

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 = Wasting

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: Transmission

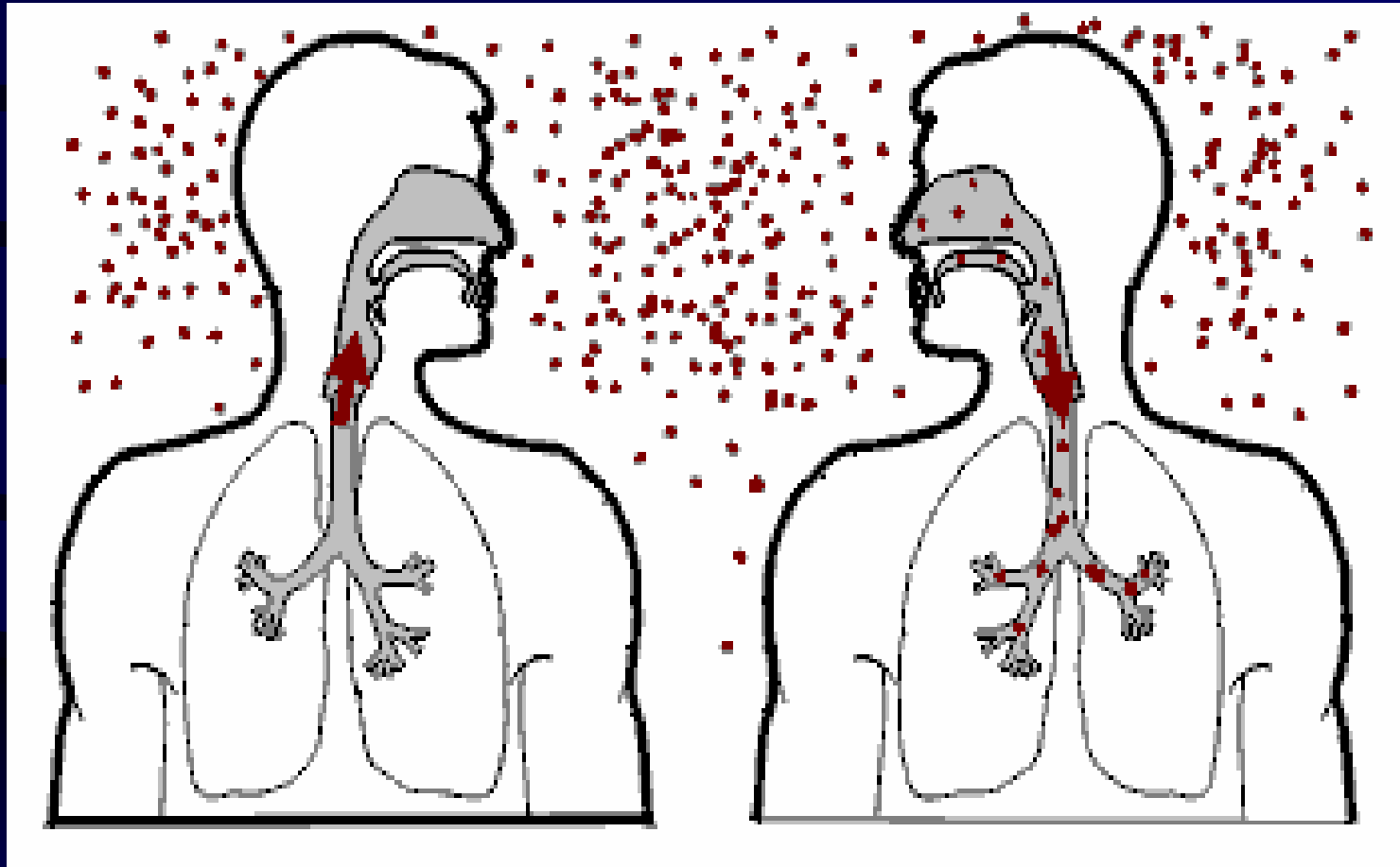
- Infection = Person to Person via Airborne Infectious Aerosol:

Coughing

Sneezing

Talking

Transmission and Pathogenesis



TB: Transmission

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

TB: Transmission

- 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

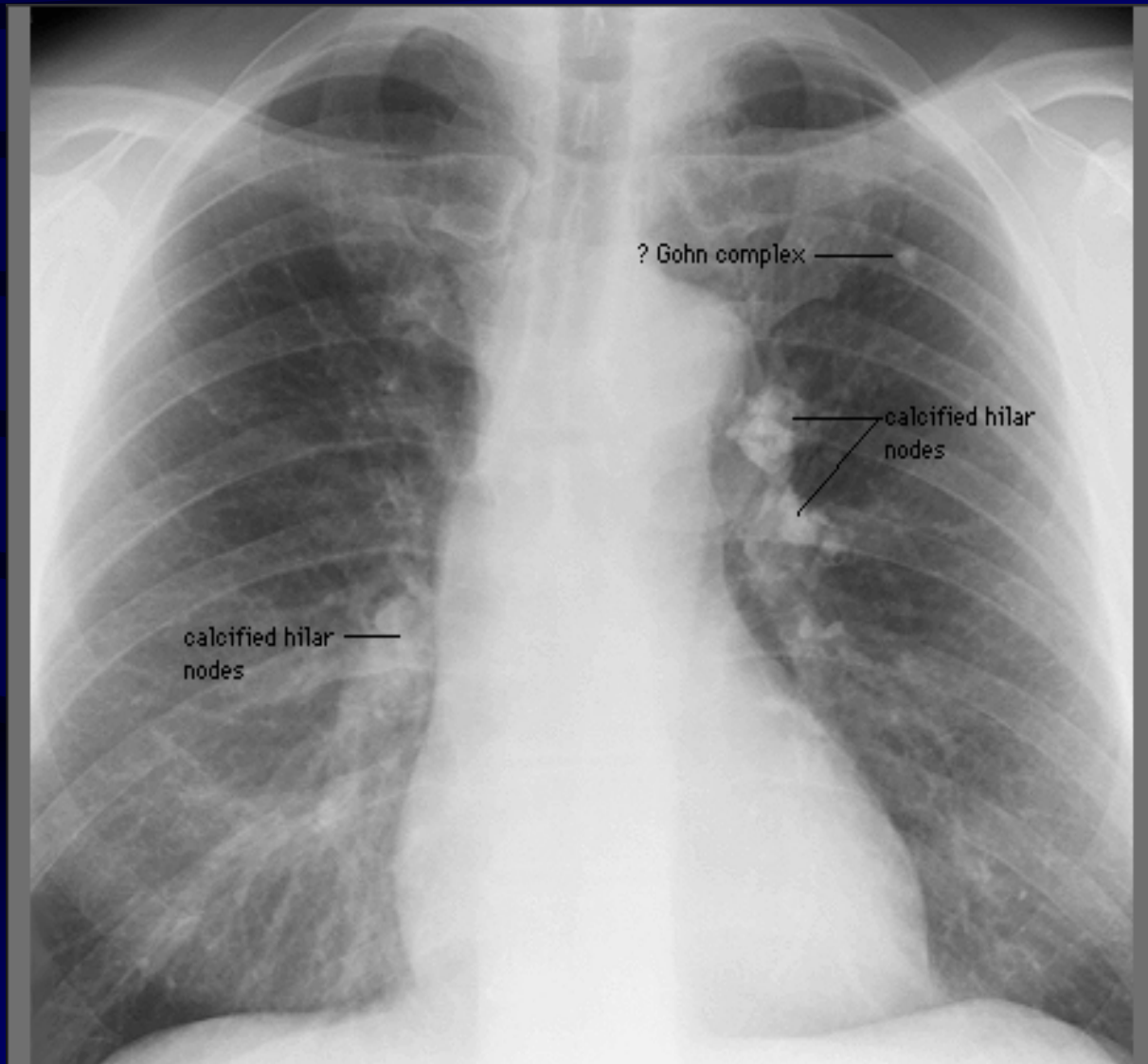
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Immune System Activation

*

Granuloma Formation

CXR with evidence of TB infection



TB: Disease

- Estimated Only 10% of Immunocompetent 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

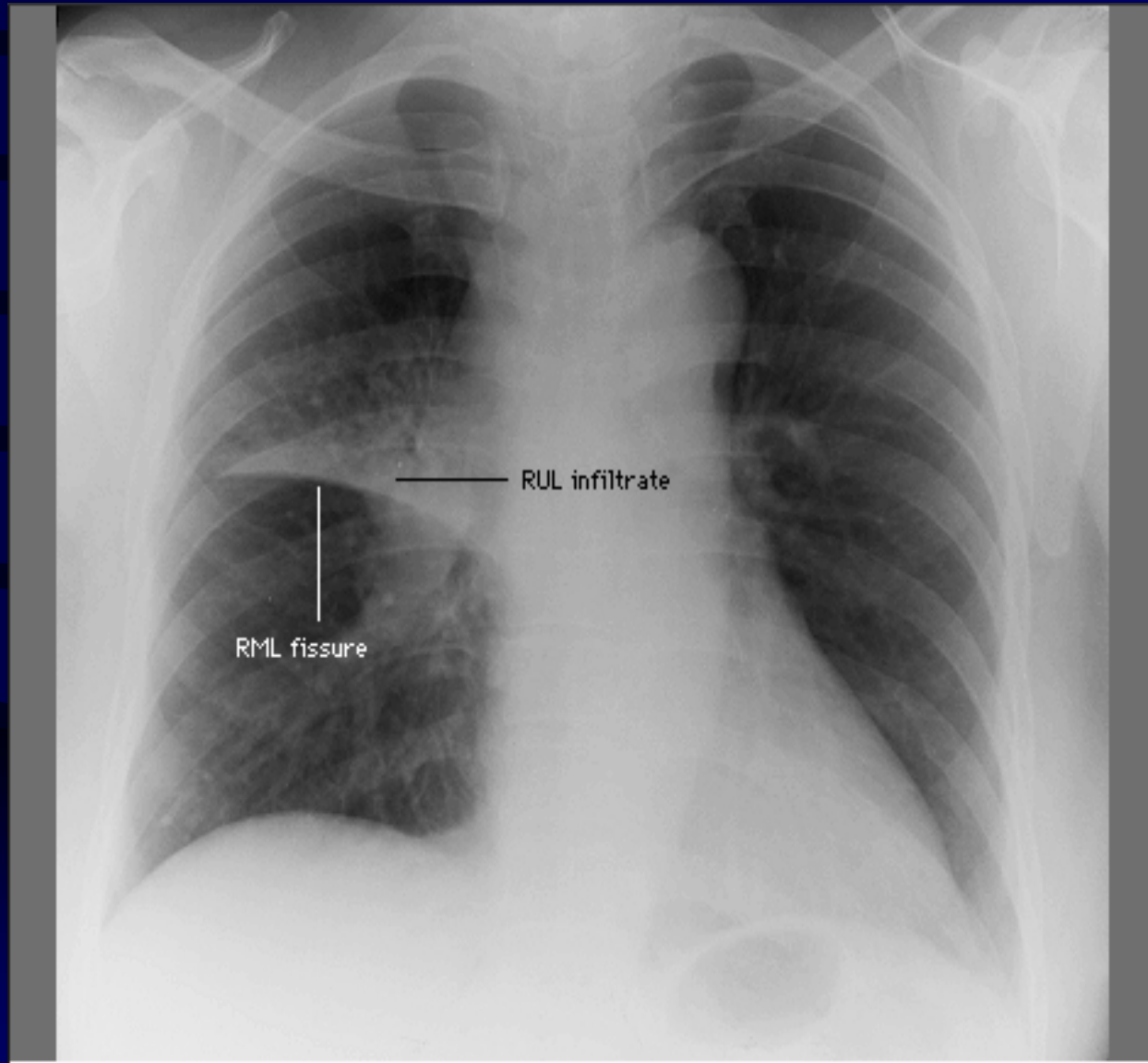
Erythema Nodosum Lower Extremities

(Women > Men)

TB: Primary Chest X-Ray

- Hilar Adenopathy 64% (Children > Adults)
- Hilar Changes Right > Left
- Pleural Effusion 29% (Adults > Children)
- Unilateral Infiltrate/Ipsilateral 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 Cavitory Disease



TB: Diagnosis

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

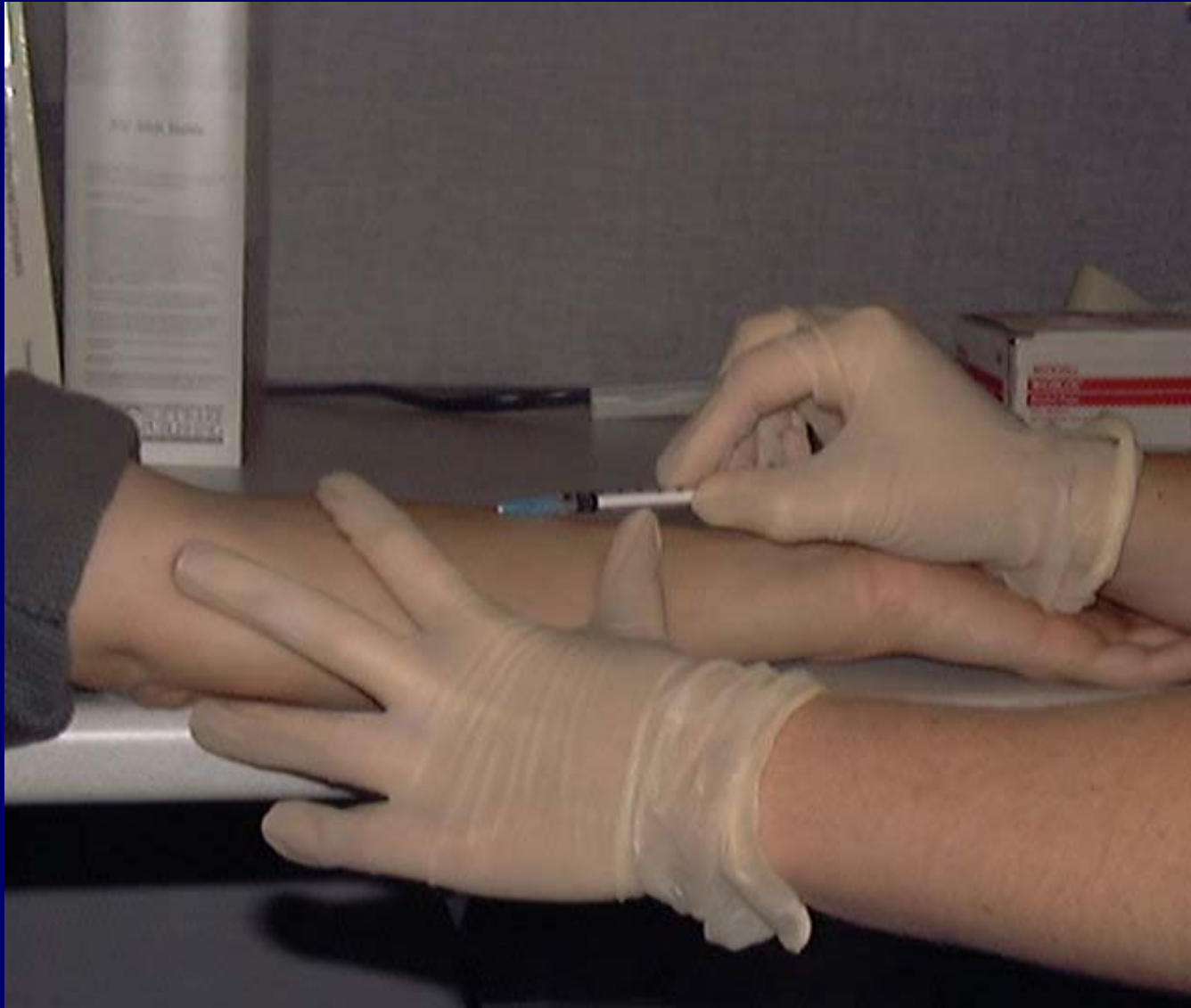
TB: PPD

- 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

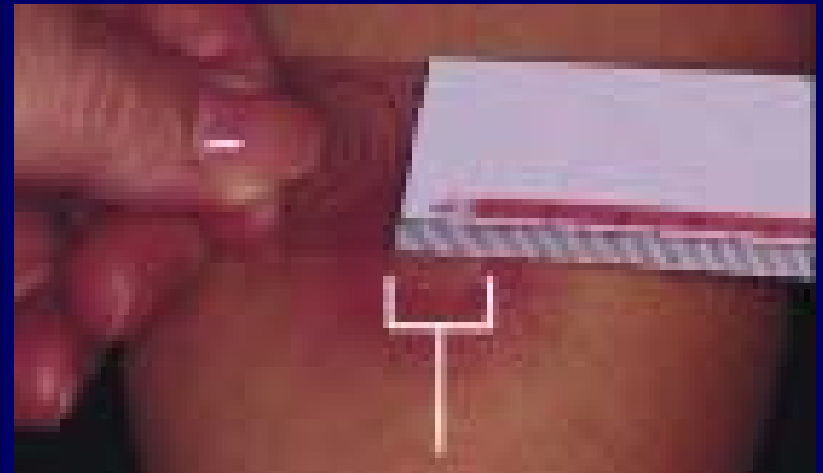


TB: PPD Resulting

- 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

< 5mm

≥ 5mm

≥ 10mm

≥ 15mm

- Considered Positive

Never = +

HIV+

Close Contact of TB+
+ Chest X-Ray

IV Drugs/HIV-
At Risk Disease

High Risk Geography

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

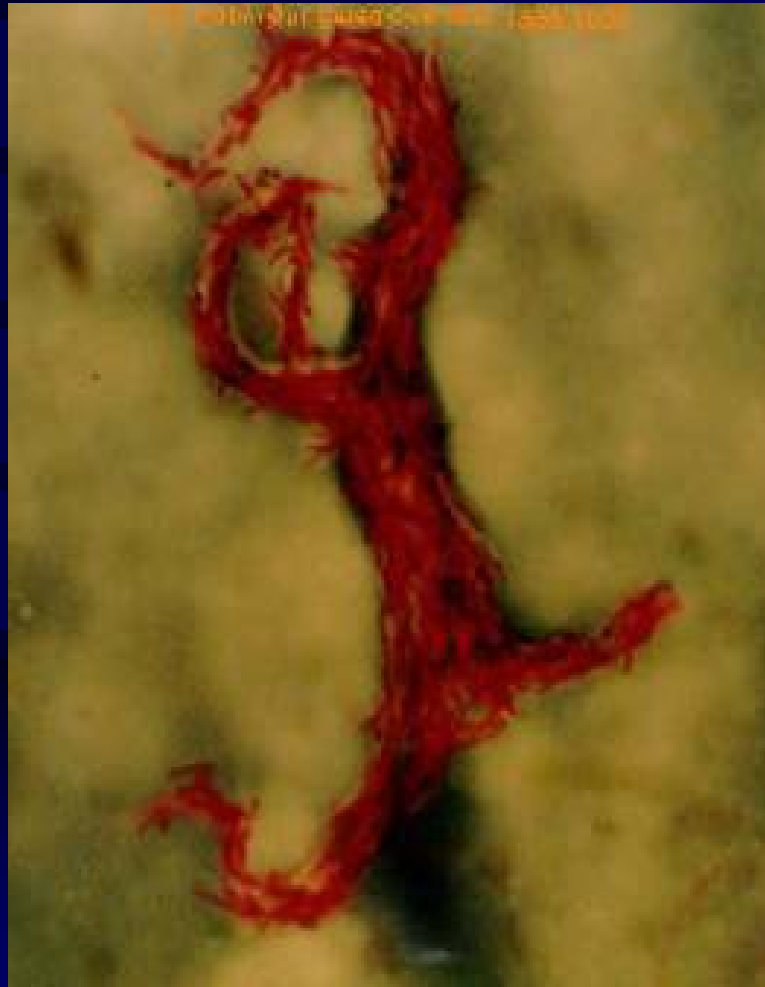
- Hepatitis = Major Toxic Effect of Isoniazid
 - < 20 Years Old = 0% Risk
 - 20-34 Years Old = 0.3% Risk
 - 35-49 Years Old = 1.2% Risk
 - 50-65 Years Old 2.3% Risk

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

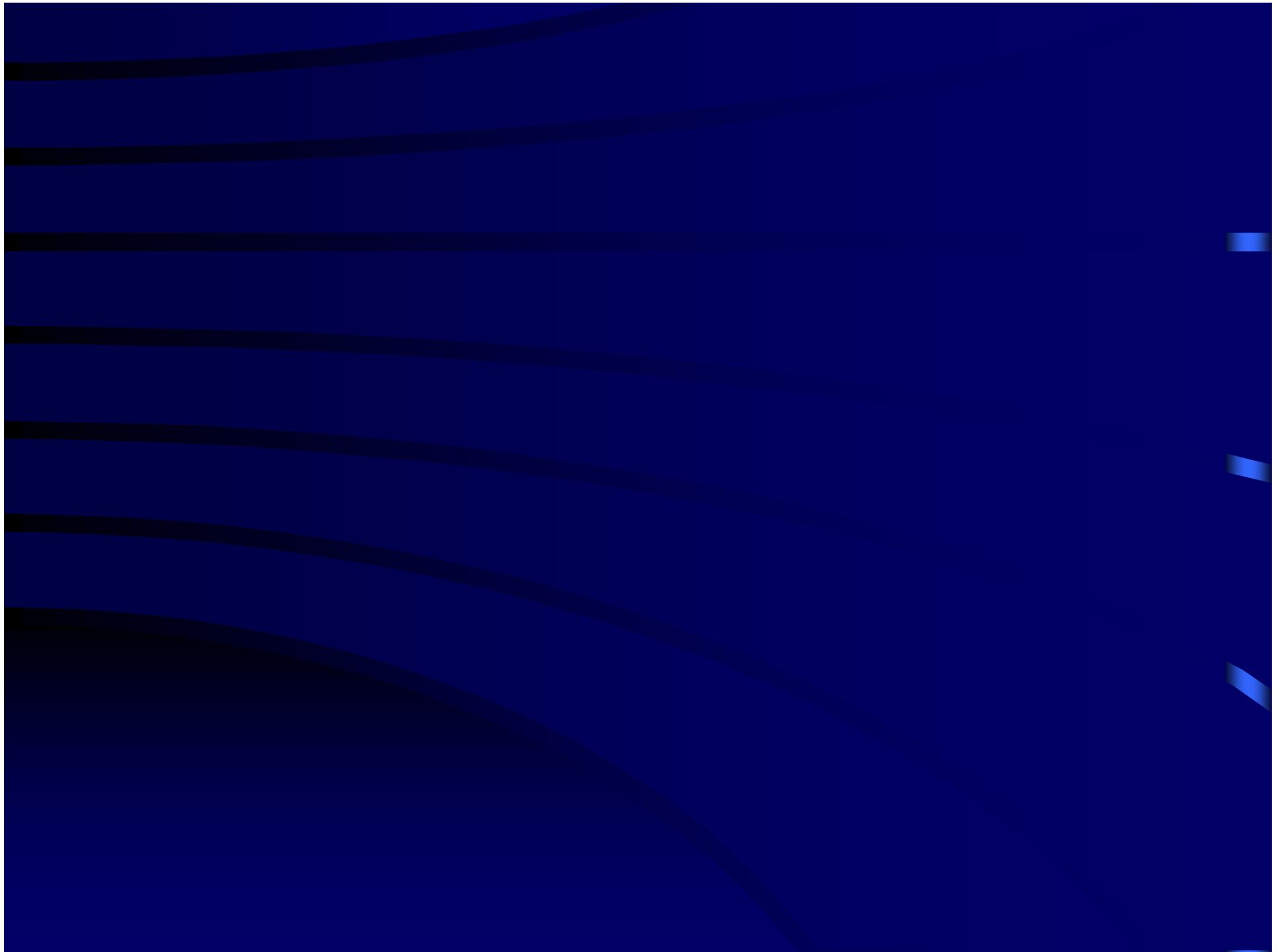
- Live Attenuated Vaccine Derived From *M. Bovis*
- WHO: Recommended For Young Children
- Vaccination = 60-80% Decrease in Disease Does Not Prevent Infection
- Effect of BCG on PPD Decreases With Time

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 Murmurs

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