

# Reading the Tuberculin Skin Test

- Read reaction 48-72 hours after injection
- Measure only induration
- Record reaction in millimeters



# PPD Guidelines for Interpretation

| • Size of Induration | • Considered Positive |
| --- | --- |
| < 5mm | Never = + |
| ≥ 5mm | HIV+<br>Close Contact of TB+<br>+ Chest X-Ray |
| ≥ 10mm | IV Drugs/HIV-<br>At Risk Disease<br>High Risk Geography |
| ≥ 15mm | All Patients |

# TB Chemo prophylaxis

- Isoniazide Prophylaxis Given to Tuberculin Reactors Reduces the Risk of Active TB by 90%

# TB Chemo prophylaxis

- Isoniazid 300mg Single Daily Dose 6-12 Months
- HIV+ Patients Isoniazid 300mg Daily 12 Months
- Alternative:  Isoniazid 15 mg/kg Twice Weekly 6-12 Months

***All Regiments Require Patient Compliance For Efficacy**

# Risk of Isoniazid

- Hepatitis = Major Toxic Effect of Isoniazid

< 20 Years Old = 0% Risk

20-34 Years Old = 0.3% Risk

35-49Years Old = 1.2% Risk

50-65 Years Old 2.3% Risk

Risk Increased With Alcohol Consumption

# Risk of Isoniazid

- Peripheral Neuropathy
- Highest Risk in Diabetes, Malnutrition, Alcoholism
- Peripheral Neuropathy Prevention Co-Administer Pyridoxine

# Micobacterium Tuberculosis in Sputum

# Principles of Tuberculosis Treatment

- Regimens Must Contain Multiple Drugs
- Drugs Must be Taken Regularly
- Treatment Must be Continued for Sufficient Time

(Minimal Acceptable Duration of Treatment = 6 Months)

# Principles of Tuberculosis Treatment

*Any Regimen is Irrelevant if Drugs Do Not Enter The Patients Body. Promoting and Monitoring Adherence to The Drug Regimen Are Essential For Treatment To be Successful*

# Principles of Tuberculosis Treatment

The World health Organization Advocates
**Directly Observed Therapy**
(DOT)

# Drugs in Current Use

- Isoniazid
- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin

# TB: Treatment Option 1

| Drug | Dose (Max) | Duration |
|---|---|---|
| • Isoniazid | 5-10mg/kg/day (300mg) | 6 Months |
| • Rifampin | 10mg/kg/day (600mg) | 6 Months |
| • Pyrazinamide | 25mg/kg/day (2.5g) | First 2 Months |
| • Ethambutol | 25mg/kg/day | First 2 Months |

# TB: Treatment Option 2

Daily: Isoniazid+Rifampin+Pyrazinamide+Ethambutol

Duration: Week 1+2

+

2 Times/Week: Isoniazid+Rifampin+Pyrazinamide+ Ethhambutol

Duration: Week 2-8

+

2 Times/Week: Isoniazid+Rifampin

Duration: Week 8-24

***Total Duration of Therapy 24 Weeks**

***Direct Observed Therapy Required For Short Course**

# TB: Treatment Option 3

3 Times/Week For Total 6 Months:

Isoniazid

+

Rifampin

+

Pyrazinamide

+

Ethambutol

*Directly Observed Therapy Required Short Course

# Adjusted Treatment Dose

| Drug | 2X/Week | 3X/Week |
|---|---|---|
| Isoniazid | 15mg/kg Max 900mg | 15mg/kg Max 900mg |
| Rifampin | 10mg/kg Max 600mg | 10mg/kg Max 600mg |
| Pyrazinamide | 50-70mg/kg Max 4g | 50-70mg/kg Max 4g |
| Ethambutol | 50mg/kg Max 2.5g | 50mg/kg Max 2.5g |

# Ethambutol Caution

- Ethambutol Should not Be Used if Unable to Monitor Visual Acuity, Including in Small Children

- Substitute with Streptomycin

Daily Dose = 15mg/kg Max 1g/dose

2x/Week Dose = 25-30mg/kg Max 1.5 g/dose

3x/Week Dose = 25-30mg/kg Max 1.5 g/dose

# Toxicities of TB Treatment

- All therapies have significant toxicity
- All drugs are associated with hepatitis and hypersensitivity reactions
- Unique toxicities
  - INH: hepatic necrosis, peripheral neuropathy
  - Rifampin: altered drug metabolism
  - Pyrazinamide: hyperuricemia
  - Ethambutol: optic neuritis
  - Streptomycin: vestibular toxicity

# Evaluation Response To Treatment

- Response To Anti TB Chemotherapy is Best Evaluated Through Sputum Examination
- Recommend Sputum Evaluation Every Month
- After 2 Months of Therapy 85% of Patients = Sputum negative

# Treatment Failure

- Consider Drug Resistance To Medical regimen
- Consider Poor Patient Compliance With Medical Regimen

# TB and HIV

- Complex synergy between HIV and TB
- Annual risk of progression to disease is 10%
  - this is up to 100-fold higher than in HIV -
- TB is aggressive in HIV, more likely to disseminate
- TB may be AIDS-defining illness
- Treatment is the same, but often a longer course
- Interactions between HIV meds and anti-TB drugs

# TB: BCG Vaccination

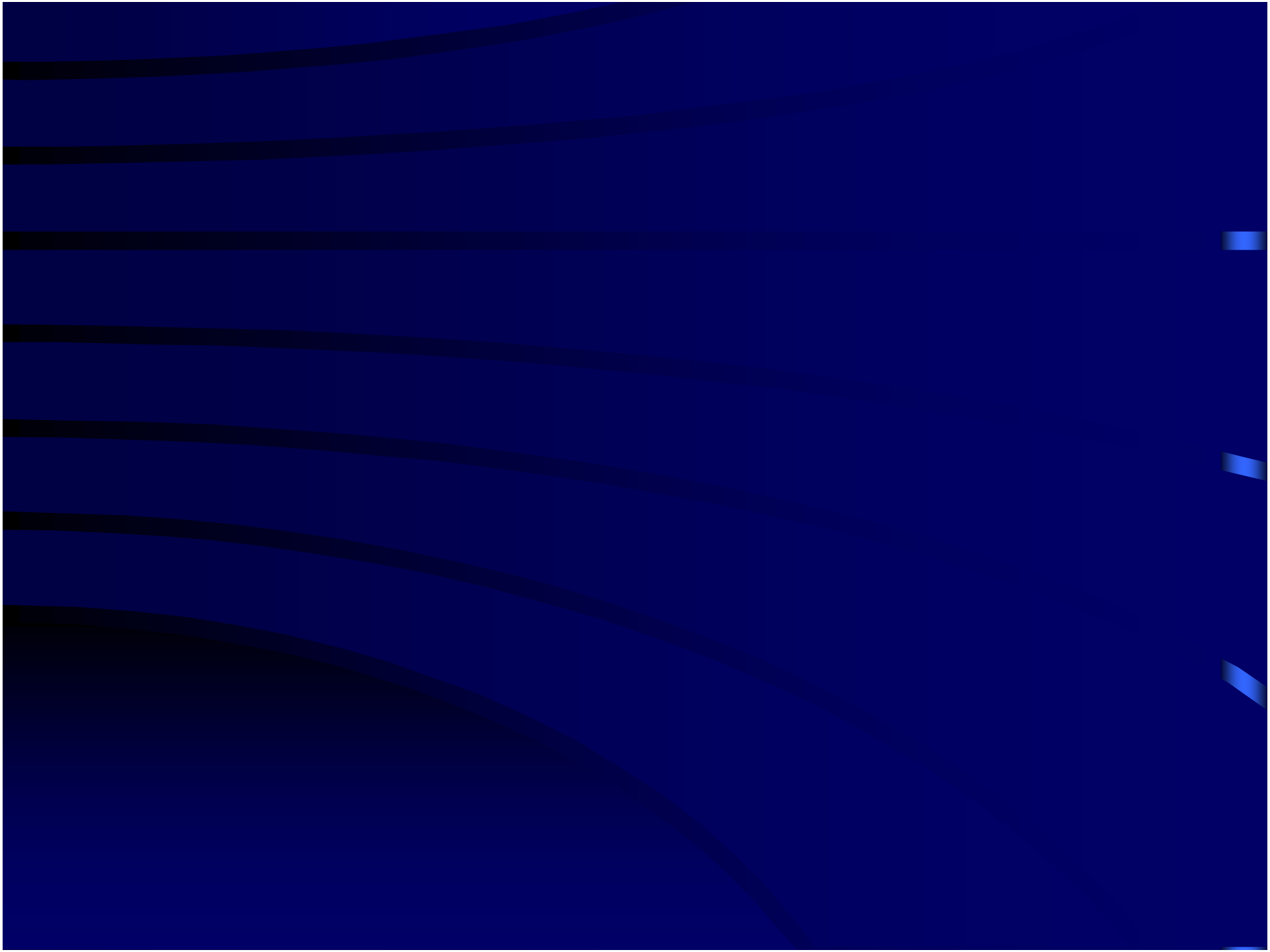
- Live Attenuated Vaccine Derived From M. Bovis
- WHO: Recommended For Young Children
- Vaccination = 60-80% Decrease in Disease Does Not Prevent Infection
- Effect of BCG on PPD Decreases With Time

# Allocation of TB Resources

- Infection Case Finding and Treatment
- Contact Investigation and Treatment

# TB: Summary

- Endemic Disease With Significant Mortality and Morbidity
- Resource Focus: Case Finding + Contact Treatment
- Treatment Requires Medication + Compliance



# CASE: I

- A 56 Year Old Previously Healthy Woman Presents for Care. She is Complaining of a Productive Cough, Fever, Night Sweats
- Past Medical History = Diabetes, She is HIV Negative
- Social = She Lives With Her Husband and 16 Year old Daughter

# CASE: I

- Physical Exam
- BP 130/70 HR 90 RR 18 T 38.6

Lung: Crackles in the Right Upper lung (RUL) Field
There is Dullness to Percussion in the RUL

Heart: Regular Rate Rhythm No Murmers

# What Studies Do You Wish to Perform?

# CASE: I

# CASE: I

- What is The Differential Diagnosis
- What is The Diagnostic Plan
- What is The Treatment Plan
- What is the Public Health Responsibility