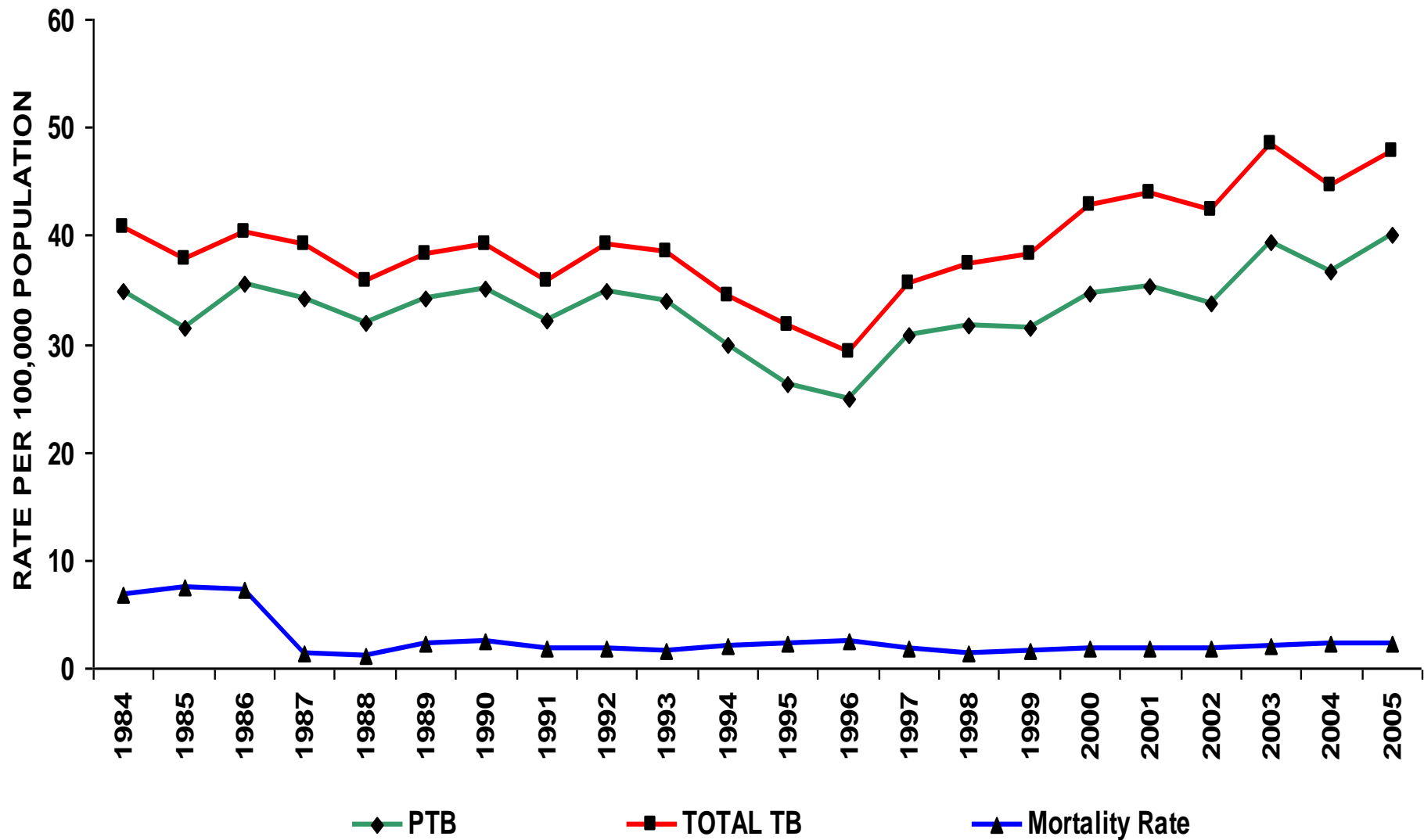




# Taking another look at Tuberculosis

**Kirithi Gunasekera**

# INCIDENCE AND MORTALITY RATES OF TUBERCULOSIS IN SRI LANKA 1984 - 2005



24y old Tamil boy is brought to A & E department of PGH Badulla with severe dyspnoea.  
He is tachypnoeic and gasping for breath  
O/E Pale, Cachectic and febrile with bilateral crepitation

Within 2 hours of admission he had a Respiratory arrest & could not be revived despite ET intubation and manual ventilation.

*He had been transferred from DH Passara where he had been treated one day and his sputum was found to be positive for AFB.*  
*20<sup>th</sup> November 2008*



*Chest x-ray revealed extensive bi lateral fibrocavitary disease with areas of consolidation*



Questioning the father in retrospect, it revealed That the patient was not resident of Passara but working tea boutique in Maradane - Colombo for 6 years

He had been unwell with cough, wheezing and episodic fever for 1 1/2y. He had sought medications from over 8 doctors and had taken in ward treatment from 2 teaching hospitals where he had been treated for bronchial asthma with repeated nebulizations.

At no point in his illness was chest x-ray or sputum examination performed !

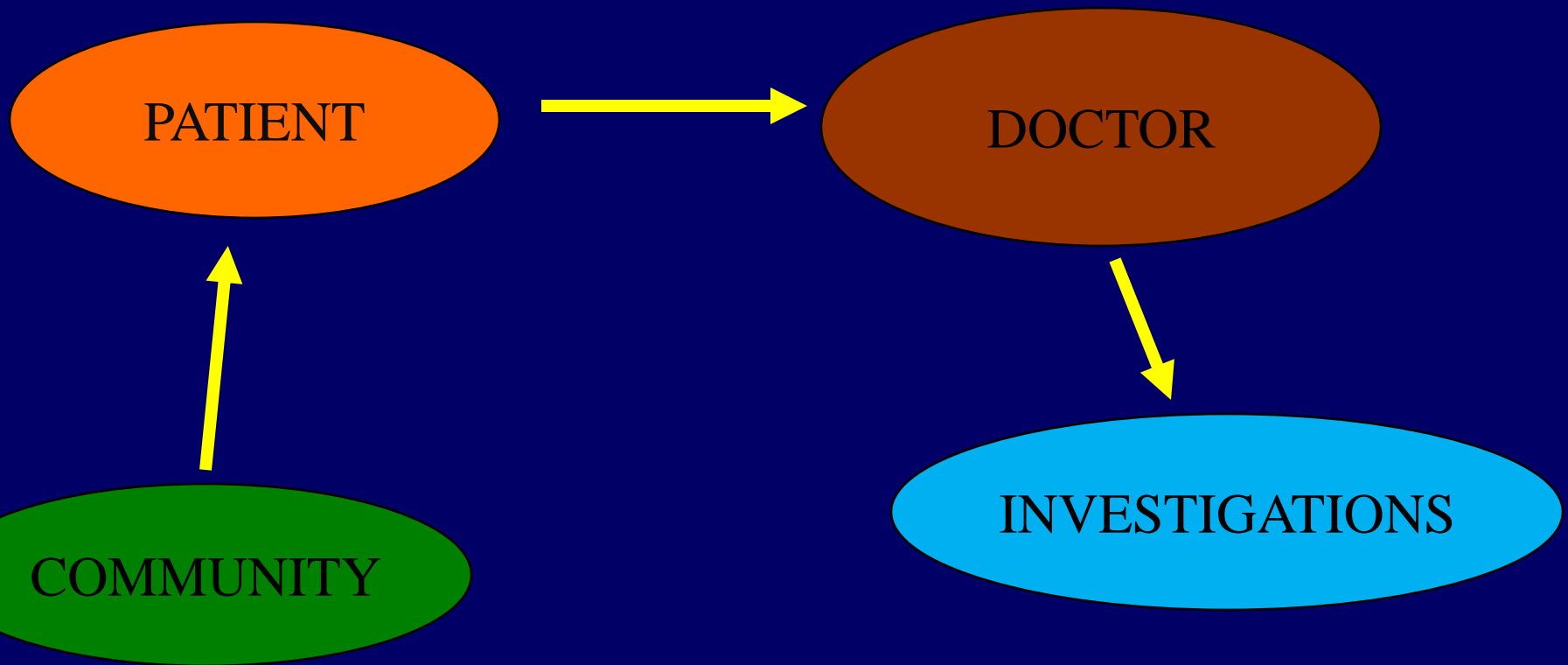
# ***The Problems Associated With Delayed Diagnosis***



Spread of disease in the community

Progression of disease in patient  
Respiratory Cripple

# ***The key factors affecting the diagnosis of TB***





PATIENT

Lack of awareness

Social stigmatization

Nature of Symptoms



COMMUNITY

Inaccessibility to Health care

Social stigmatization

Myths

# SYMPTOMS OF PULMONARY TUBERCULOSIS

## Nonspecific and Constitutional

Unusual fatigue

Tiredness

Malaise

Anorexia

Pyrexia

Weight Loss

Night sweats

Amenorrhoea



## Respiratory

Cough-2 wks

Haemoptysis

Chest pain

SOB



*THE SUBTLE NATURE OF THE  
EARLY SYMPTOMS  
OF  
TUBERCULOSIS*

*WITH*

*POOR ACESSEBILTY TO  
DIAGNOSTIC FACILITIES*

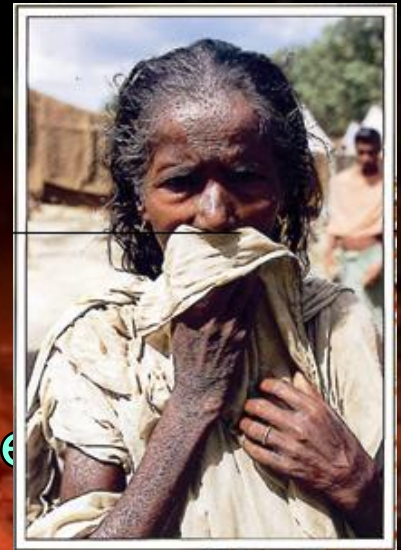
*PLAYS A KEY ROLE*

*IN*

*THE DELAYED DIAGNOSIS OF THE DISEASE*

# SOCIAL STIGMA – IS IT REAL in 2009?

- Rejection by family
- Rejection by society
- Loss of employment
- Disqualification for middle east employment



- *Social isolation*
- *Depression*
- *Homelessness*
- *Rejection at Marriage*
- *Suicide*



**Does TB deprive you of all Human Rights?**

# DOCTOR

Lack of awareness

Nature of Clinical signs

Misdiagnosis

False image

Paucity of diagnostic aids

Low priority



# CLINICAL SIGNS OF PULMONARY TUBERCULOSIS

**Mild to moderate disease may have no clinical signs**

**Generalized**

**Pallor (Anaemia)**

**fever**

**weight loss**

**Chronic Tuberculosis**

**Tracheal deviation**

**flattened chest**

**cavity - amphoric**

**breath sounds**

**Respiratory**

**upper zone crackles**

**- post tussive**

**signs of consolidation**

**Localized wheeze**

# Differential Diagnosis

## Differential Diagnosis

- Asthma
- COPD
- Bronchiectasis
- Bronchial carcinoma
- Other infections, Eg:  
Bacterial pneumonia  
Lung abscess  
Pneumocystis carinii

## Pointers to the Correct Diagnosis

- Intermittent symptoms,  
Expiratory wheeze
- Smoking, Chronic symptoms,  
generalized wheezing
- Large amounts of purulent  
Sputum / Haemoptysis
- Risk factor (Smoking) / clubbing
- Response to antibiotic
- Abscess with fluid level on CXR
- Dyspnoea prominent

## High Risk Groups with Increased Susceptibility to Tuberculosis

### Nonspecific Decrease in Resistance

Adolescence

Senescence

Malnutrition

Post gastrectomy states

Diabetes mellitus

Alcoholism

Drug addicts

### Decrease in Resistance Due to Hormonal Effects

Pregnancy

Therapy with adrenocortico steroids

### Decrease in Local Resistance

Silicosis

### Decrease in Specific immunity

Lymphomas Uremia Immunosuppressive therapy

Sarcoidosis

Live virus vaccination

### Acquired immunodeficiency syndrome (AIDS)

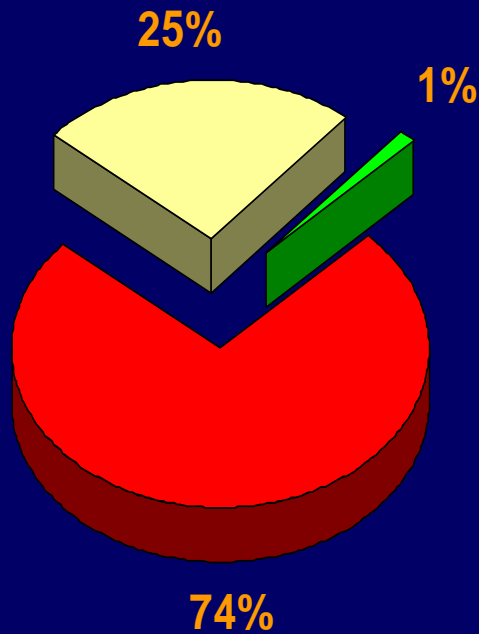
### Exposure to TB Patients

- Family / close contacts
- People living / working in institutionalized Settings  
Eg: Prisons, Nursing homes, Refugee Camps
- Healthcare Workers



# FALSE IMAGE ?

# Changing Profiles



■ 0-14

■ 15-55

■ >55

AGE DISTRIBUTION

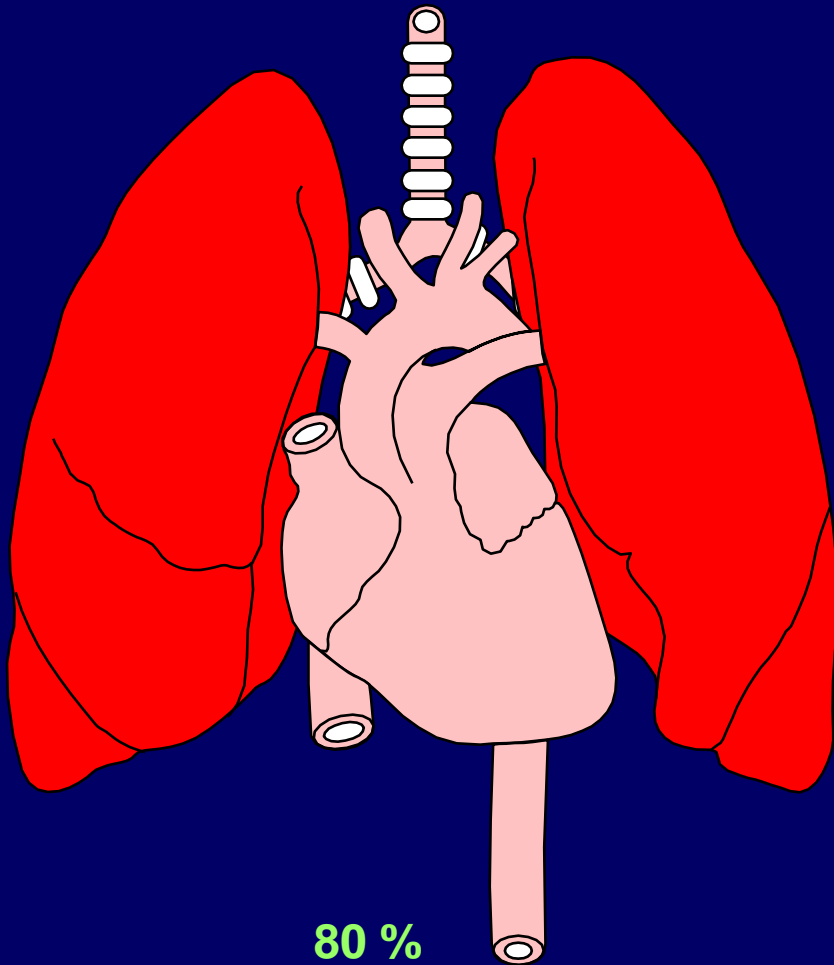


Wasted  
Cache tic  
Haemoptysis  
Elderly

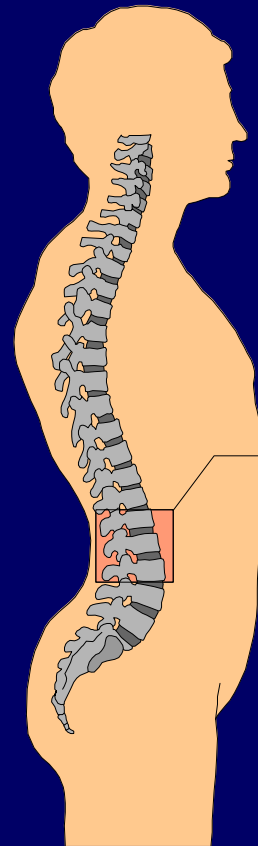


Healthy looking  
Mild cough  
Low grade fever  
Young

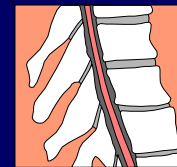
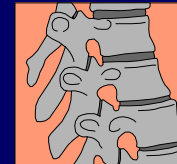
# Sites of Attack



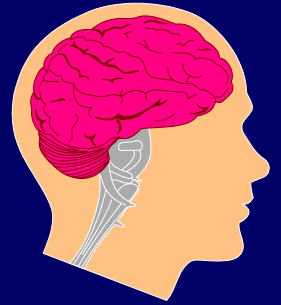
80 %  
PREDOMINANTLY  
LUNGS



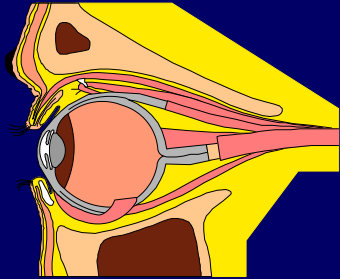
SPINE



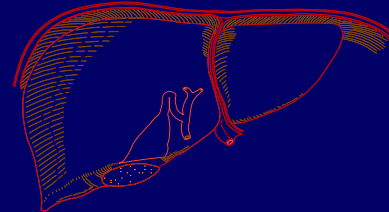
BRAIN



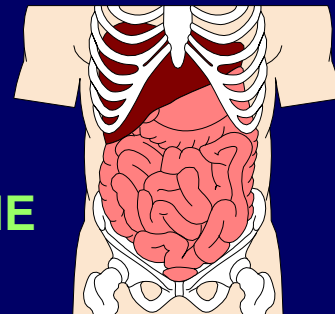
EYES



LIVER



INTESTINE





# PRIMARY TUBERCULOSIS

Lung - most important portal of entry



Disease transmission

Inhalation

Aerosol of

TB Bacilli

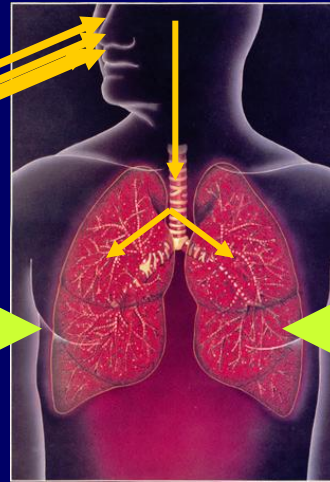
Coughed up by  
a smear (+) TB  
patient

# PRIMARY TUBERCULOSIS

## WHAT HAPPENS TO THE INHALED BACILLUS

**TB Germ** →

(Magnified Approximately 30,000 times)



← **Natural Immunity**

Majority

**INFECTED**

**Germ - inactive**  
**No Symptoms**  
**Do not feel sick**  
**Do not spread the disease**  
**TB skin test (+)**

Immunity

10%  
Minority

**DISEASE**

**Germ - active**  
**Symptoms**  
**Mild & Non Specific**  
**Pleurisy**  
**Signs unusual**

# POST PRIMARY TUBERCULOSIS

## Clinical Features

### Nonspecific and Constitutional

Unusual fatigue

Tiredness

Malaise

Anorexia

Pyrexia

Weight Loss

Night sweats

Amenorrhoea



Respiratory

Cough

Haemoptysis

Chest pain

SOB

# POST PRIMARY TUBERCULOSIS

## Signs

Mild to moderate disease may have no clinical signs

### Generalized

Pallor (Anaemia)

fever

weight loss

clubbing

### Respiratory

upper zone crackles

- post tussive

signs of consolidation

Localized wheeze

## Chronic Tuberculosis

Tracheal deviation flattened chest

cavity - amphoric

breath sounds

EPTB- 10% (Cervical lymphnodes

pleural effusions)

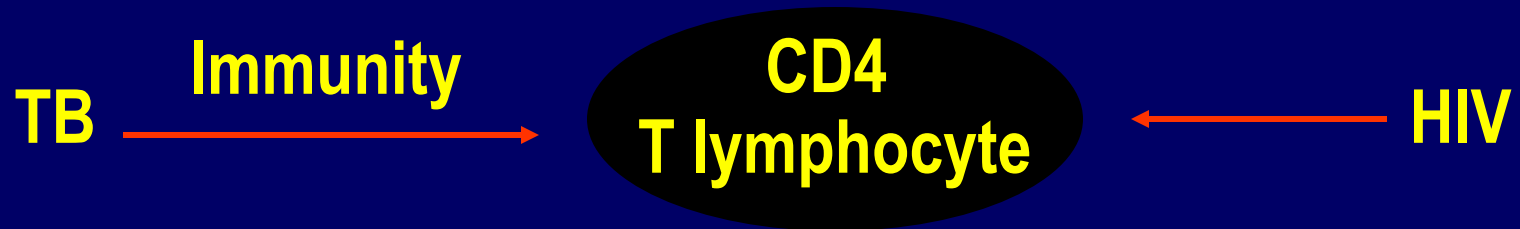
**WORKING TOGETHER**



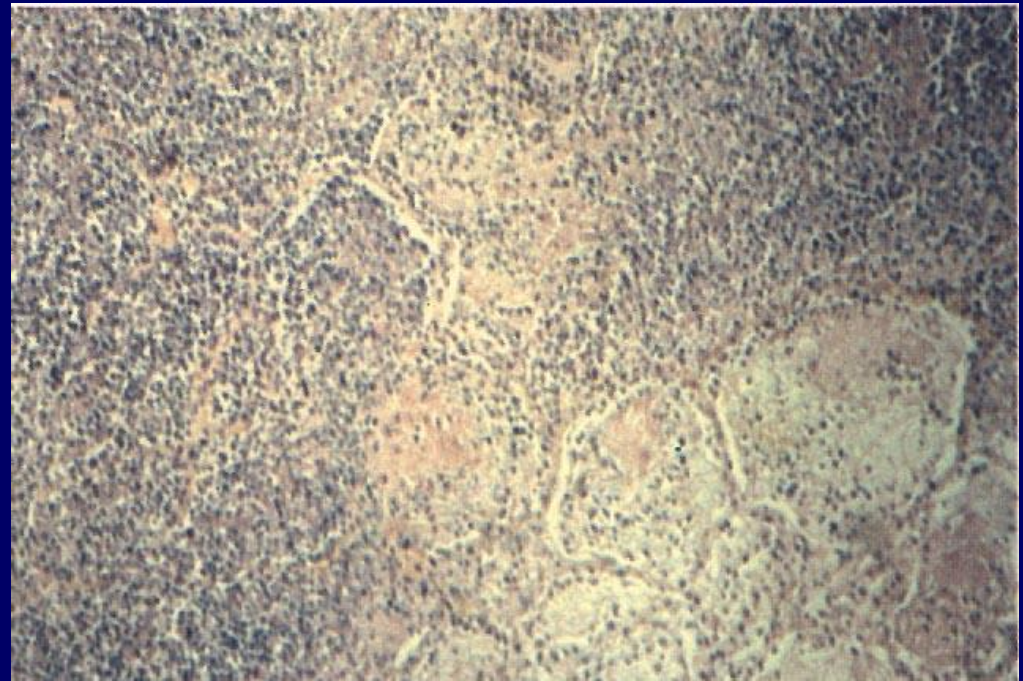
**6 MILLION PEOPLE ARE CO-INFECTED - HIV- TB  
HIV PATIENTS ARE 25 TIMES MORE LIKELY TO GET TB**

**AGAINST US**

# Pathogenesis of TB / HIV



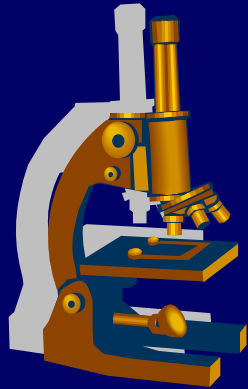
- Active TB | CD4
- Immune Stimulation – TNF  $\alpha$
- HIV / TB - | Opp Infection



# Clinical Picture of Pulmonary TB In HIV Seropositive Persons

Features of Pulmonary TB	Stage of HIV Infection	
	Early	Late
Clinical Picture	Often resembles Post –primary TB	Often resembles primary TB
Sputum smear result	Often positive	Often negative
Chest X-ray	Often cavities are seen	Often infiltrates With no cavity

# INVESTIGATIONS



Sputum Microscopy

Chest X ray

Mantoux Test

TB Culture



*PCR*

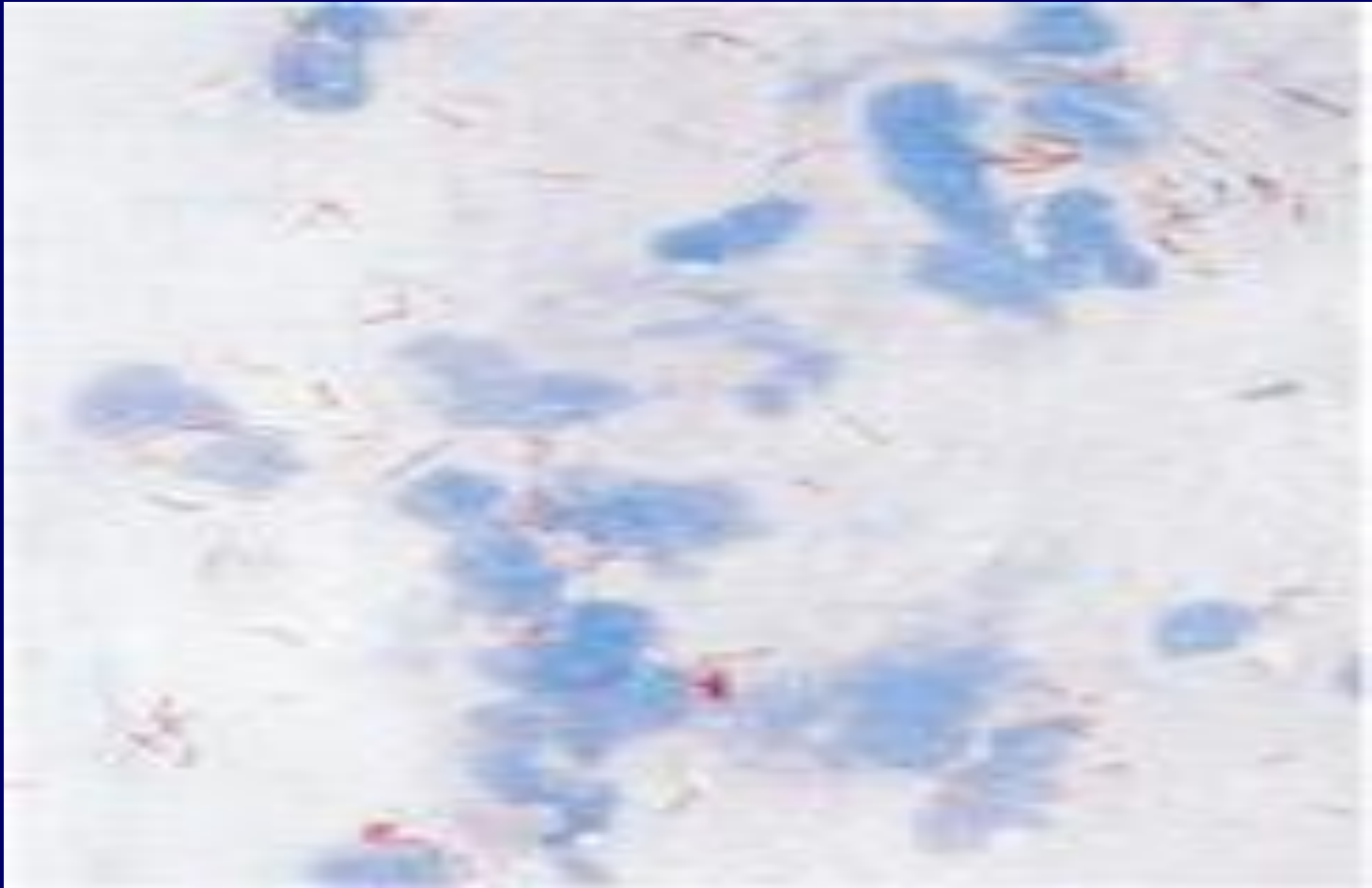
*Gamma Interferon*

*Rapid Culture*

*Adenosine De Aminase*



## Sputum microscopy



**Mycobacterium Tuberculosis**

# SPUTUM MICROSCOPY

Major tool for rapid diagnosis

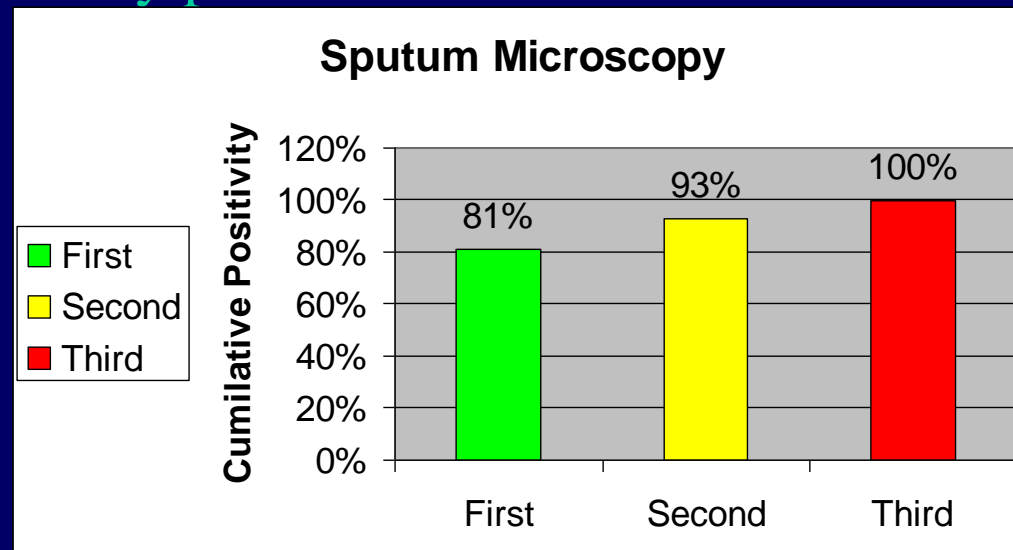
- Not popular among Doctors & patient
- Lack of facility
- Incorrect sample collection – saliva
- Inadequate samples
- Improper reading



# SPUTUM MICROSCOPY

## Three Specimens Optimal

- Spot sample - – 1<sup>st</sup> visit – give container
- Early morning sample- collected by patient
- Spot sample – 2<sup>nd</sup> visit

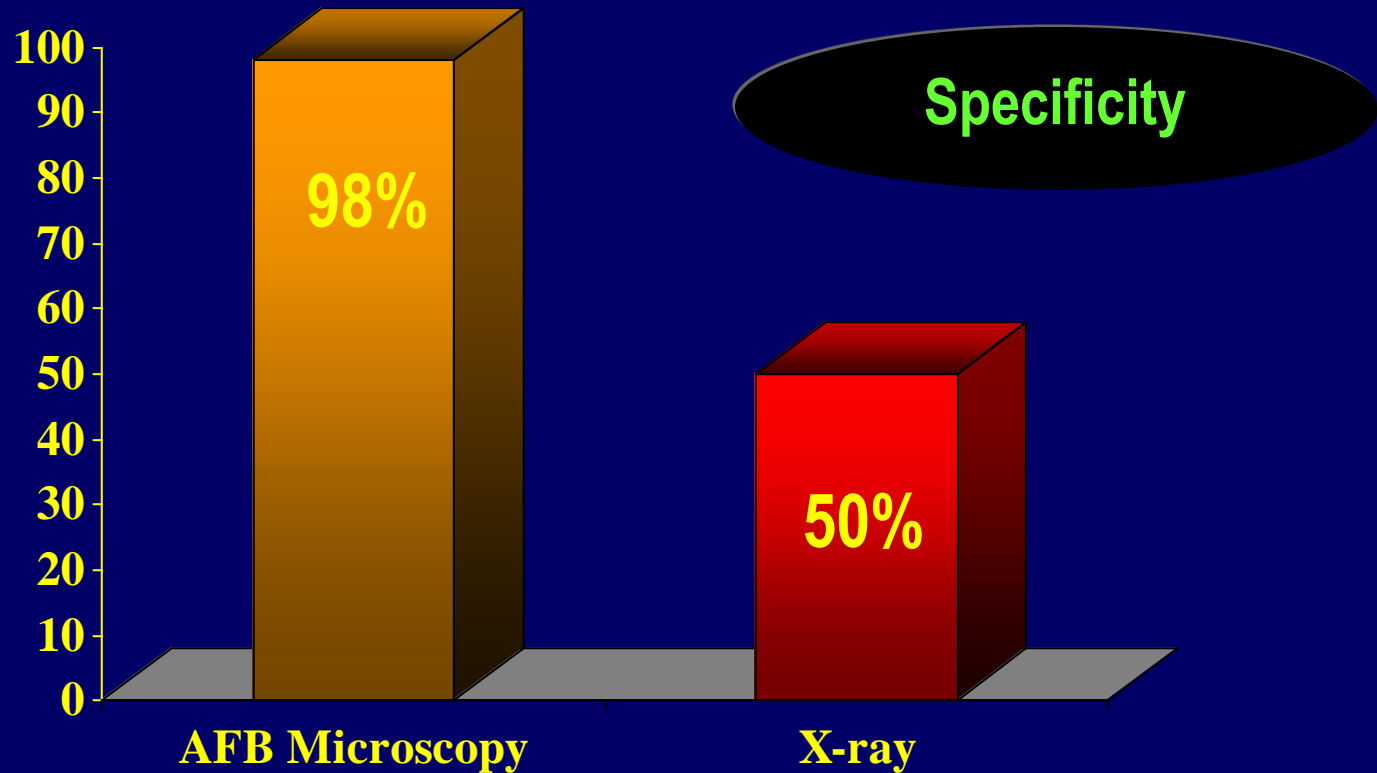


# Sputum collection



**? Deterrent to the Diagnosis**

# TB Diagnosis



**Microscopy is appropriate technology**

*Indicates*

**Infectiousness**

**Risk of death**

**Priority for treatment**

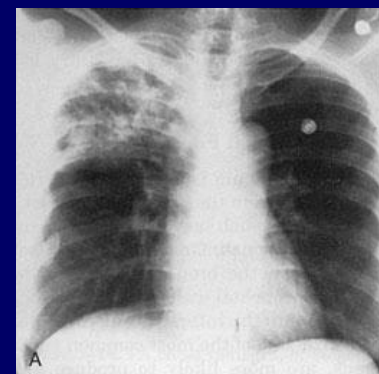
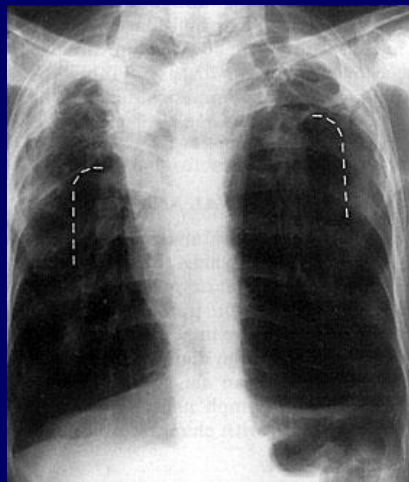
# CURRENT TRENDS IN INVESTIGATING PTB IN SRI LANKA THE FACTS

## The 1<sup>st</sup> line investigation

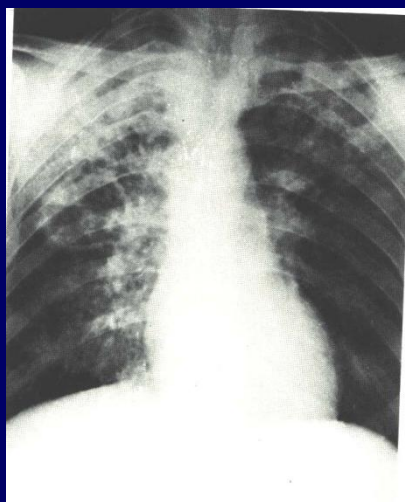
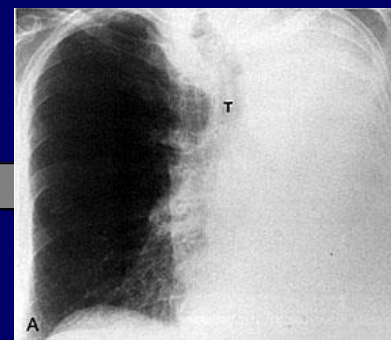
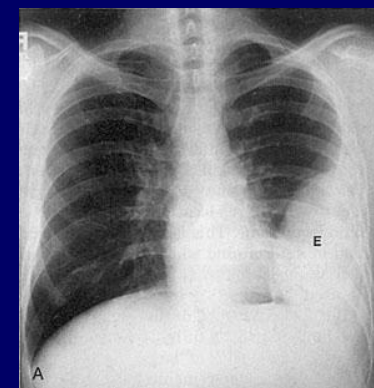
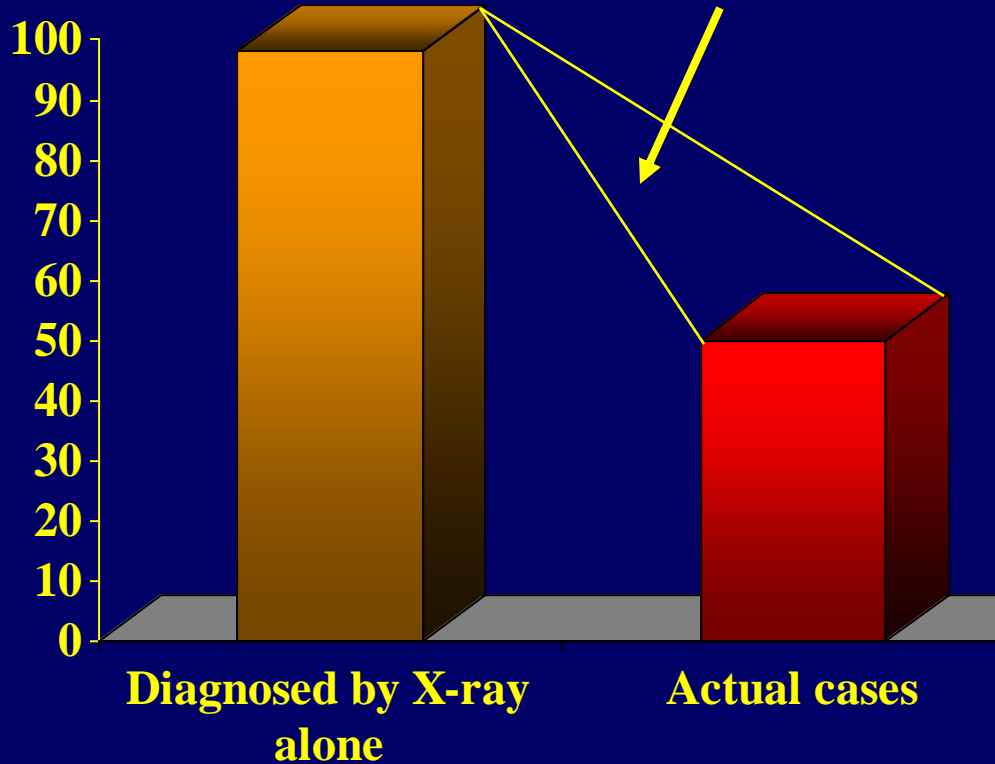
- Sputum microscopy - mainly confined to Chest Clinics
- ESR and Chest X ray - main tools used by the majority followed by Sputum Microscopy

NEED WE RELOOK AT INCEASING X RAY FACILITIES  
ALONG WITH SPUTUM MICROSCOPY ?

# TB Diagnosis



Over-diagnosed



# Tuberculin Skin Test

Limited Value if TB prevalence is high

## Results:

0 - 9 mm

- Negative

> 10mm

- Positive

> 20mm

- Strongly Positive



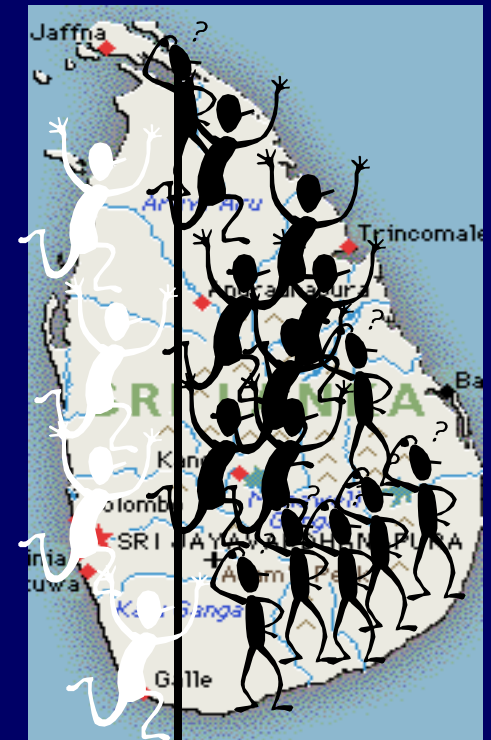
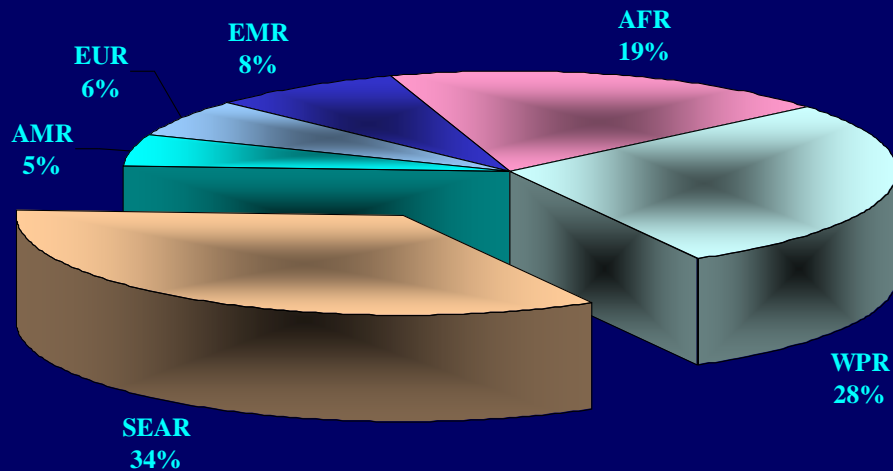


# TB INFECTED POPULATION



1/3 OF THE WORLDS POPULATION  
- 1.7 BILLION

South – East Asia accounts for nearly  
1/3<sup>rd</sup> of all Tuberculosis cases



> 50% IN SRI LANKA.

## ARE WE OVER RELIANT ON MATOUX AND ESR ?



- Mantoux is non specific and influenced by many factors
- ESR does not correlate well with disease activity
- ESR may be normal with active disease though a very high ESR may indicate TB

MICROBIOLOGICAL / HISTOLOGICAL CONFIRMATION OF  
TUBERCULOSIS

SHOULD BE GIVEN TOP PRIORITY

# Gamma Interferon

## MTB produces antigens

– *not seen in BCG & Non TB Myco bacteria*

- *Early Secretory Antigen Target 6 – ( ESAT 6)*
- *Culture Filtrate Protein 10 – ( CFP 10)*

*Pt's Lymphocytes – culture with Antigens*

*Gamma Interferon*



# TB CULTURE

- Highly specific
- Grossly underutilized
- Time consuming
- Luxury test in state sector

Very helpful in species identification

Identify Drug sensitivity patterns

EPTB

Smear negative TB



## Rapid Culture Methods

Radiometric methods

Oxygen consumption

TB growths 7 – 10 days earlier

Costly

# TB Diagnosis

- Polymerase Chain Reaction (PCR)
  - Mycobacterial Antibodies
  - TB - Gamma Interferon
  - Adenosine De Aminase
- 
- A female scientist with long brown hair, wearing a white lab coat over a dark top, is working in a laboratory. She is using a pipette to transfer liquid into a multi-well plate. In the foreground, there is a black bucket filled with white ice. The background shows a laboratory bench with various equipment, including a sink and a box labeled 'M'. The overall scene is brightly lit, typical of a clinical or research laboratory.

# TB **THOUGH** DEADLY IS COMPLETELY CURABLE

- **Completely Free**
- **Very Cheap**
- **Long Duration**
- **Multiple Drugs.**



**4 Antibiotics x 2 months**  
**2 Antibiotics x 4 months.**

# Essential Anti-TB Drugs

Drug	Mode of Action	Potency	Side Effects
Isoniazide (H)	- Bactericidal	- High	- Peripheral Neuropathy / Hepatitis
Rifampicin (R)	- Bactericidal	- High	- Nausea / Hepatitis / OCP
Pyrazinamide (Z)	- Bactericidal	- Low	- Joint Pains / Hepatitis
Ethambutol (E)	- Bacteriostatic	- Low	- Optic Neuritis
Streptomycine (S)	- Bactericidal	- Low	- Auditory / Vestibular Damage Nephrotoxic

**Intensive Phase**

- RHEZ Two Months

Non Infective in Two Weeks

**Continuation Phase**

- R H Four Months

Smear Negative in Two Months

# Prophylaxis in TB

**INAH – 6/12**

**INAH + Rifampicine – 3/12**

**Primary Chaemoprophylaxis**

**Person exposed but not infected**

**Eg: Breast Fed Baby with sputum +  
Mum.**

**HIV Positive / Mx Negative**

**Secondary Chaemoprophylaxis**

**Person infected but no clinical  
disease**

**Eg: HIV + / Mx +**

**Recent Mx Converters**

**Mx > 10mm with Risk factor**

**Mx > 10mm High prevalence groups**





# TREATMENT PROBLEMS

- **Incorrect Chemotherapy Dose / Duration**
- **Non compliance / Incomplete treatment**
- **Irregular Drug Supply**
- **Poor Quality Drugs**

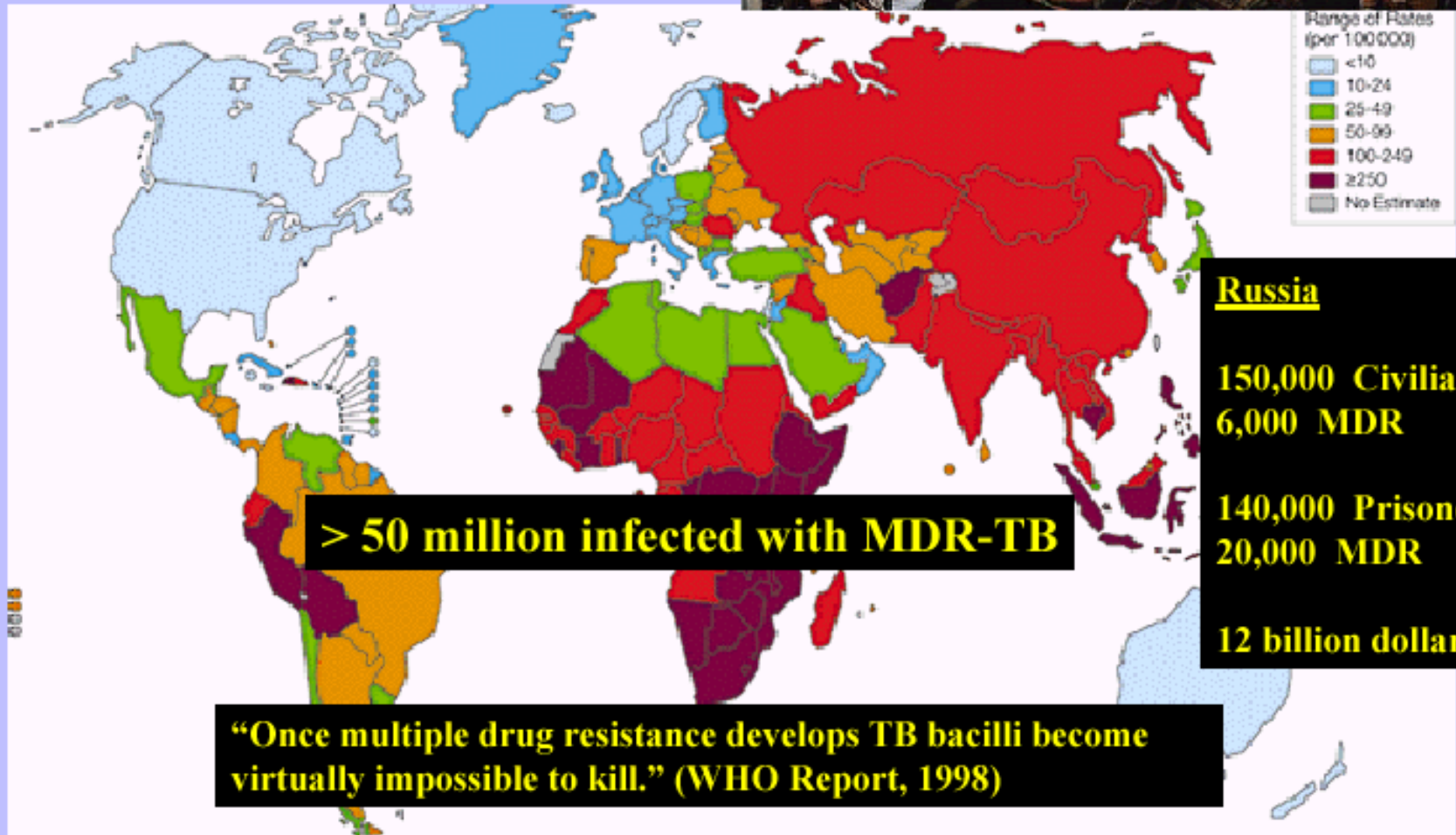
**Multi Drug Resistant TB**



## CONSEQUENCES

- Common Drugs Ineffective
- Second line drugs – Severe adverse reactions / not very effective
- Very High cost
- High Mortality.

# The “New” TB MDR-TB



# Second Line Drugs

**Amikacin Kanamycin Capreomycin**

**Ethionamide, Prothionamide**

**Cycloserine,**

**PAS**

**Ofloxacin, Ciprofloxacin,**

**Surgical Resection**



## XDR – TB

- **Extreme Drug Resistant TB**
- **Form of MDR TB – resistant to**
- **Quinolones + Injectables – Amikacin, Capreomycin, Kanamycin -classes of the second line drugs**
- **4 – 19% of MDR Cases**  
South Africa – Kwazulu – Natal – HIV positive population  
Very high mortality – 52 out of 53 cases dead within 25 days

## TDR – TB

- **Totally Drug Resistant TB**  
2009 – Iran

A woman in a white uniform, likely a health worker, is standing and talking to a family in a rural setting. The family includes a woman in a blue dress, a young boy in blue shorts, and a young girl in an orange dress. They are standing in front of a structure with a thatched roof. The text 'DOTS - Directly Observed Treatment Short Course' is overlaid on the image in yellow and red.

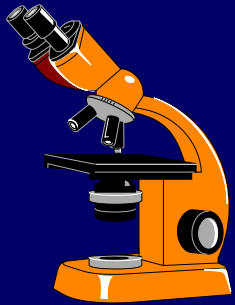
**D** - Directly  
**O** - Observed  
**T** - Treatment  
**S** - Short Course

*DOTS is the most cost effective strategy available  
for controlling the TB epidemic*

# DOTS Ensures Treatment

- **With the right drugs**
- **In the right dose**
- **At the right intervals**

- **Political commitment**



- **Diagnosis by microscopy**

- **Adequate supply of SCC drugs**



- **Directly observed treatment**

- **Accountability**



*The key factor to the diagnosis of Tuberculosis is the*

**Awareness that  
this Disease  
still Exists.**

Thank you