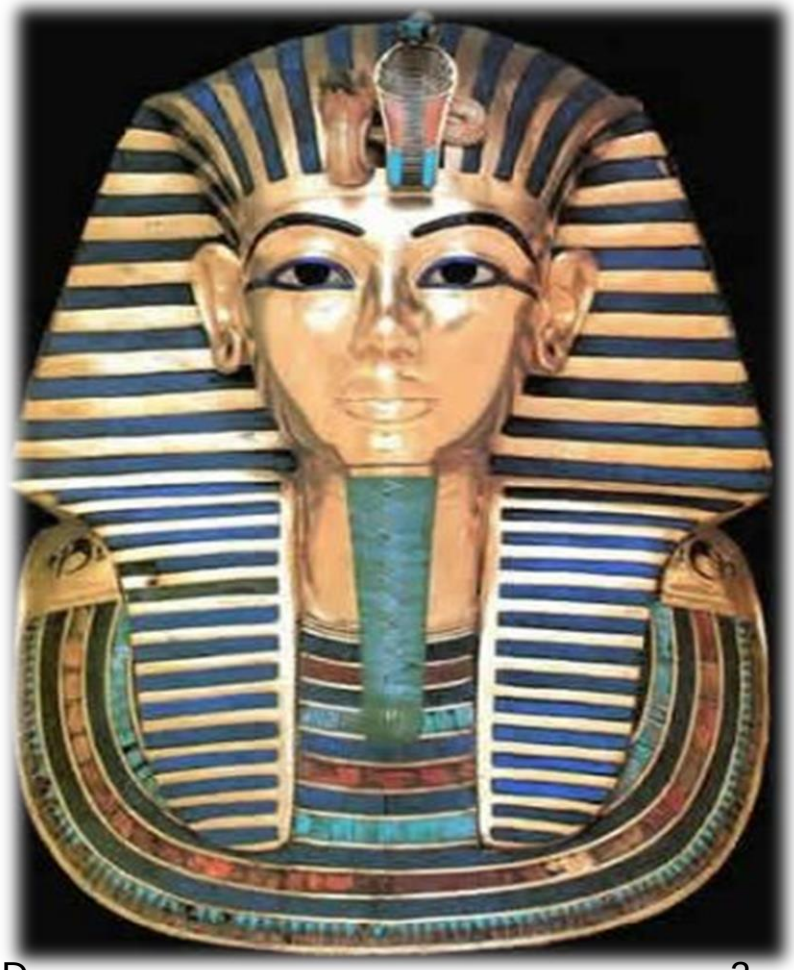
Tuberculosis

Student Update

Dr.T.V.Rao MD

HISTORY of Tuberculosis

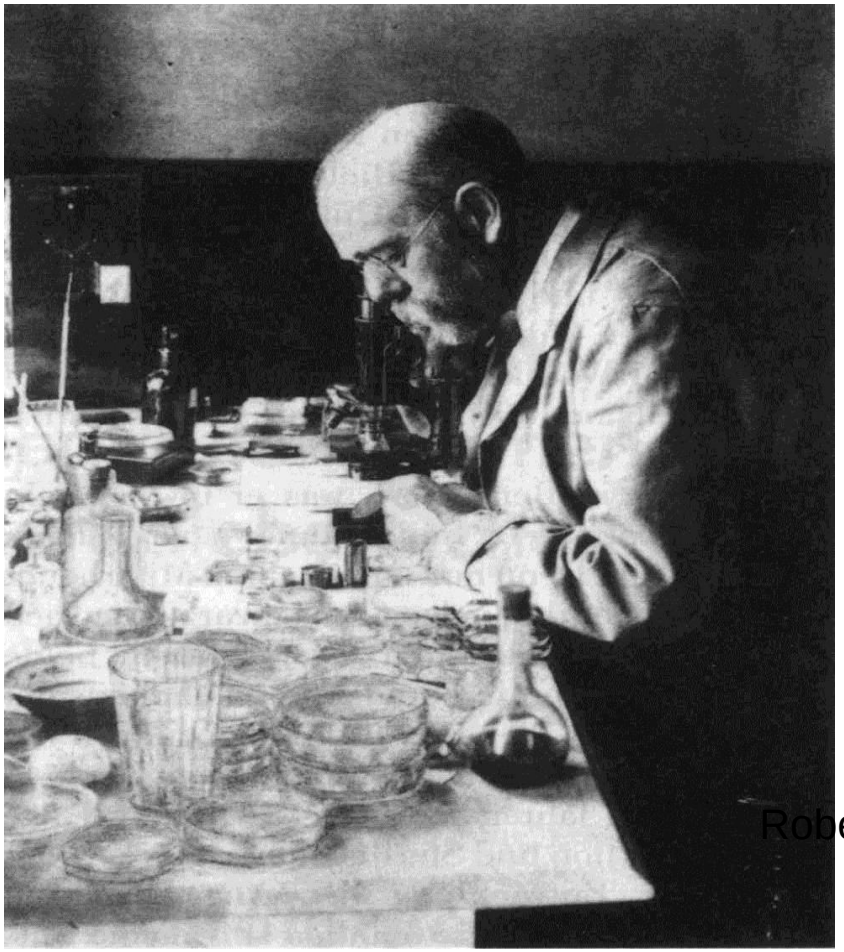
- Tuberculosis Is an Ancient Disease
- Spinal Tuberculosis in Egyptian Mummies
- History dates to 1550 – 1080 BC
- Identified by PCR



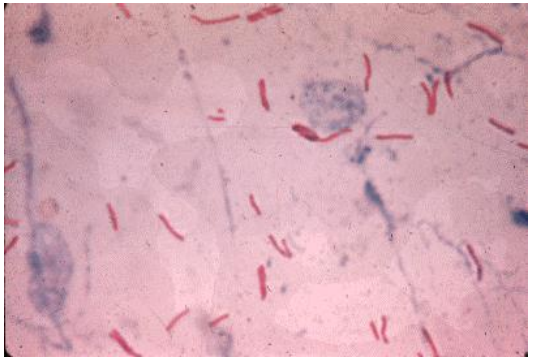
- Aristotle said…

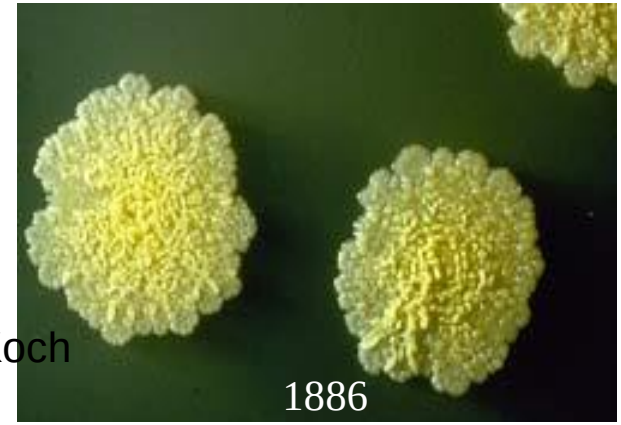
- 354-322 BC - Aristotle – “When one comes near consumptives… one does contract their disease… The reason is that the breath is bad and heavy…In approaching the consumptive, one breathes this pernicious air. One takes the disease because in this air there is something disease producing.”

M tuberculosis as causative agent for tuberculosis
Robert Koch



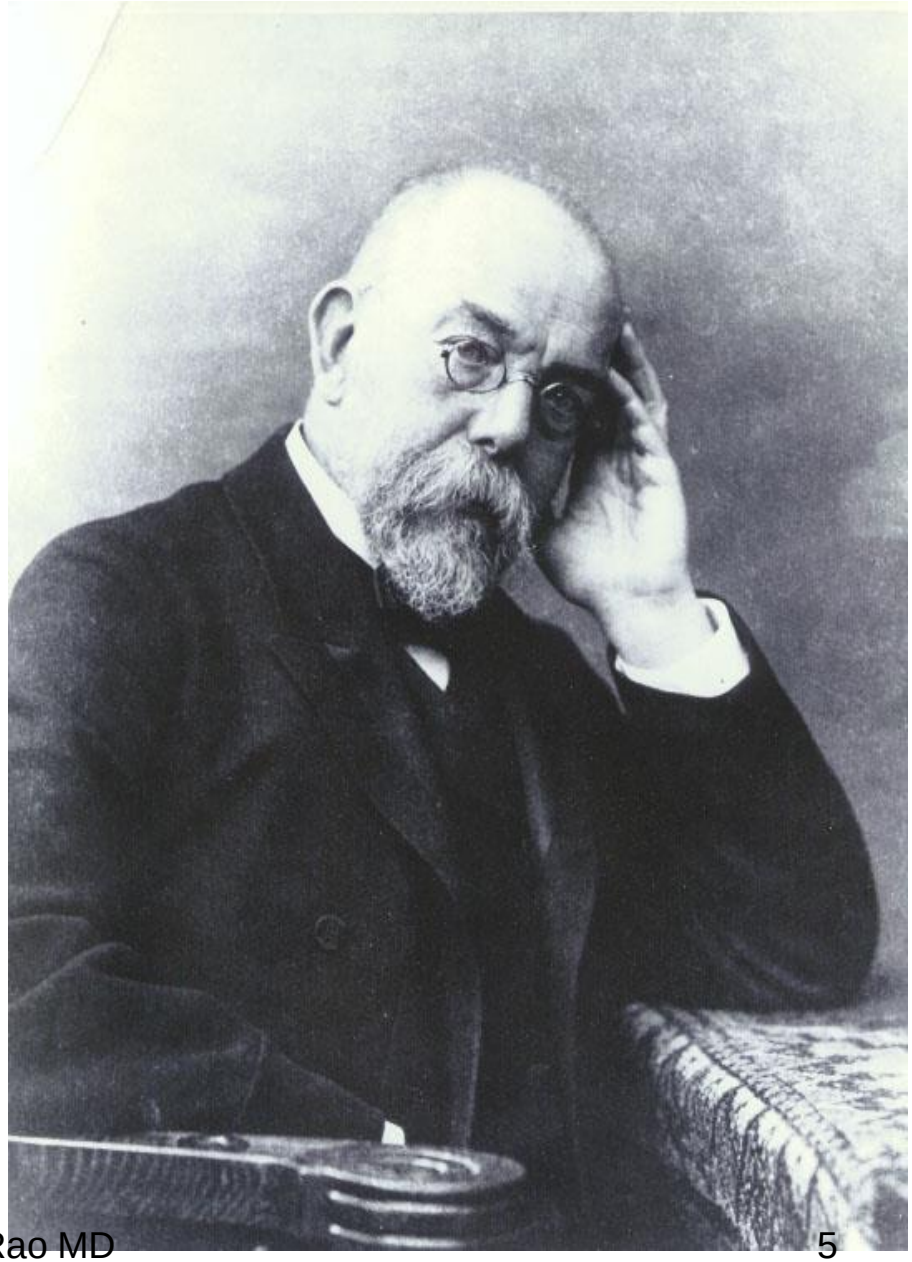
Robert Koch





1886

Robert Koch Discoverer of Mycobacterium Tuberculosis



What are Mycobacteria?

- **Obligate aerobes** growing most successfully in tissues with a high oxygen content, such as the lungs.
- Facultative **intracellular pathogens** usually **infecting mononuclear phagocytes** (e.g. macrophages).

Mycobacterium differ from other routinely isolated Bacteria

- **Slow-growing** with a generation time of 12 to 18 hours (c.f. 20-30 minutes for *Escherichia coli*).
- **Hydrophobic** with a high lipid content in the cell wall. Because the cells are hydrophobic and tend to clump together, they are impermeable to the usual stains, e.g. **Gram's stain**

Acid fast bacilli

- Known as “**Acid-fast bacilli"** because of their lipid-rich cell walls, which are relatively impermeable to various basic dyes unless the dyes are combined with phenol.

How they are Acid fast

- Once stained, the cells resist decolourization with acidified organic solvents and are therefore called "acid-fast". (Other bacteria which also contain mycolic acids, such as *Nocardia*, can also exhibit this feature.)

Mycobacterium tuberculosis complex

- Includes Human and Bovine mycobacterium
- M.africanum Tropical Africa
- M.microti do not cause human infections but small mammals Can be infected

Avian Tuberculosis

- Transmitted by ingestion and inhalation of aerosolized infectious organisms from feces.
- Oral ingestion of food and water contaminated with feces is the most common method of infection.
- Once ingested, the organism spreads throughout the bird's body and is shed in large numbers in the feces.
- If the bacterium is inhaled, pulmonary lesions and skin invasions may occur
- transmission of avian TB is from bird to human not from human to human.

Bovine Tuberculosis

- Bovine TB is most likely going to effect the joints and bones.
- people contract Bovine TB today,by eating food that has been contaminated by the bacteria or from drinking un-pasteurized milk from cows that are infected with the virus.

M.bovis

- Primarily infection among the cattle
- M.bovis infects Tonsils, Cervical nodes, can produce Scrofula.
- Enter through Intestines – infects the Ileocecal region.

What are atypical Mycobacterium

- Infects birds, cold blooded animals worm blooded animals
- Present in environment
- Opportunistic pathogens
- Others – Saprophytic bacteria

  M butryicum present in butter

  M.phlei

  M smegmatis – present in Smegma

Atypical Mycobacterium

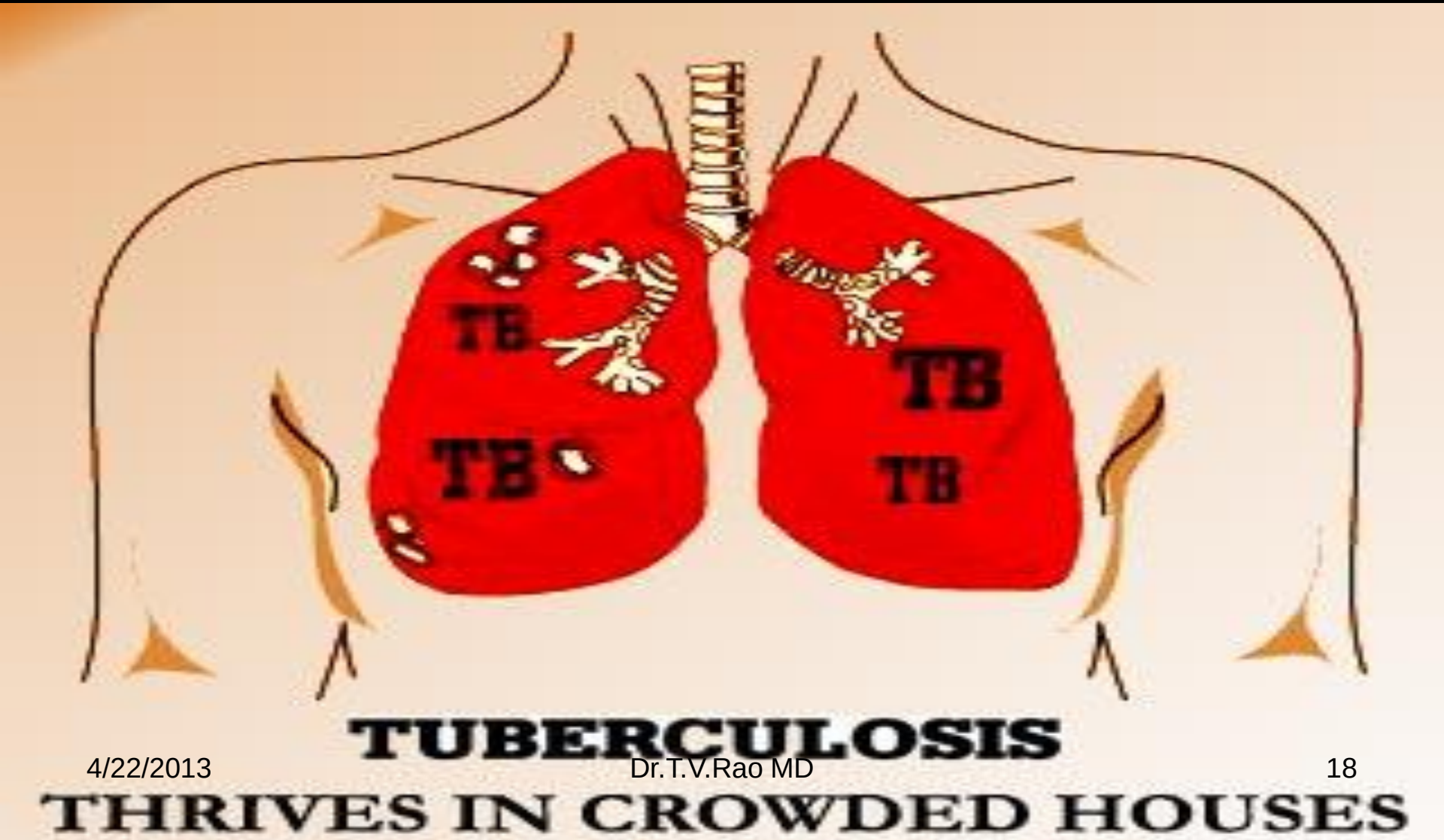
- 1 Photochromogens
- 2 Scotochromogens
- 3 Nonphotochromogens
- 4 Rapid growers

MOST IMPORTANT AMONG INFECTIOUS DISEASES

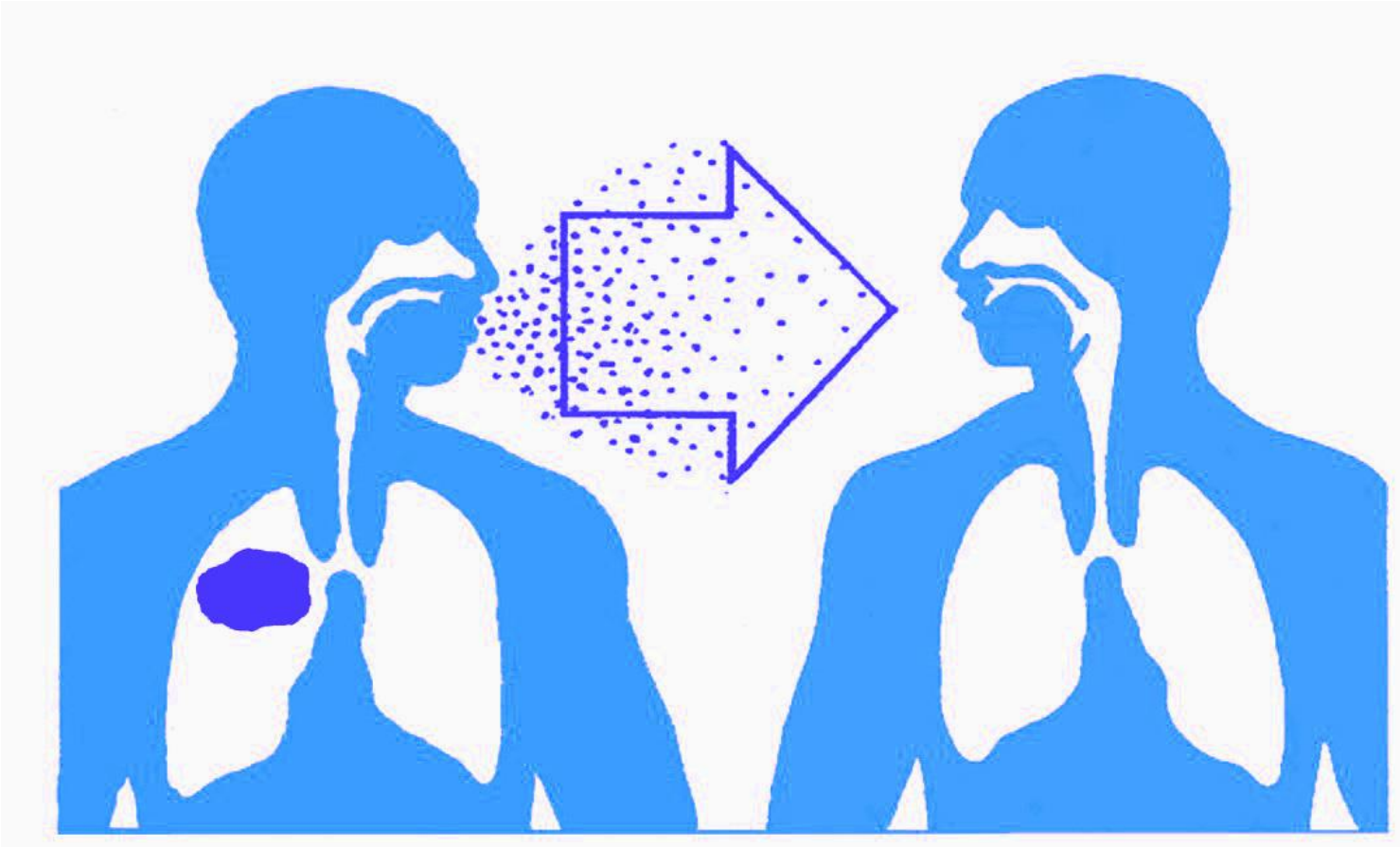
- **Tuberculosis (TB)** is the leading cause of death in the world from a bacterial infectious disease. The disease affects 1.8 billion people/year which is equal to one-third of the entire world population.

Tuberculosis kills not only poor but rich and famous

Poverty and Crowded living spreads Tuberculosis



How Are TB Germs Spread?

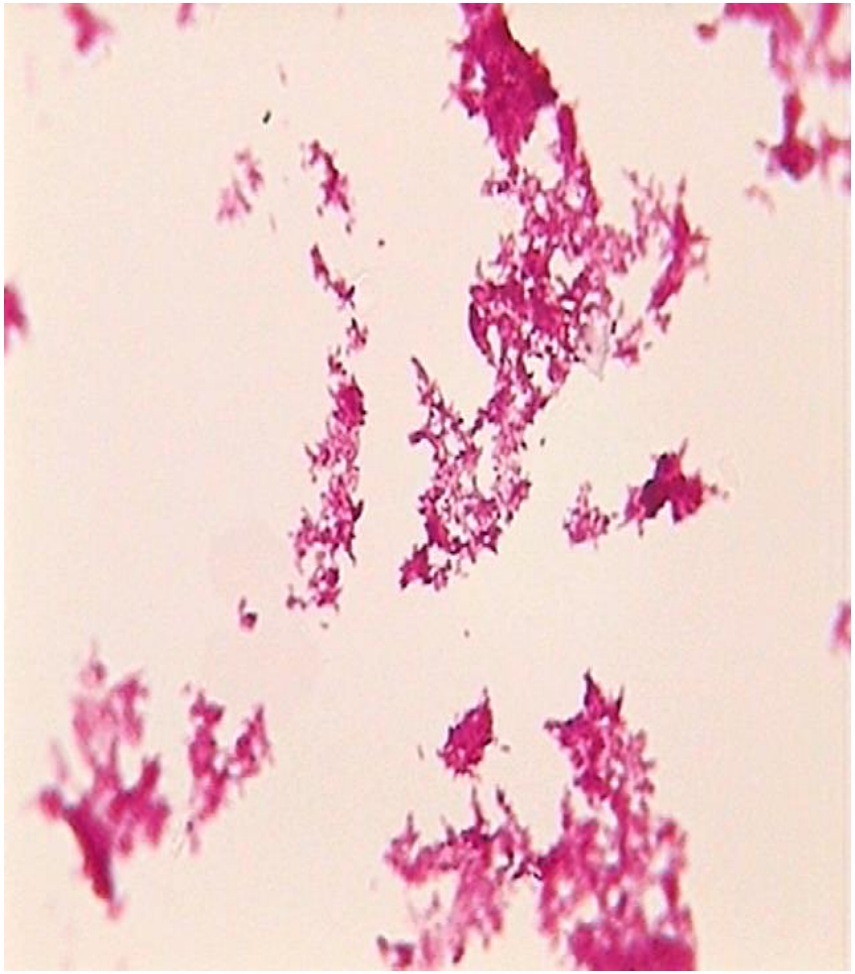


What are Mycobacteria?

- Obligate **aerobes** growing most successfully in tissues with a high oxygen content, such as the lungs.
- Facultative **intracellular pathogens** usually infecting **mononuclear phagocytes** (e.g. macrophages).

Morphology of Mycobacterium tuberculosis

- Straight, slightly curved Rod shaped 3 x 0.3microns
- May be single, in pairs or in small clumps
- On conditions in growth appears as filamentous, club shaped, or in Branched forms.



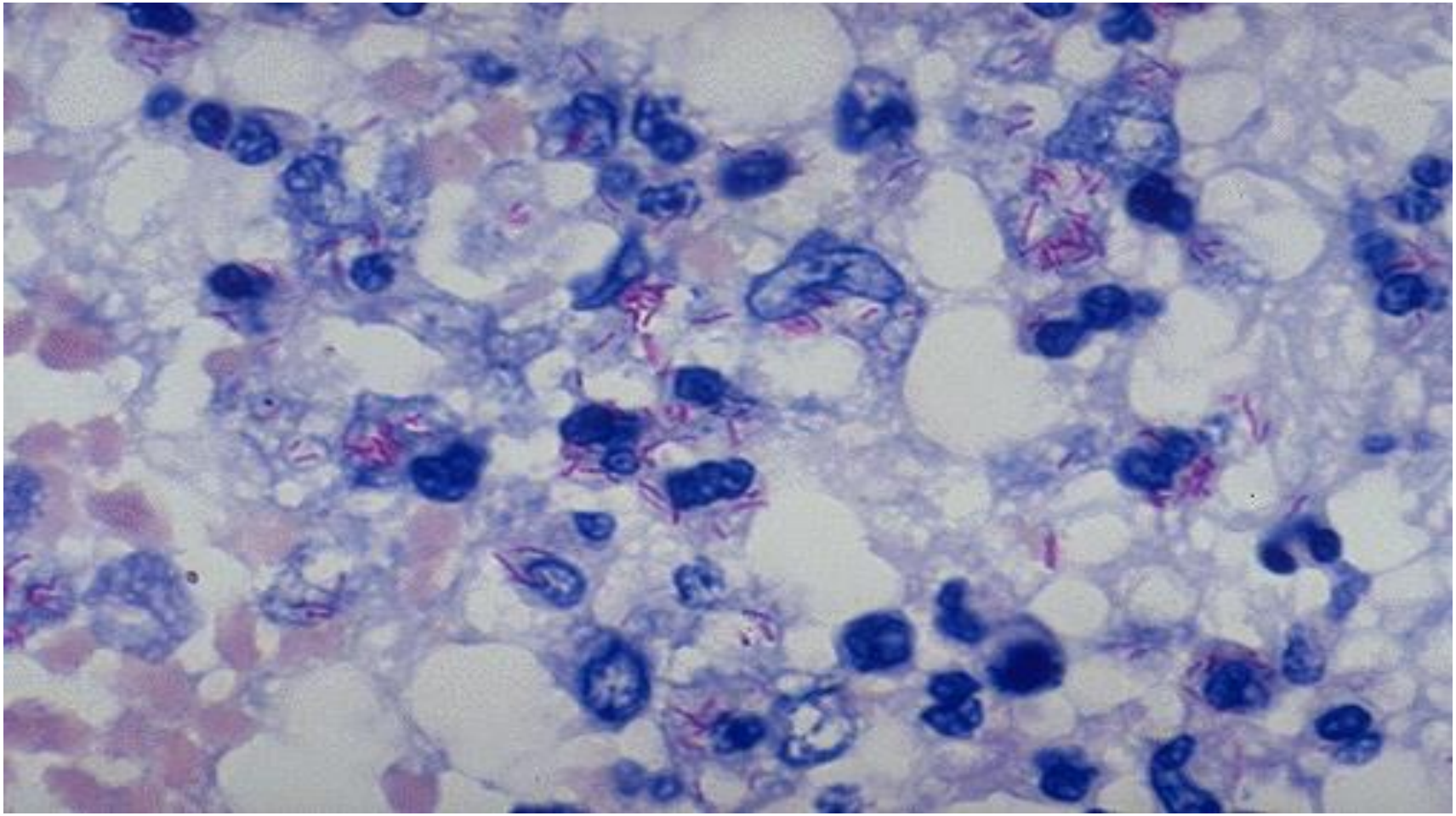
ACID FAST BACILLI

- Known as "**Acid-fast bacilli"** because of their lipid-rich cell walls, which are relatively impermeable to various basic dyes unless the dyes are combined with phenol.

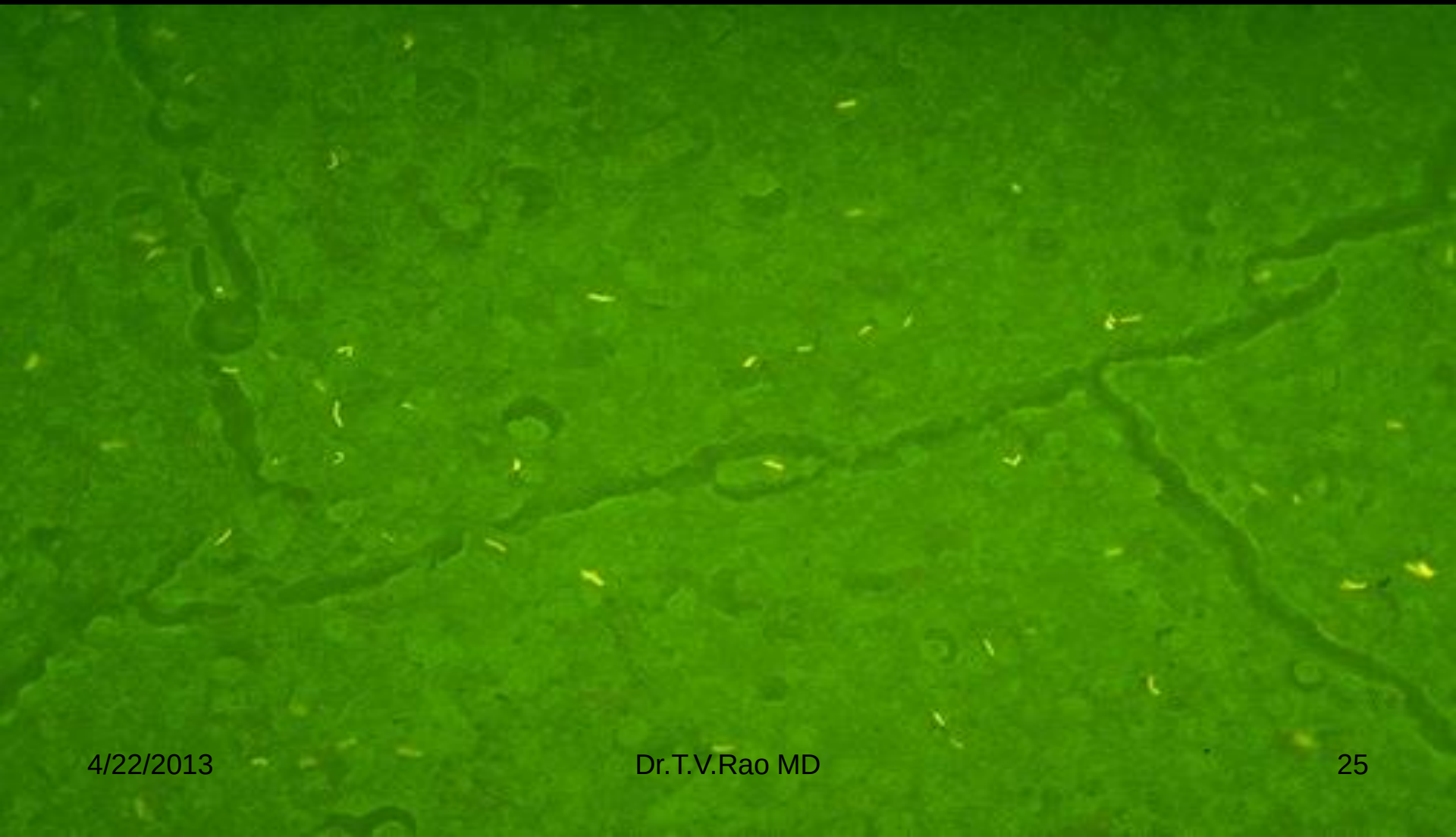
Important Mycobacterium

- *Mycobacterium tuberculosis*, along with *M. bovis*, *M. africanum*, and *M. microti* all cause the disease known as tuberculosis (TB) and are members of the tuberculosis species complex. Each member of the TB complex is pathogenic, but *M. tuberculosis* is pathogenic for humans while *M. bovis* is usually pathogenic for animals

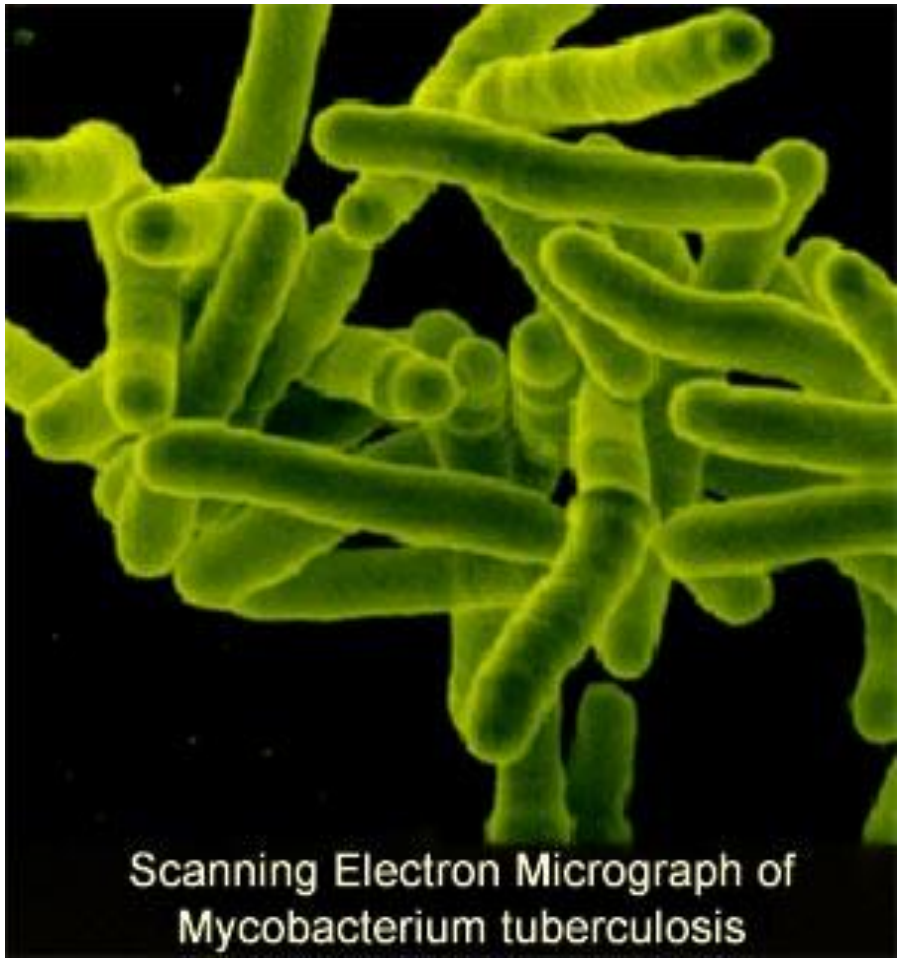
Acid Fast Bacilli seen in a specimen of Sputum



Acid fast Bacilli seen as in Florescent Microscope



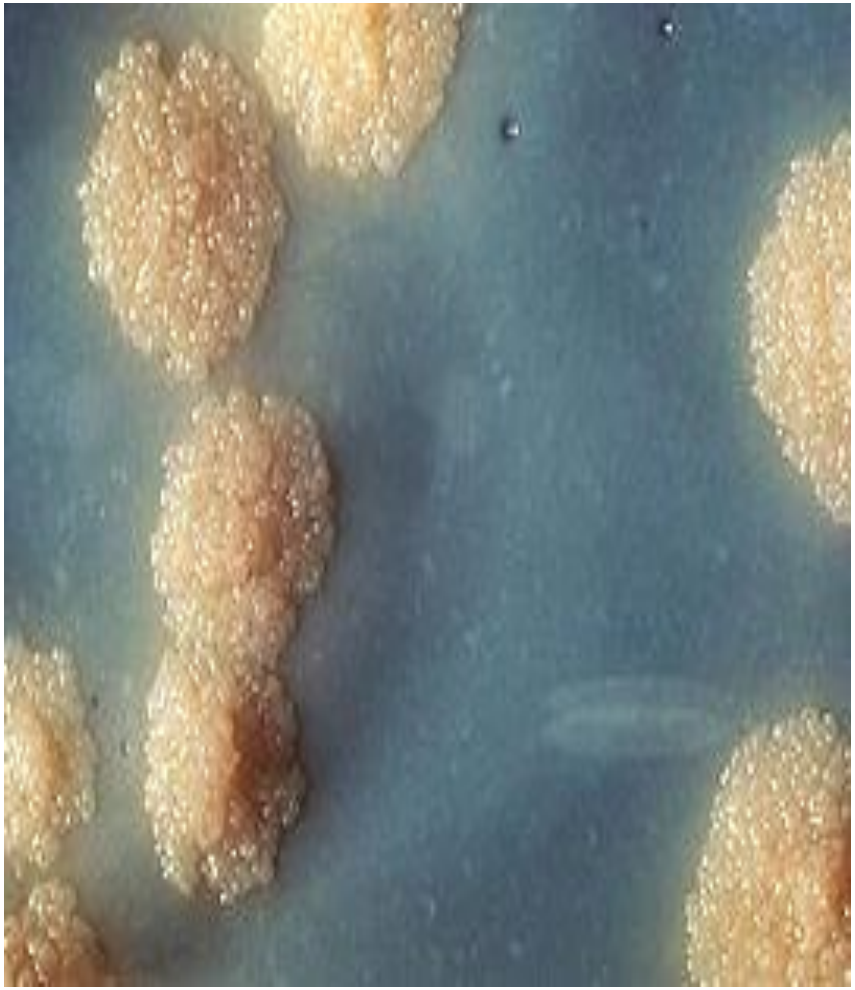
Why they are Acid Fast



- The character of Acid fastness is due to presence of Unsapnofiable wax (My colic acid and semi permeable membrane around the cell)

Culturing Acid Fast Bacilli

- Slow to grow ,
- Generation time is 14 – 15 hours
- > 2 weeks minimal required period
- Grows at 37^0c do not grow below 25^0c
- Ph between 6.4 to 7.0



Nature of Media Used

- Helps the growth needs
- Solid Medium is commonly used
- Lowenstein Jensen’s medium
- Petrangini
- Middle brook medium

Lowenstein Jensen's Medium

- Contain coagulated egg
- Mineral salt solution
- Asparagine's
- Malachite green
- Agar

Other Medium

- Middle brook
- Sula”s medium
- But not routinely used

Nature of Growth Characters

- M tuberculosis is obligate aerobe
- M.bovis Microaerophilic
- M.tuberculosis grwoth luxierently
- M.tuberculosis eugonic
- M bovis is dysgonic
- When grown on 0.5% glycerin M tuberculosis growth improves
- Sodium pyruvate improves the grwoth of both organism.

On L J Medium

- M.tuberculosis appear dry, rough raised irregular colonies
- Appear wrinkled
- They appear creamy white
- Become yellowish
- M.bovis appear as flat smooth, moist, white and break up easily

On Liquid Medium

- Appear as long serpentine cords in liquid medium
- Virulent strains grow in a more dispersed manner.

Immunological Testing

- Tuberculin skin test/Mantoux: tuberculin purified protein derivative (PPD) injected intradermally & cell-mediated response at 48-72h . +ve 5-14mm induration, strongly +ve >15mm
- +ve test indicated immunity (may be previous exposure, BCG) Strong +ve test = active infxn. False neg tests in immunosuppression (miliary TB, sarcoid, AIDS, lymphoma)

Resistance of Mycobacterium

- Mycobacterium are killed at 60^0c in 15 – 20 mt
- In sputum they survive for 10 – 30 mt
- Relatively resistant to several chemicals including Phenol 5 %
- Sensitive to Glutaraldehyde and Formaldehyde
- Ethanol is suitable application to superficial surfaces and skin gloves

Resistance to several agents

- **Bacilli survive in Droplets for 8 – 10 days**
- **Survive in**

  5% phenol,

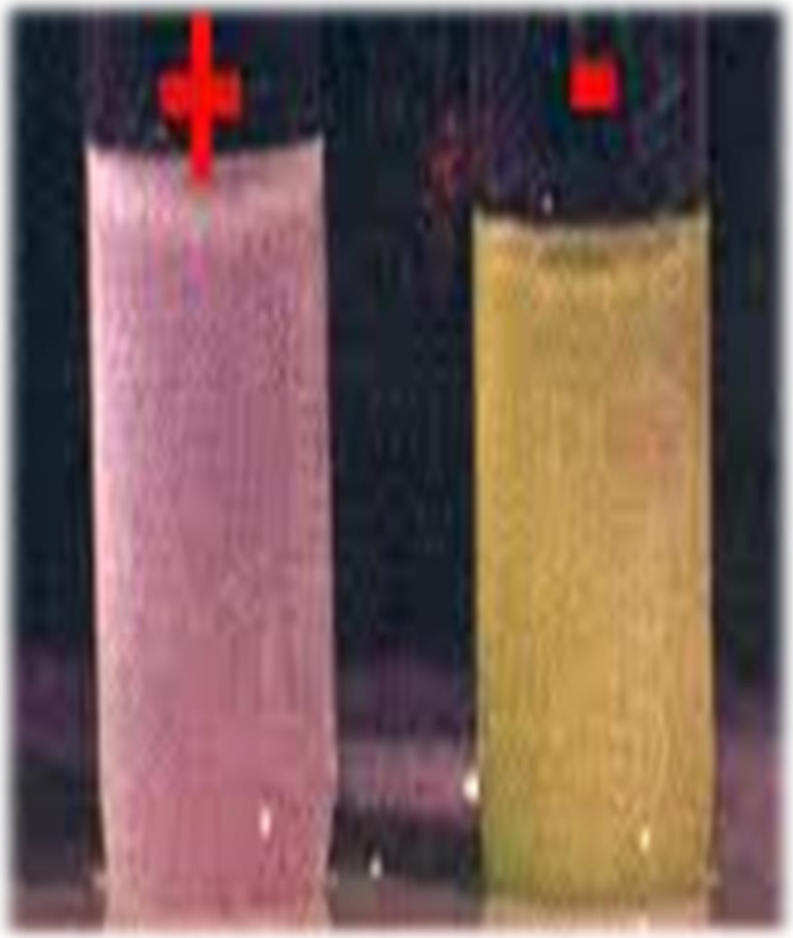
  15% Sulphuric acid

  3% Nitric acid,5% oxalic acid,

  4% Sodium hydroxide

Biochemical Tests on Mycobacterium spp

- Niacin test – 10% cyanogens bromide and 4% Aniline in 96% ethanol are added to suspension of – C canary yellow color indicates postive test.



Biochemical Tests

- Aryl sulphatase test – Positive in Atypical Mycobacterium
- Bacilli grown in 0.001 tripotassium phenolpthalein disulphide / 2 N. Na oH added drop by drop a pink color develops
- Catalase peroxidase test –

  Differentiates Atypical from Typical

  Most Atypical are strongly Catalase positive

  Tubercle bacilli are weakly positive

  Tubercle bacilli are peroixidae positve – not atypical

  INH resistant strains are negative for test

Catalase Test

- 30 vol of H_2O_2 and 0.2 % alcohol in distilled water is added to 5 ml of test culture
- Effervescence indicates Catalase positive
- Other test

  Amidase test

  Nitrate reduction test

Antigenic Characters

- Group specificity due to Polysaccharides
- Type specificity to protein antigens
- Delayed hypersensitivity to proteins
- Related to each other species
- Some relation between lepra and tubercle bacilli
- Serology – Tests not useful

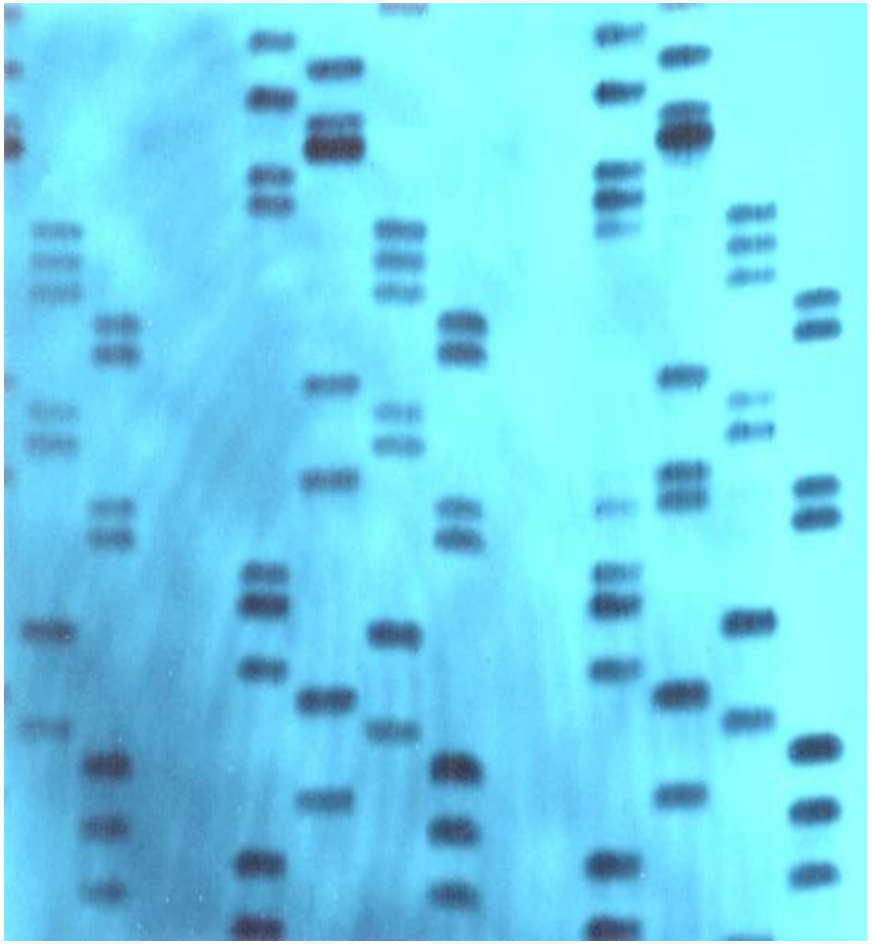
Antigenic homogeneity between < bovis and M.microti

Bacteriophages

- There are 4 Bacteriophages A B C D
- A worldwide
- B. Europe and -American
- C rare
- I type nature between A and B and common in India
- Phage 33 D M tuberculosis and not in BCG strains

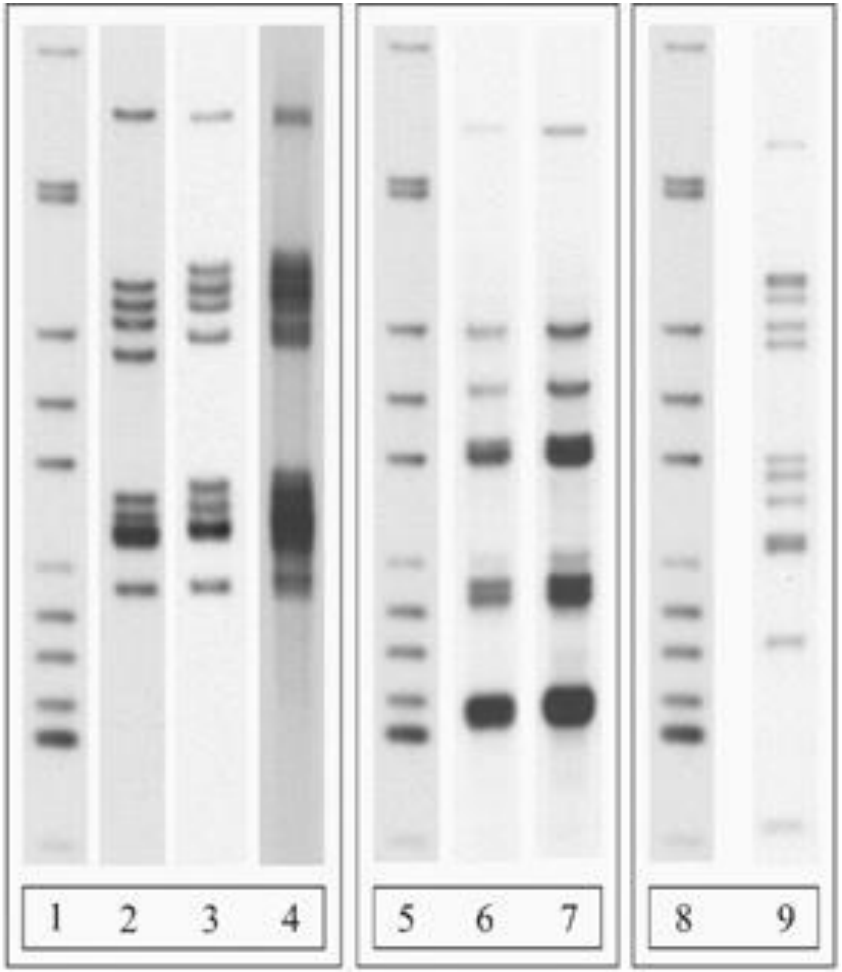
Molecular Typing

- DNA finger printing differentiates different strains of Mycobacterium species
- Treating the organism with Restriction endonulease yields Nucleic acid fragments of varying length and strain specific
- Use in epidemiological studies

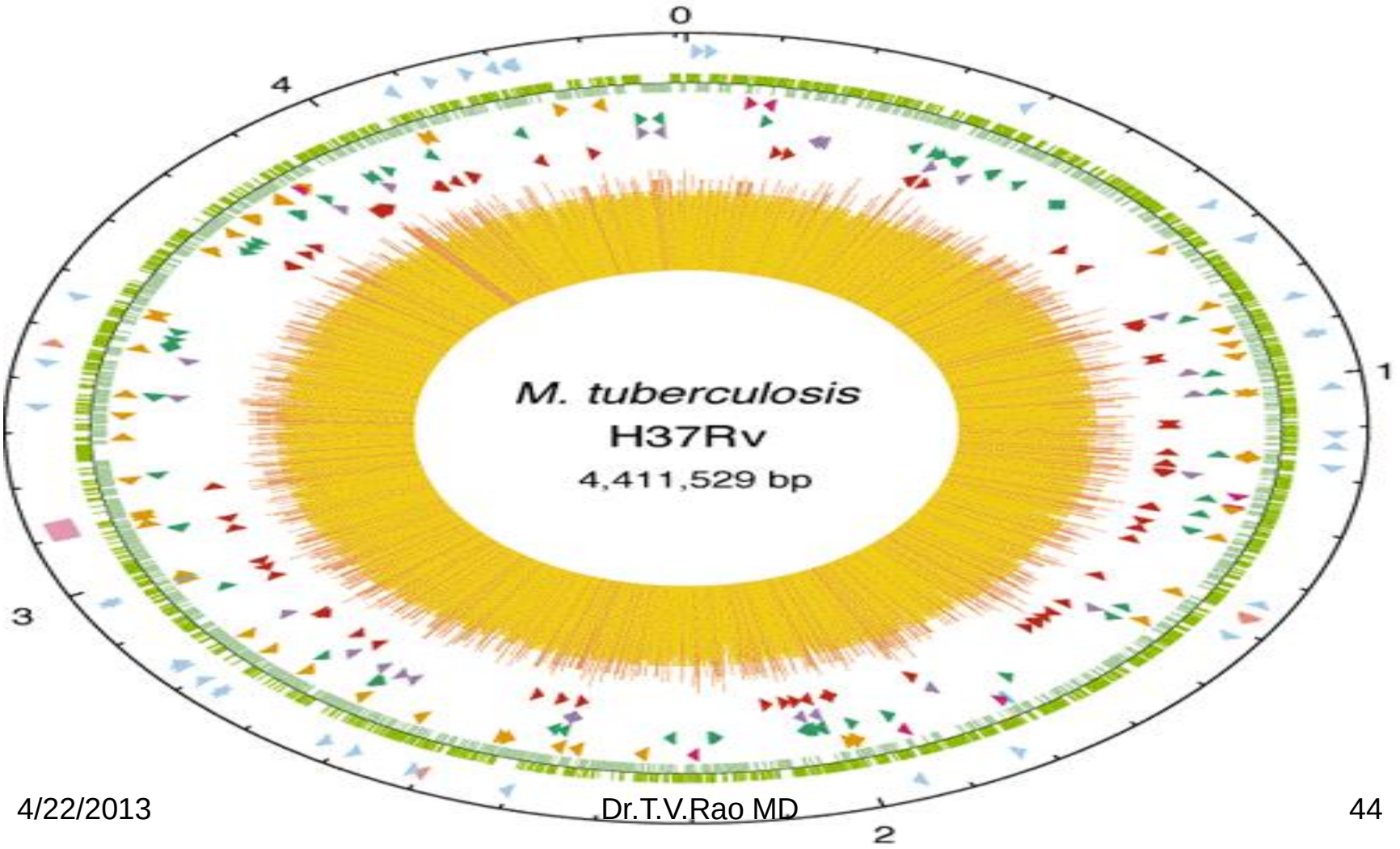


Finger printing Methods

- Finger printing is done with Chromosomal insertion sequence IS 6110 present in most strains of Tubercle bacilli
- Now entire genome of M tuberculosis is sequenced
- Several Molecular methods are avialble for studies



Genome of Mycobacterium tuberculosis

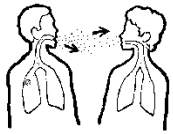


How tuberculosis spreads

- Tuberculosis (TB) is a contagious disease. Like the common cold, it spreads through the air. Only people who are sick with TB in their lungs are infectious. When infectious people cough, sneeze, talk or spit, they propel TB germs, known as bacilli, into the air. A person needs only to inhale a small number of these to be infected.

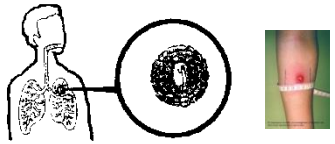
Natural History of TB Infection

Exposure to TB



No infection
(70-90%)

Infection
(10-30%)



Latent TB
(90%)

Active TB
(10%)

Never develop
Active disease

Untreated

Treated

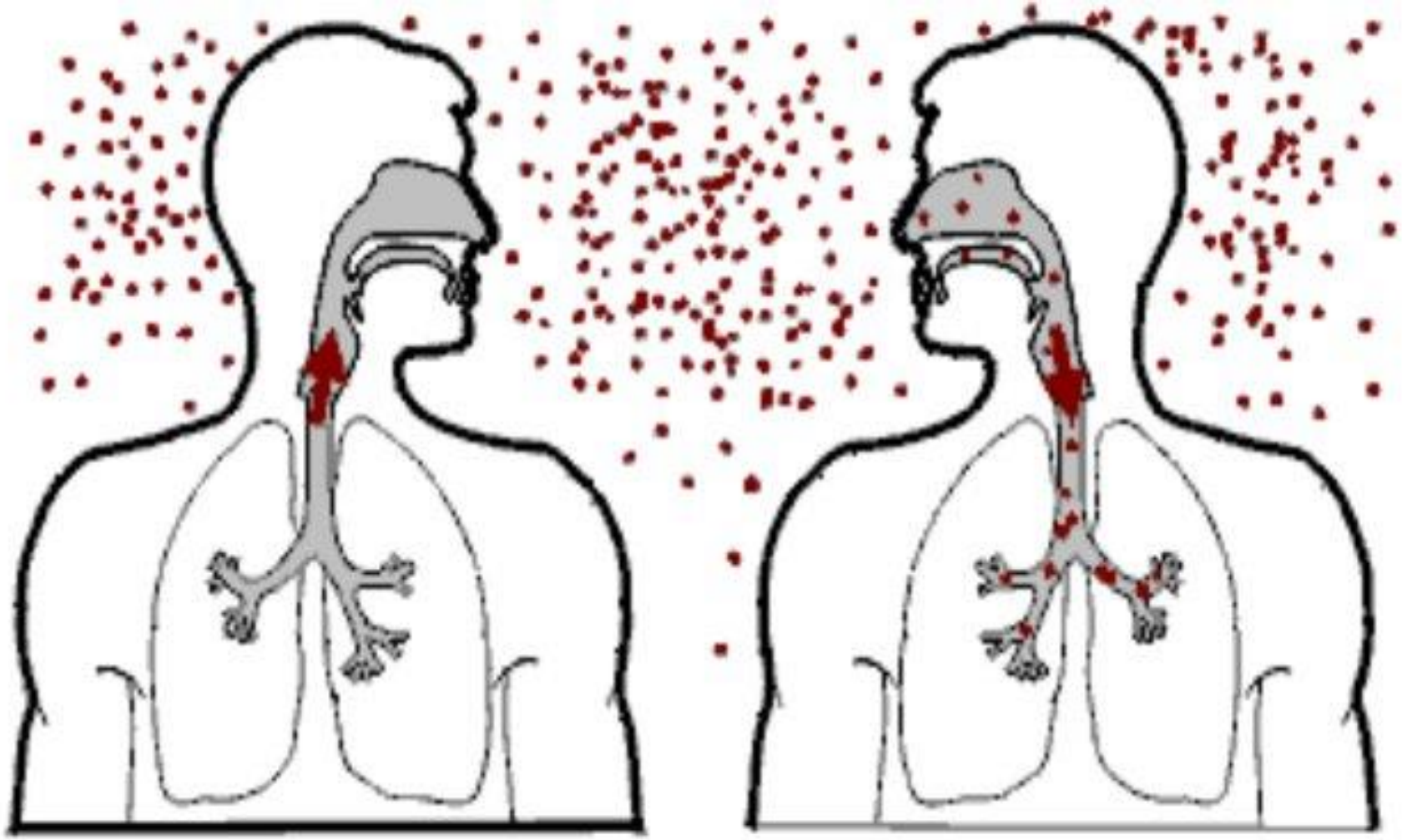
Die within 2 years

Survive

Die

Cured

Tuberculosis spread by Respiratory route



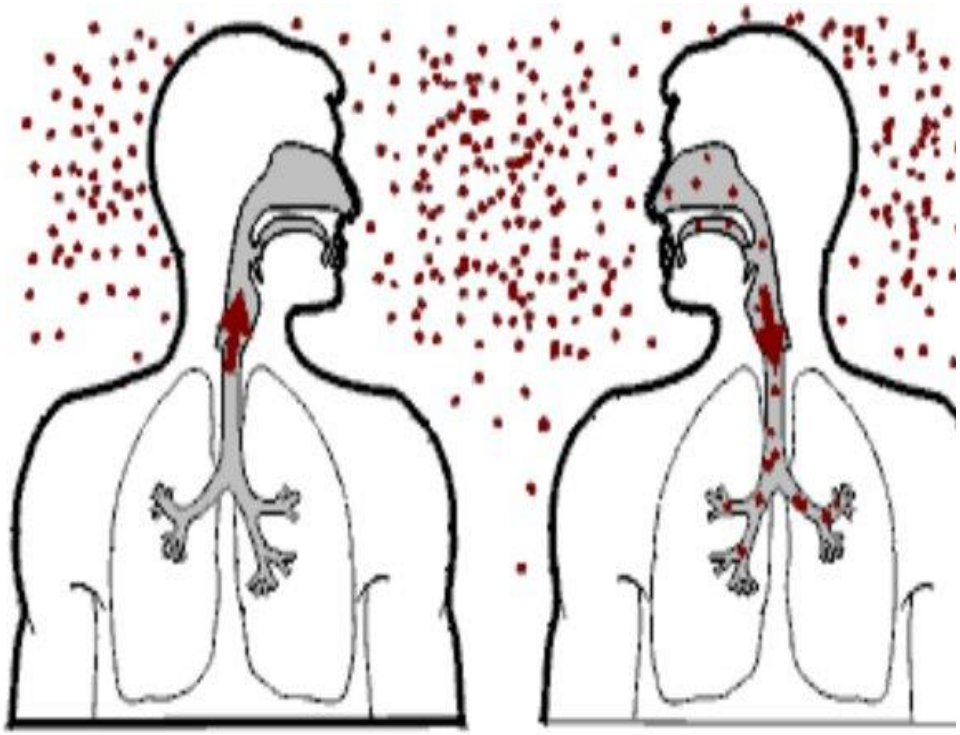
Importance of Tuberculosis

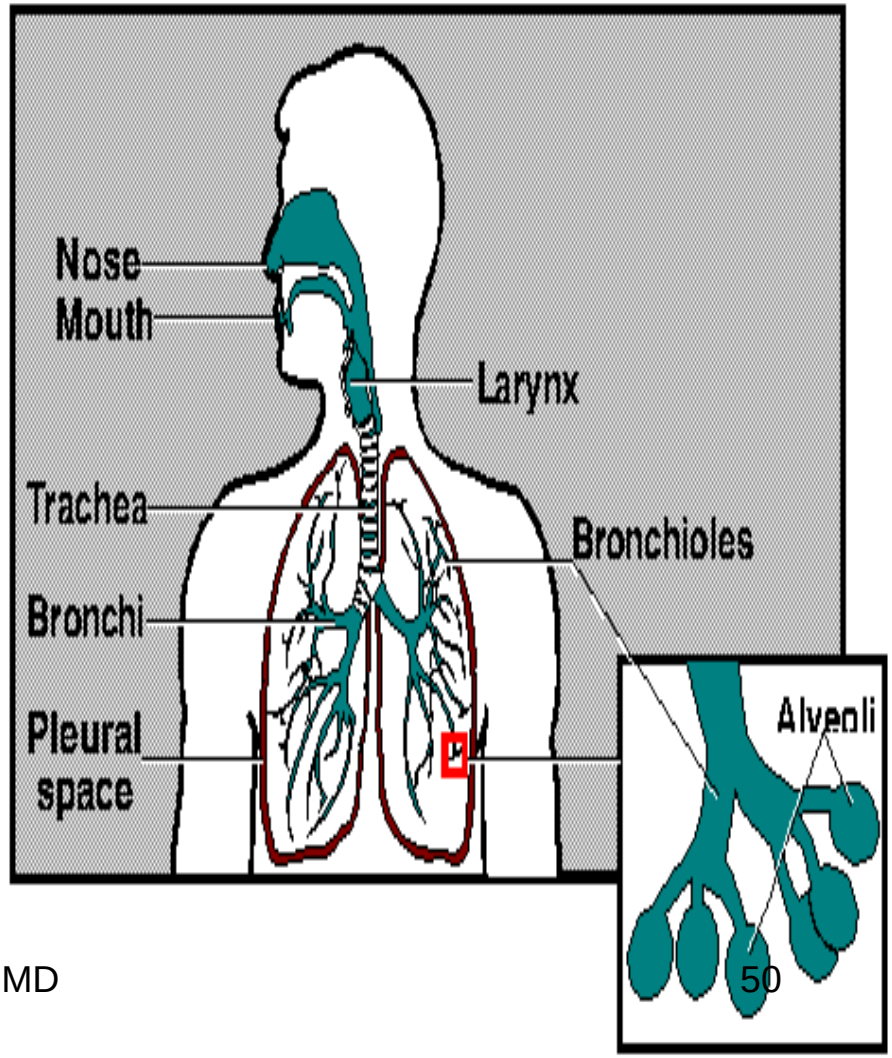
- Someone in the world is newly infected with TB bacilli every second.
- Overall, one-third of the world's population is currently infected with the TB bacillus.
- 5-10% of people who are infected with TB bacilli (but who are not infected with HIV) become sick or infectious at some time during their life. People with HIV and TB infection are much more likely to develop TB.

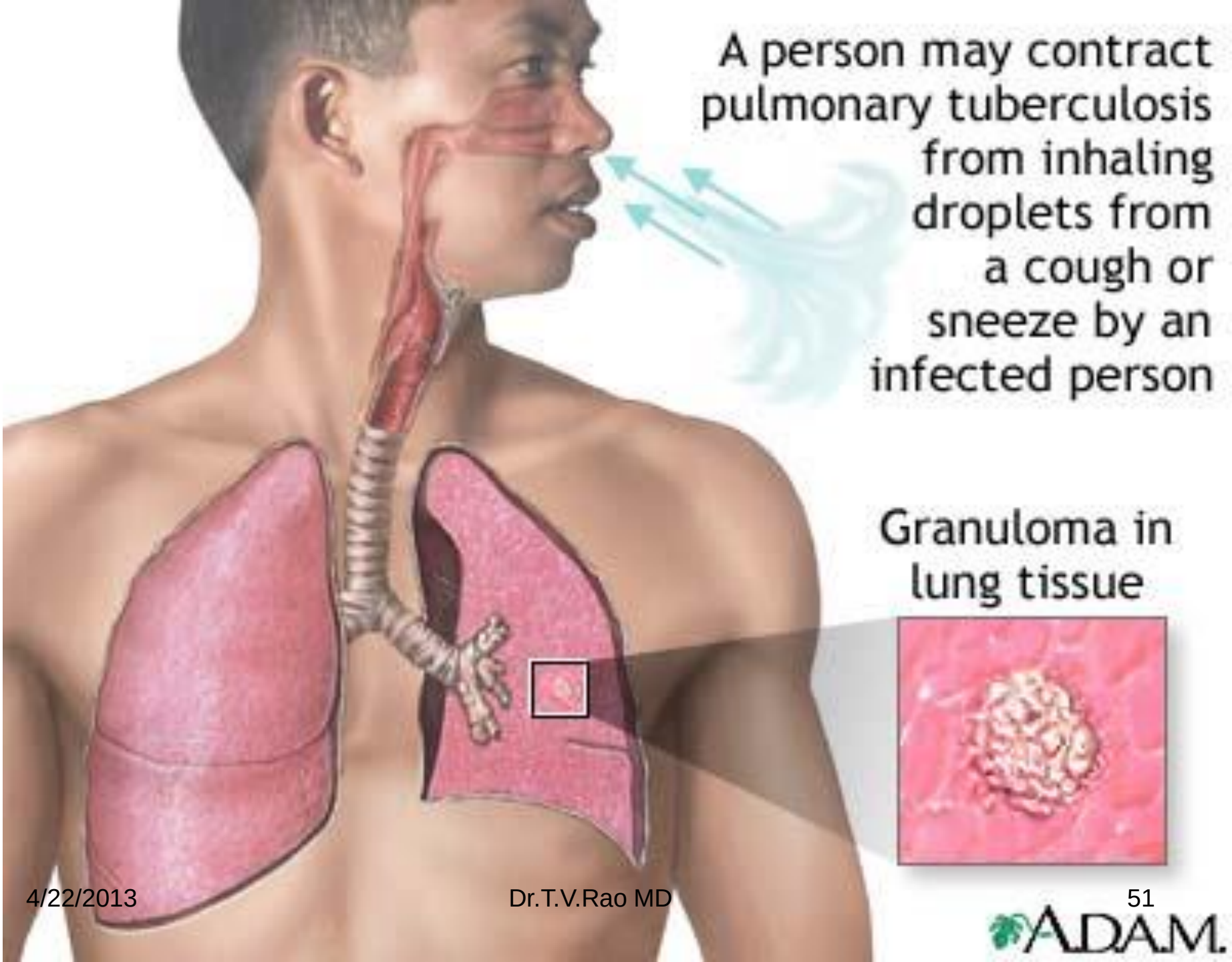
Pathology and Pathogenesis of Tuberculosis

- Source of Infection – Open case of Pulmonary Tuberculosis.
- Every open case has potential to infect 20 – 25 healthy persons before cured or dies
- Coughing , Sneezing, or Talking.
- Each act can spill 3000 infective nuclei in the air,
- Infective particles are engulfed by Alveolar Macrophages.

Spread of Tuberculosis






A person may contract pulmonary tuberculosis from inhaling droplets from a cough or sneeze by an infected person
Granuloma in lung tissue
A.D.A.M.

Predisposing Factors

- Genetic basis,
- Age
- Stress,
- Nutrition,
- Co existing infections Eg HIV

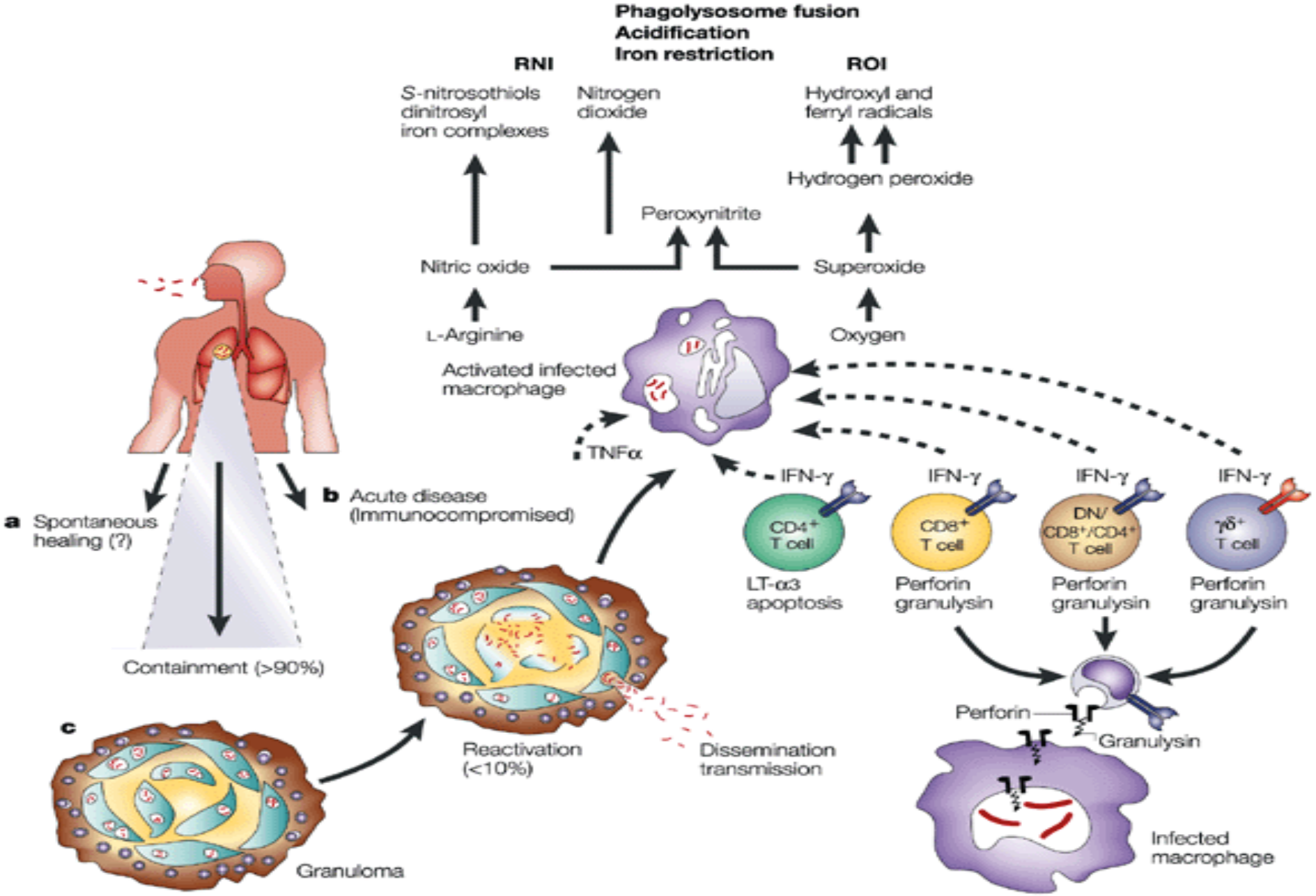
Mechanisms of Infection

- Mycobacterium do not produce toxins.
- Allergy and Immunity plays the major role.
- Only 1/10 of the infected will get disease.
- Cell Mediated Immunity plays a crucial role.
- Humoral Immunity – not Important.
- CD_4 Cell plays role in Immune Mechanisms.

Mechanisms of Infection

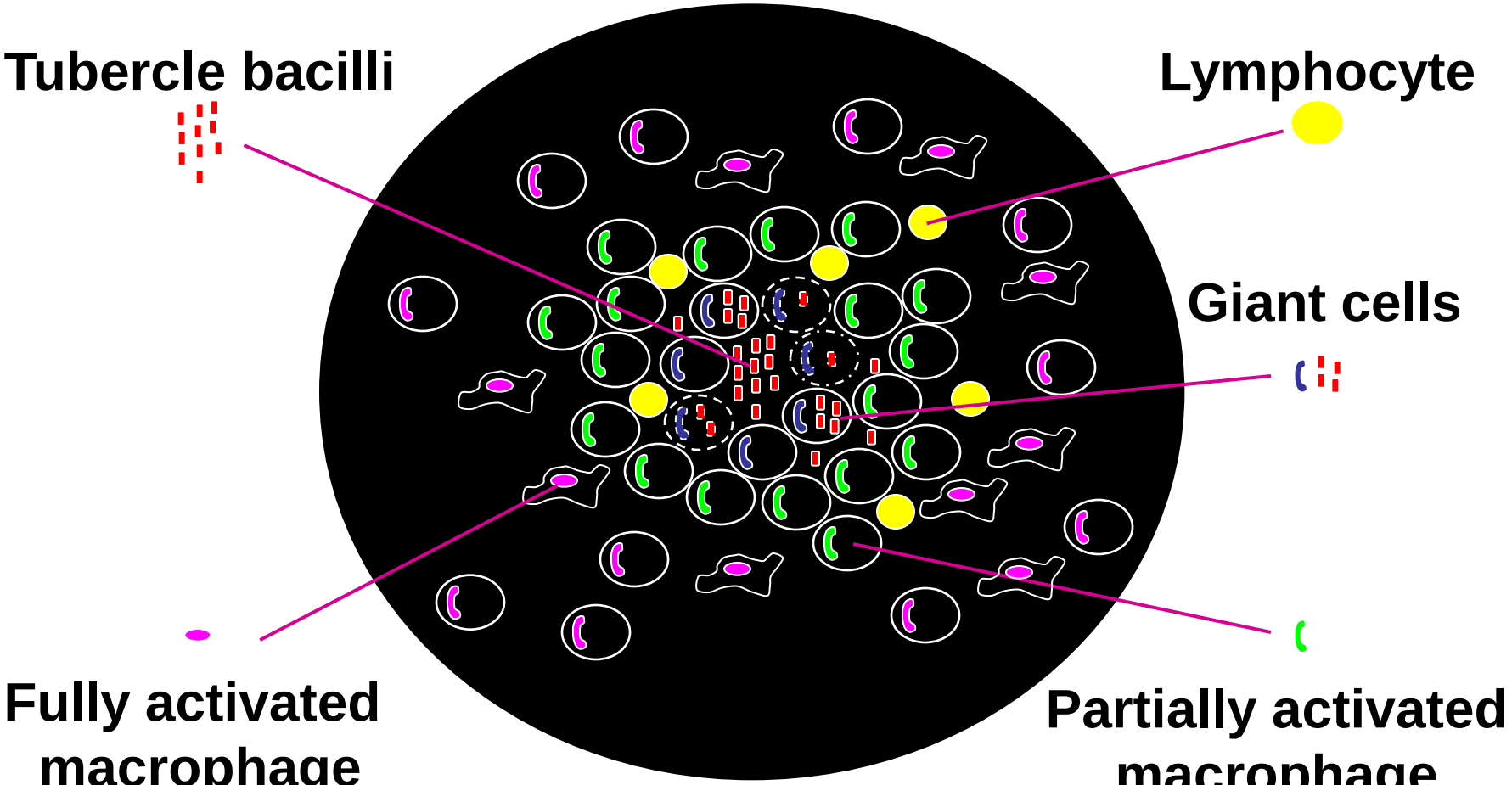
- Within 10 days of entry of Bacilli clones of Antigen specific T Lymphocytes are produced
- Can actively produce Cytokines,

  Interferon γ which activate Macrophages form cluster or Granuloma

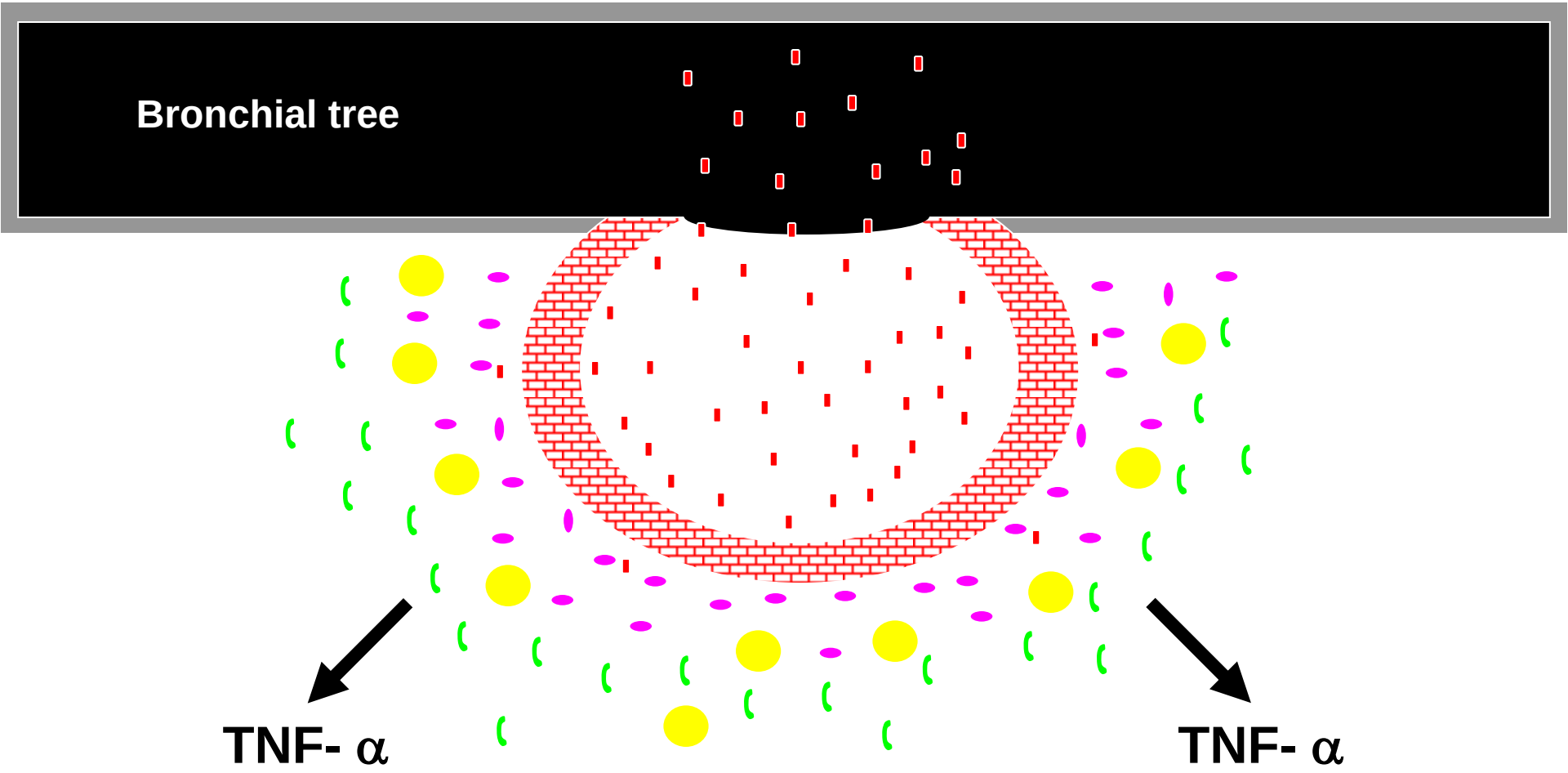


Nature Reviews | Immunology

Tubercle with Caseous Necrosis



Tubercle discharging



Immunity in Tuberculosis.

- CD_4 T Lymphocytes with Th 1 or Th 2 secrete - 1 Cytokines,2 Interleukin 1,and 2 , 3 Interferon's γ ,4.Tumor necrosis factor.
- The mechanisms with Th 1 secrete

  Cytokines Activate Macrophages

  Results in protective Immunity,

  and contain Infection.

  Th 2 manifests with Delayed Hypersensitivity

  DTH causes Tissue destruction. and disease will progress.

Pathogenesis

Activated Macrophages - Epitheliod cells

Forms cluster a granuloma

Activated macrophages turn into Giant cells.

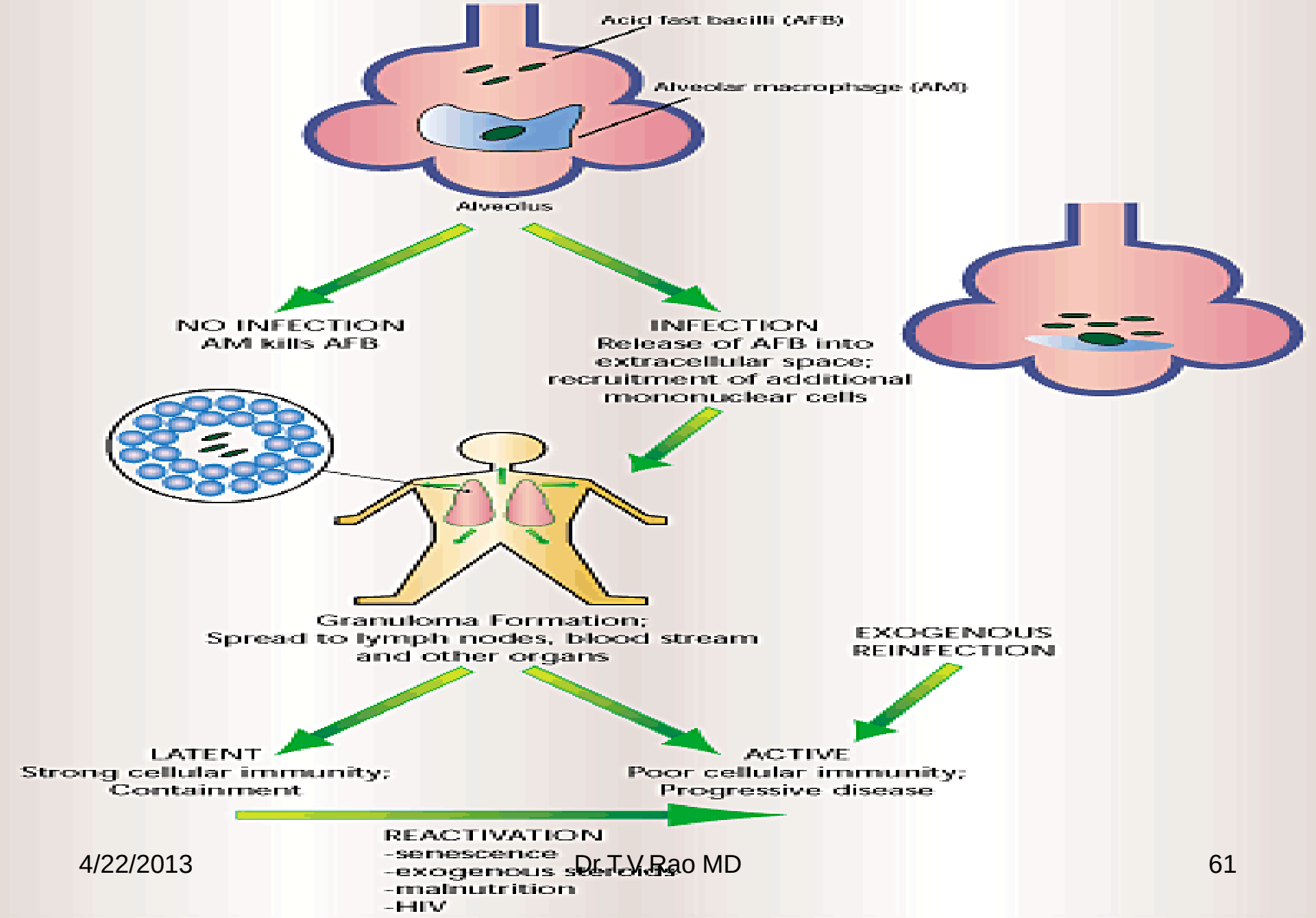
Granuloma contains necrotic tissue Dead macrophages cheese like caesiation.

Apoptosis of bacteria laden cells

Contribute to protective immunity.

Basis of Tubercle formation.

- Tubercle is a A vascular granuloma Contain central zone of giant cells with or without caseation and peripheral zone of Lymphocytes and Fibroblasts.
- Produce lesions may be Exudative or Productive


Acid fast bacilli (AFB)
Alveolar macrophage (AM)
Alveolus
NO INFECTION
AM kills AFB
INFECTION
Release of AFB into extracellular space; recruitment of additional mononuclear cells
Granuloma Formation;
Spread to lymph nodes, blood stream and other organs
EXOGENOUS REINFECTION
LATENT
Strong cellular immunity;
Containment
ACTIVE
Poor cellular immunity;
Progressive disease
REACTIVATION
-senescence
-exogenous steroids
-malnutrition
-HIV

Lesions in Tuberculosis

- Exudative – and Productive

Exudative – Acute inflammatory reaction with edema fluid – contains Polymorphs-

Lymphocytes – later Mononuclear cells.

Bacilli are virulent - Host responds with DTH Injurious.

Productive Type protective Immunity

Primary Tuberculosis

- Initial response
- In Endemic countries Young children
- Events of Primary complex

1 Bacilli are engulfed by Alveolar Macrophages

2 Multiply and give raise to Sub pleural focus of Tuberculosis,Pneumonia,involve lower lobes and lower part of upper lobes.

Called as Ghon's focus.

The Hilar Lymph nodes are also involved

Koch's Phenomenon

- Tuberculosis infected Guinea pig if injected with Living Tubercle bacilli
- The site around the injection becomes necrotic.
- Koch found the same reaction when injected with old Tuberculin (heated and concentration of the tubercle bacilli)
- It has produced the same reaction
- This is called as Koch's Phenomenon.

Primary complex

- Ghon's focus with Enlarged lymph nodes appear after 3- 8 weeks after infection.
- Heals in 2 – 6 months calcified,
- Some bacteria remain alive and produce latent infections.
- Infection activated in Immunosupressed conditions Eg. HIV infections and AIDS
- Can produce Meningitis, Miliary tuberculosis, other disseminated Tuberculosis.

Post Primary Tuberculosis

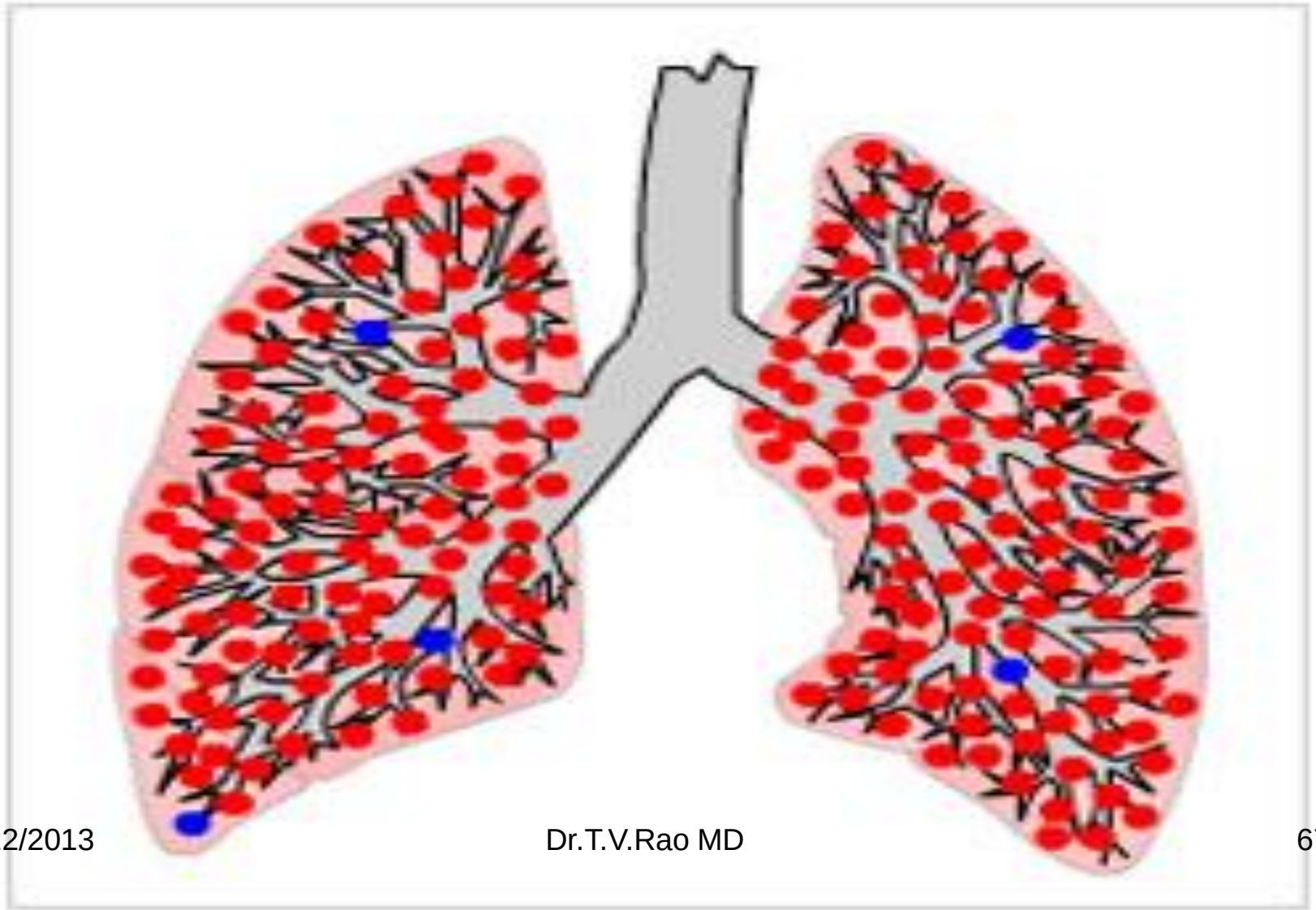
- Mainly occurs due to Reactivation of Latent infection.
- May also due to Exogenous reinfection
- Differs from Primary Infection.
- Leads to –

  Cavitation's of Lungs, Enlargement of Lymph nodes,

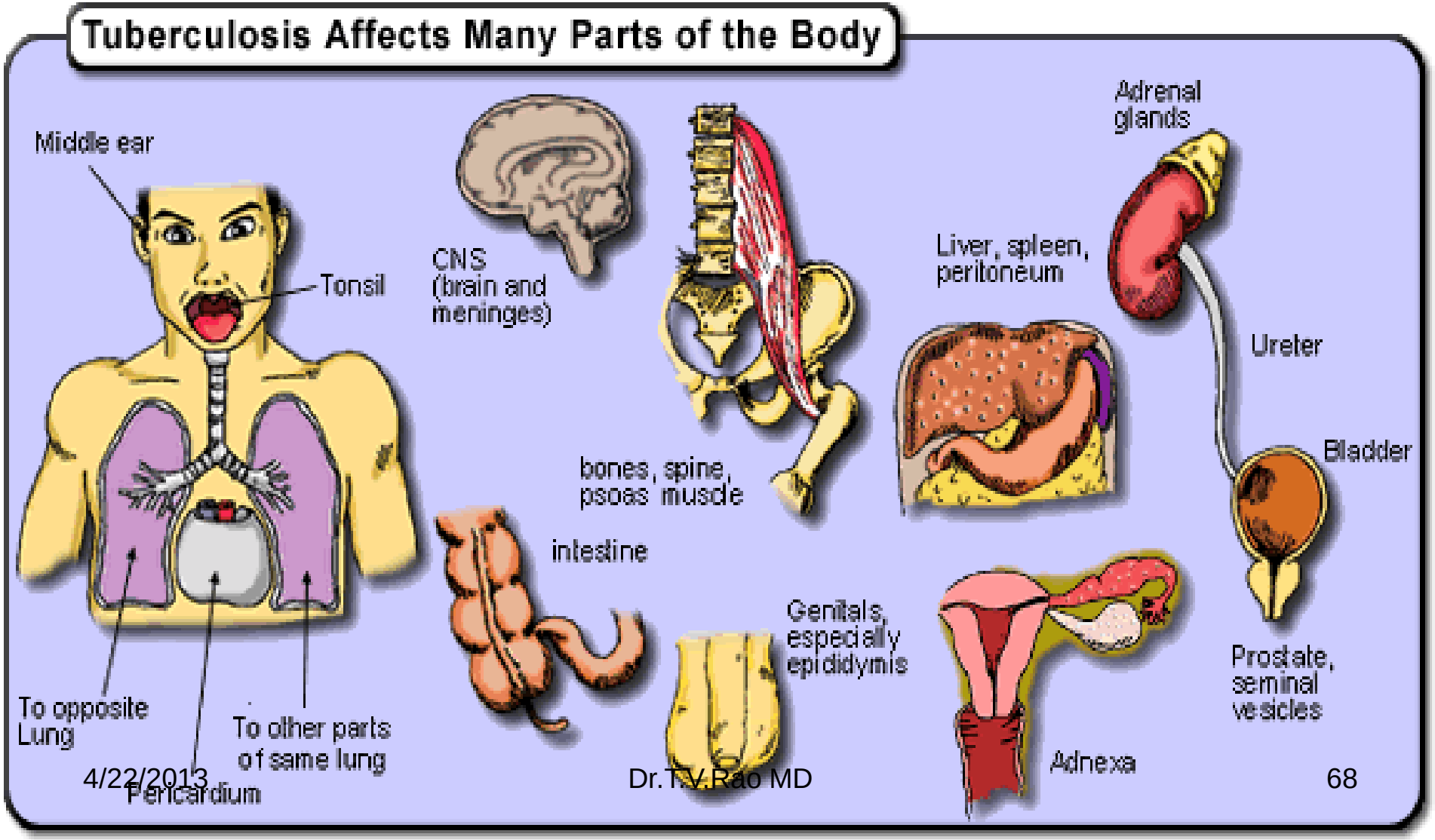
  Expectoration of Bacteria laden sputum

  Dissemination into Lungs and other extra pulmonary areas.

Majority of the Tuberculosis are Pulmonary

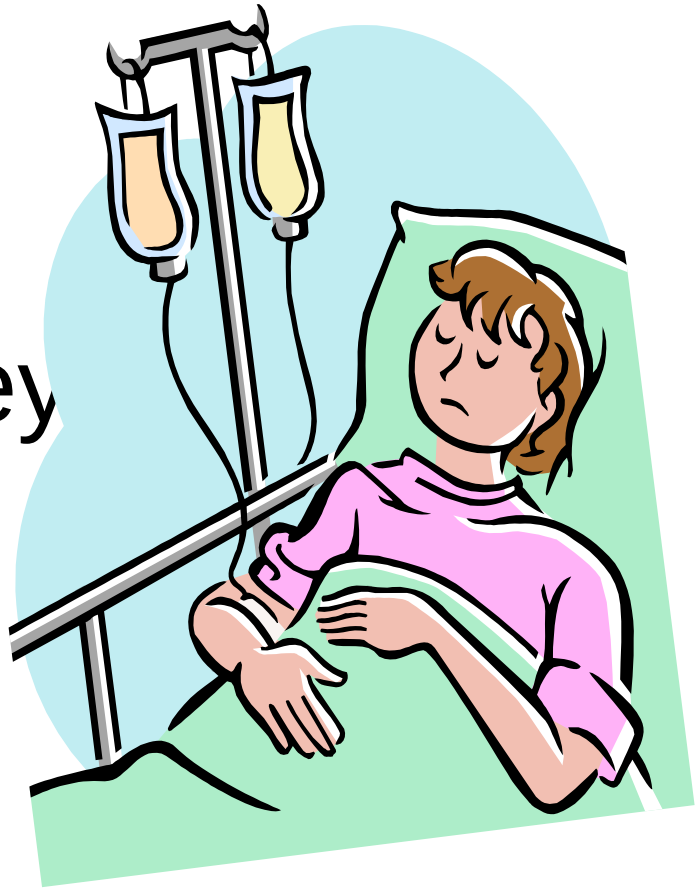


Multiorgan Involvement in Tuberculosis.

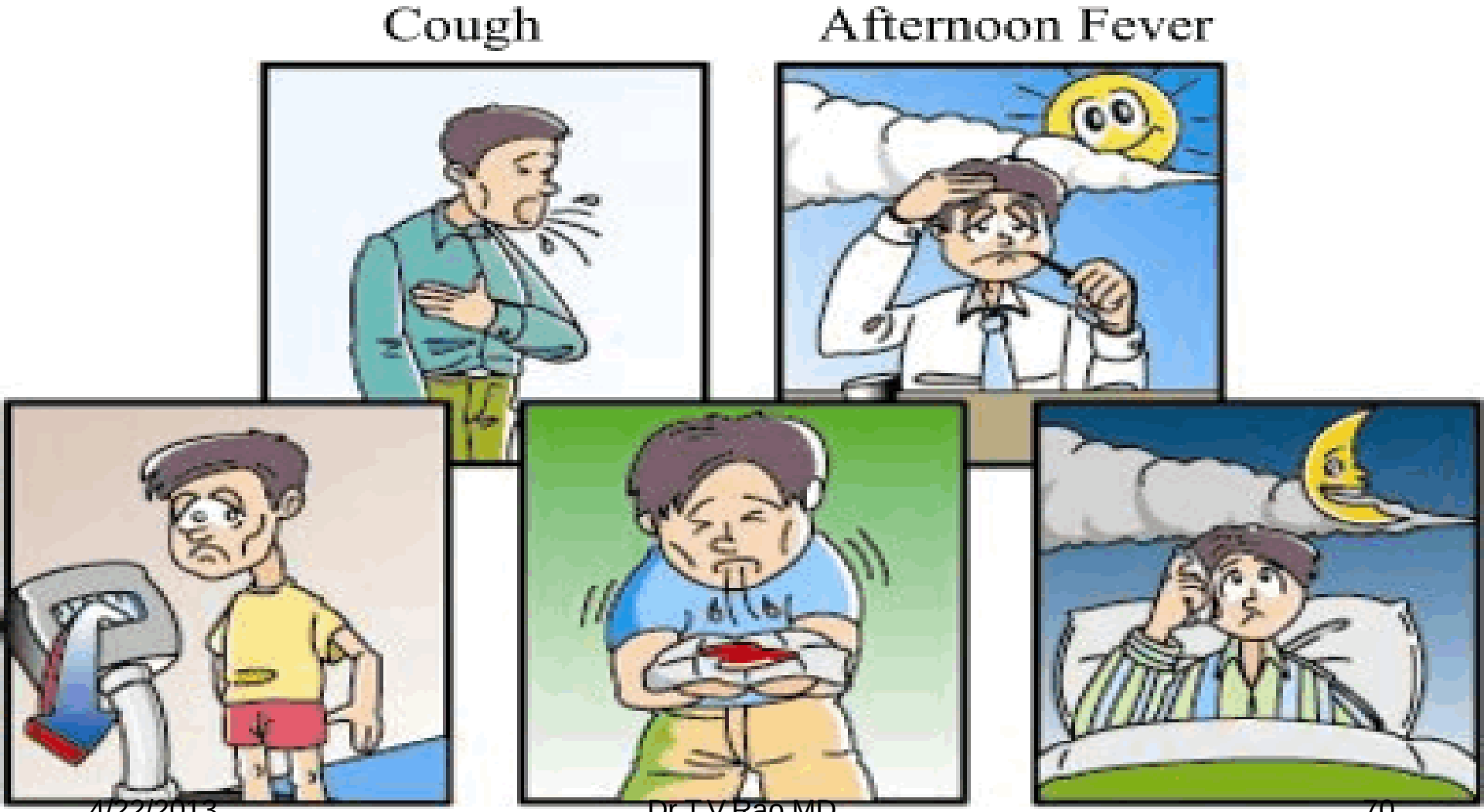


Complication of Tuberculosis.

1. Meningitis.
2. Pleurisy,
3. Involvement of Kidney
4. Spine (Potts spine)
5. Bone Joints,
6. Miliary tuberculosis



Symptoms and Sings of Tuberculosis



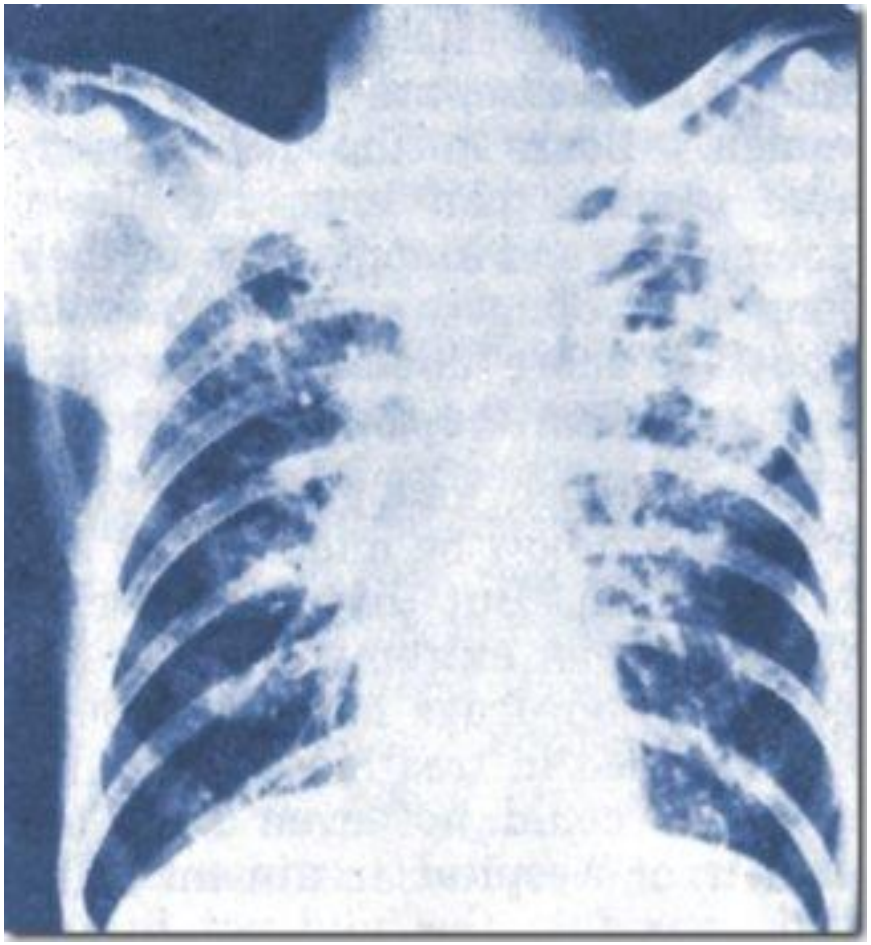
Clinical Illness with Tuberculosis

- Pulmonary Disease – Major manifestation with involvement of Lungs

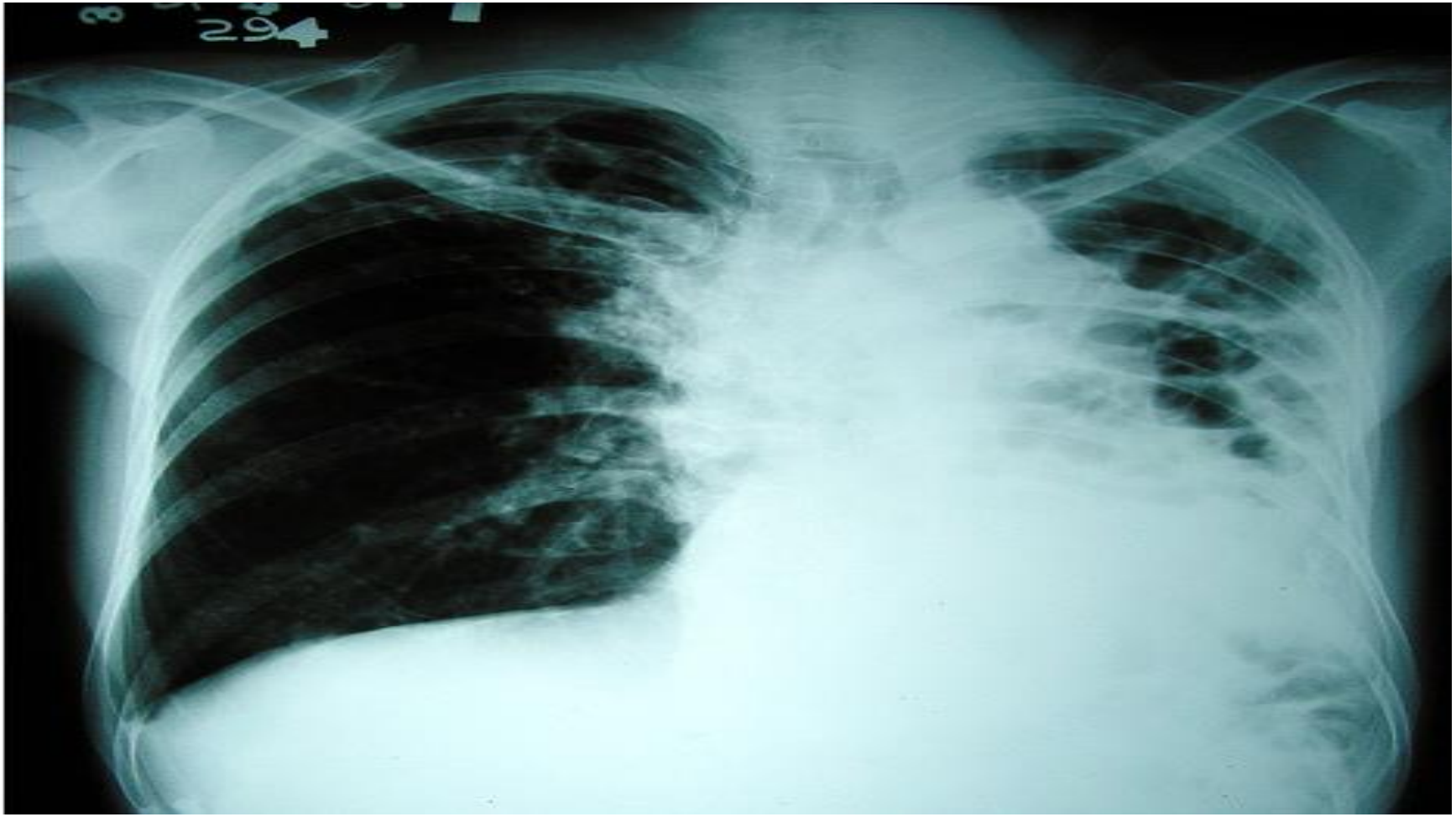
  Haemoptysis, Chest pain Fever sweets

  Anorexia

  Cavity formation in Lungs



Tuberculosis - Pneumothorax



Extra pulmonary Tuberculosis

- Bacteria on circulation leads to bacteremia leads to involvement of

  GUT, Genito urinary system, Meningitis

  Gastro Intestinal system, skin, Lymph nodes Bone marrow.

  Spinal infection Potts spine, Arthritis

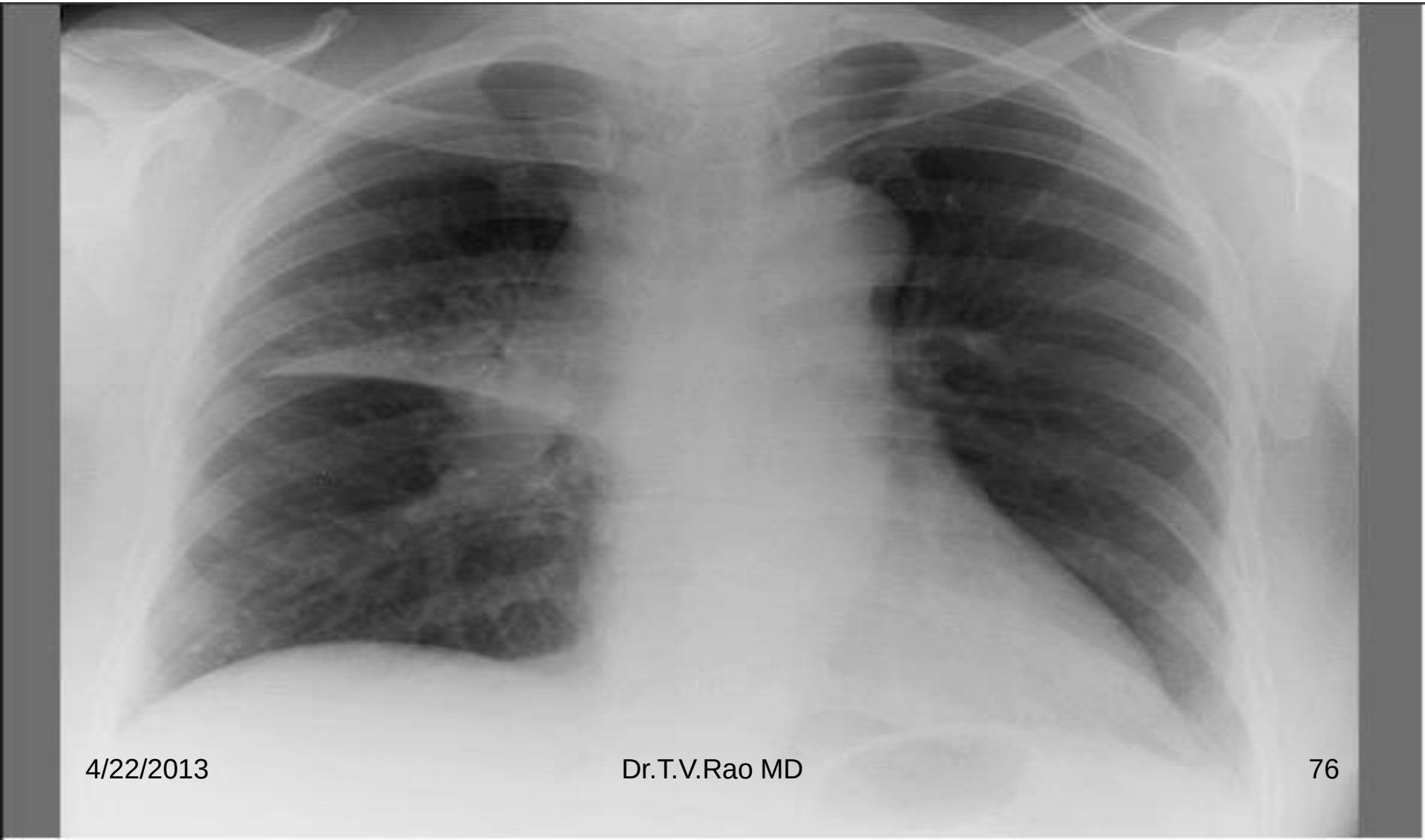
Tuberculosis - Lymphadenitis

Microbiologic Diagnosis of TB

Overview:

- Significance of microbiologic testing in TB care
- Sputum staining and processing
  - Direct smears, unconcentrated
  - Fluorochrome staining and fluorescence microscopy
  - Concentration and chemical processing
  - Specimen collection and transport
- Culture and drug-susceptibility testing
- Rapid diagnostic testing

X - ray examination of chest most easily available Investigation.

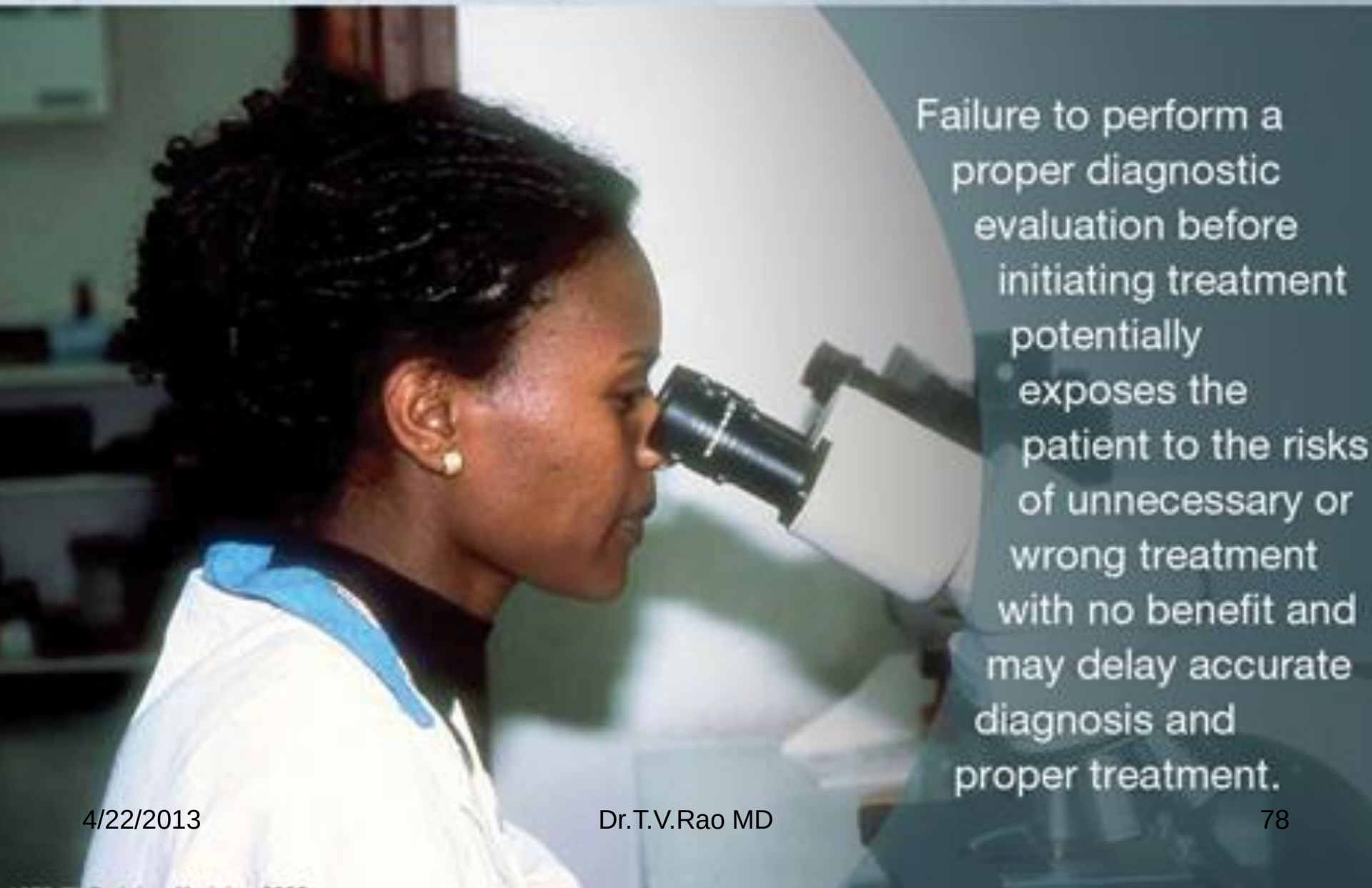


Microscopy and Tuberculosis

Microscopy with Ziehl – Neelsen's staining

A century old procedure

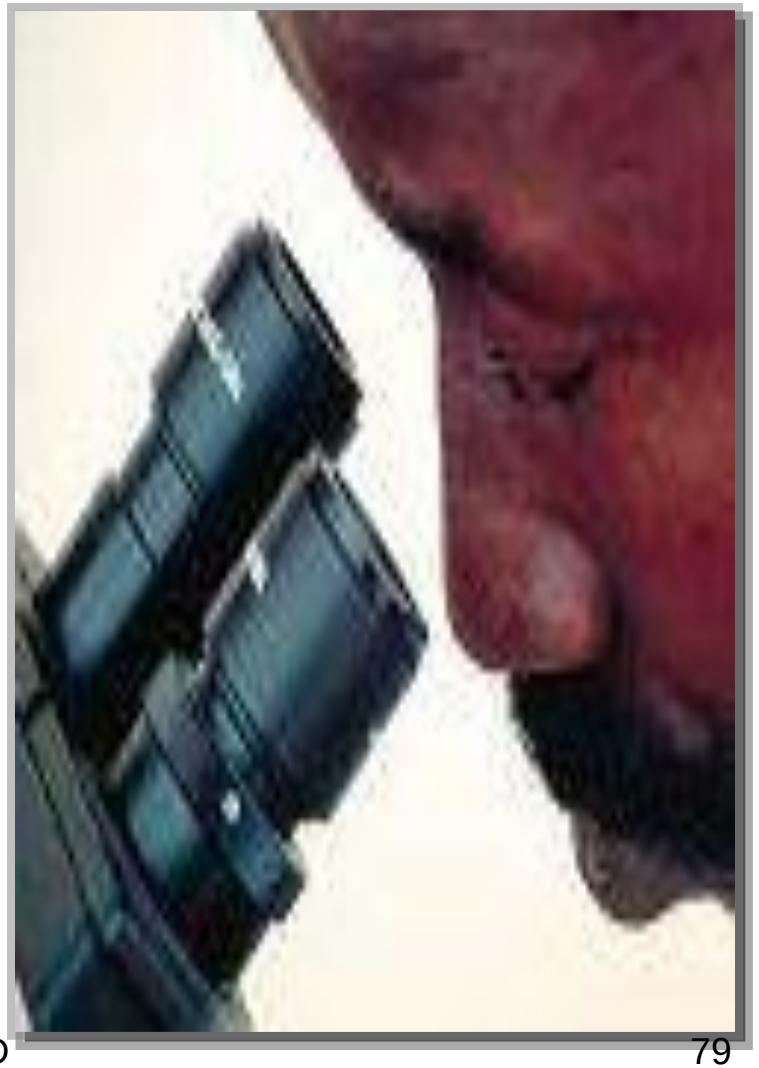
Standards for Diagnosis



Microbiologic Diagnosis of TB

Summary:

- Smear microscopy plays a central role in the diagnosis and management of tuberculosis.
- It is important to understand the aspects of specimen handling and processing that can ensure or enhance accurate results.



Sputum Smear Microscopy

- Sputum smear microscopy is the most important test for the diagnosis of pulmonary TB in many areas of the world
- Direct smears (unconcentrated specimen) are most common
- Fluorescence microscopy and chemical processing can increase sensitivity

Sputum Smear Microscopy

Carbol fuchsin-based stains

- Utilize a regular light microscope
- Must be read at a higher magnification
- Two types: Ziehl-Neelsen and Kinyoun. Both use carbol fuchsin/phenol as the primary dye
- Smear is then decolorized with acid (HCl) alcohol and counter-stained with methylene blue

Fluorescence Microscopy

Advantages:

- More accurate: 10% more sensitive than light microscopy, with specificity comparable to ZN staining
- Faster to examine = less technician time

Disadvantages:

- Higher cost and technical complexity, less feasible in many areas

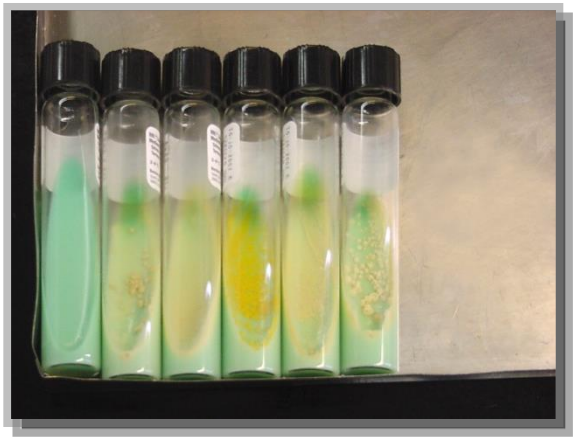
Steingart KR, et al. *Lancet Infect. Dis.* 2006; 6 (9):570-81

Culture and Drug Susceptibility Testing

Although sputum microscopy is the first bacteriologic diagnostic test of choice, both culture and drug susceptibility testing (DST) can offer significant advantages in the diagnosis and management of TB.

Culture: Solid Media

- Solid media have the advantage that organisms (colonies) can be seen on the surface of the medium
- Types most commonly used are:
  - Lowenstein-Jensen: egg-based
  - Middlebrook 7H 10 or 7H11: agar-based
  - Ogawa

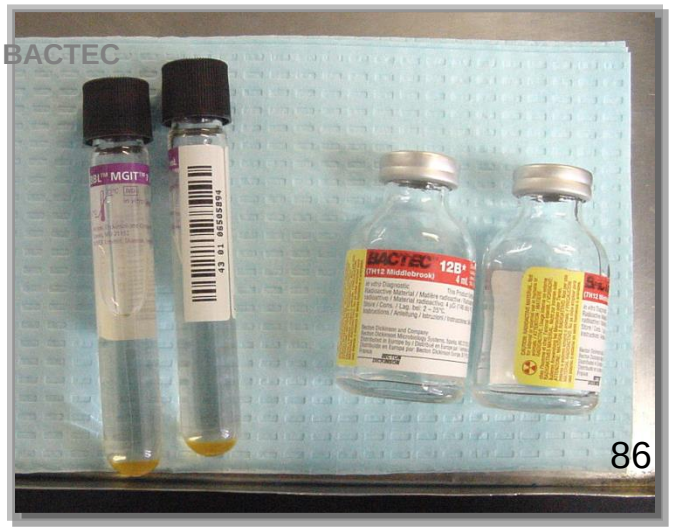


Methods of Culturing.

- **Culturing on Lowenstein Jenson's culture medium remain the affordable economical method in developing world.**

Culture: Liquid Media

- More sophisticated equipment
- Faster detection of growth
- Higher sensitivity than solid media
- Can also be used for drug-susceptibility testing
- Two examples:
  - BACTEC
  - MGIT

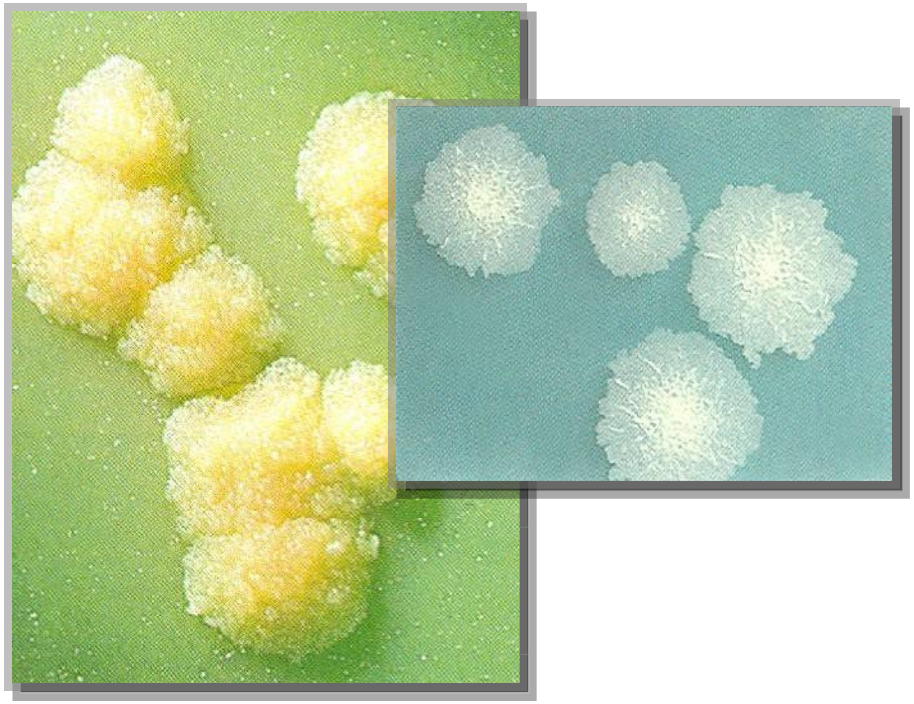


MGIT →

Culture: Identification of Mycobacteria

Visual assessment of colony morphology:

Smooth, buff-colored colonies suggestive of *Mycobacterium avium* complex

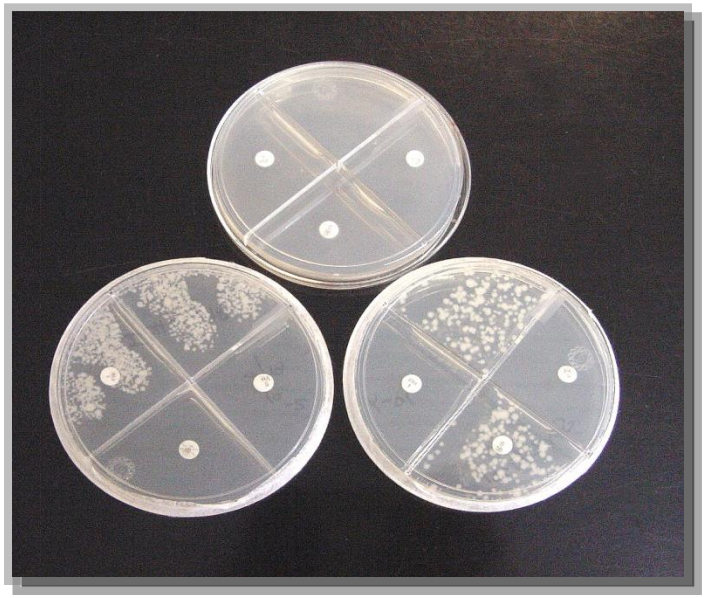


Rough, buff-colored colonies suggestive of *Mycobacterium tuberculosis*

Culture: Drug Susceptibility Testing

Methods for susceptibility testing

- Agar proportion method: Compares growth on solid agar media with and without one of the four primary drugs (on discs)
- Broth based (BACTEC, MGIT): Liquid broth is inoculated with each test drug; growth in vial indicates resistance to that drug



Rapid Diagnostic Testing

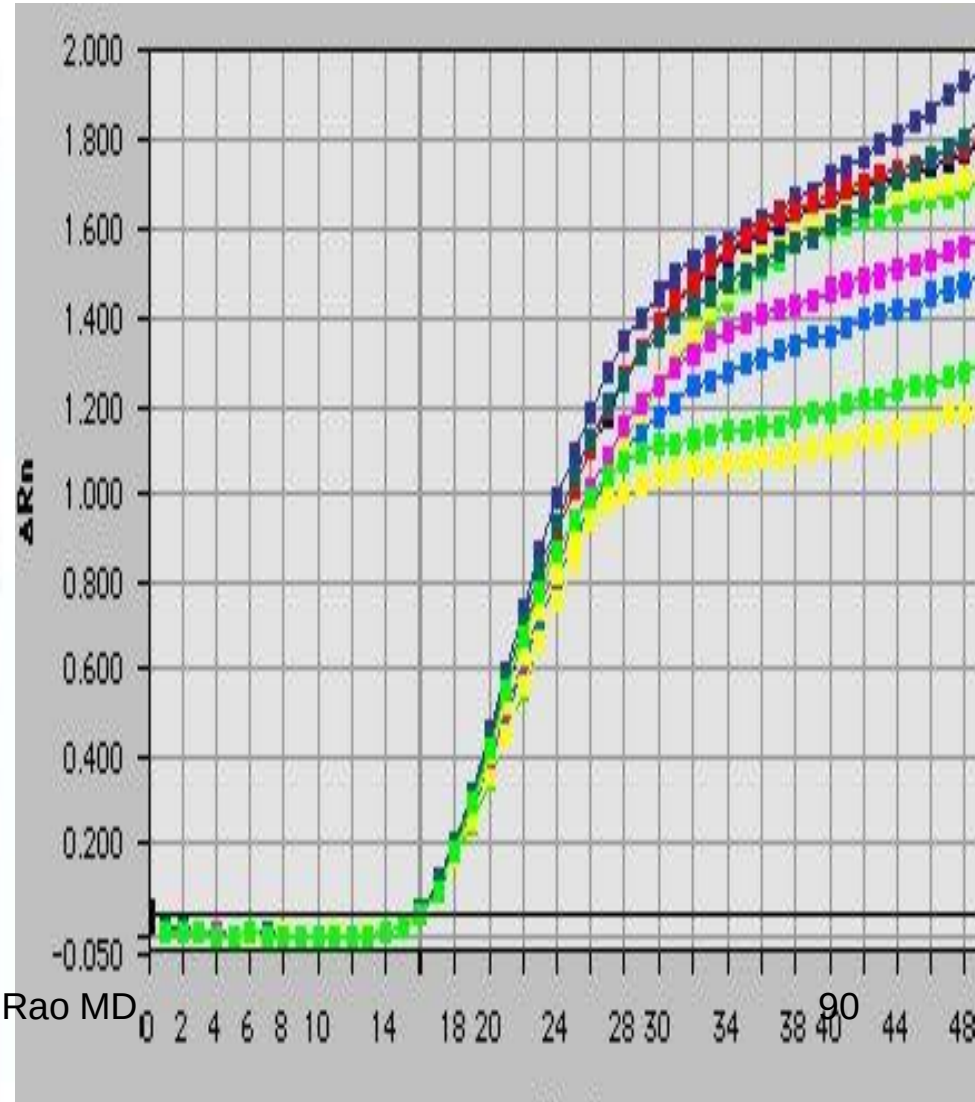
Nucleic acid probe tests (non-amplified) to identify organisms grown in culture:

- DNA probe tests are species or complex specific
  - Commercial probes are available for *M.tb* complex, MAC, *M. kansasii* and *M. gordonae*

Nucleic acid amplification tests (NAAT):

- These tests are designed to amplify and detect DNA specific to *M.tb*
- Enables direct detection of *M.tb* in clinical specimens

Real Time PCR replacing older Methods

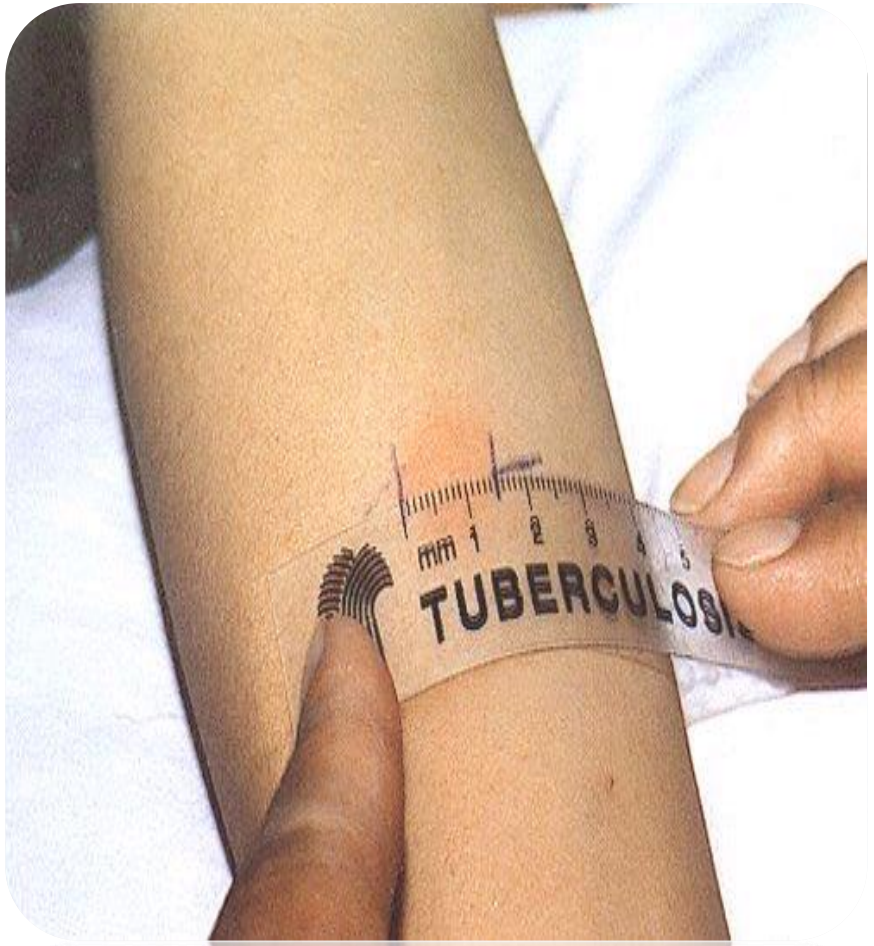


Other Rapid Diagnostic Tests

- Loop-mediated isothermal amplification (LAMP)
  - Rapid, simplified NAAT still under investigation
  - May be more feasible in lower resource settings
- Immunological tests
  - Serologic tests for antibody, antigens, and immune complexes; not currently accurate enough to replace microscopy and culture.

Tuberculin Test (Mantoux Test)

- **Test to be interpreted in relation to clinical evaluation.**
- **Even the induration of 5 mm to be considered positive when tested on HIV patients.**
- **Lacks specificity.**



GeneXpert MTB/RIF

- The Xpert MTB/RIF is a cartridge-based, automated diagnostic test that can identify Mycobacterium tuberculosis (MTB) and resistance to rifampicin (RIF). It was co-developed by Cepheid, Inc. and Foundation for Innovative New Diagnostics, with additional financial support from the US National Institutes of Health (NIH) and technical support from the University of Medicine and Dentistry of New Jersey

How the test works

- The Xpert MTB/RIF detects DNA sequences specific for Mycobacterium tuberculosis and rifampicin resistance by polymerase chain reaction It is based on the Cepheid GeneXpert system, a platform for rapid and simple-to-use nucleic acid amplification tests (NAAT).

Microscopy in Tuberculosis TODAY

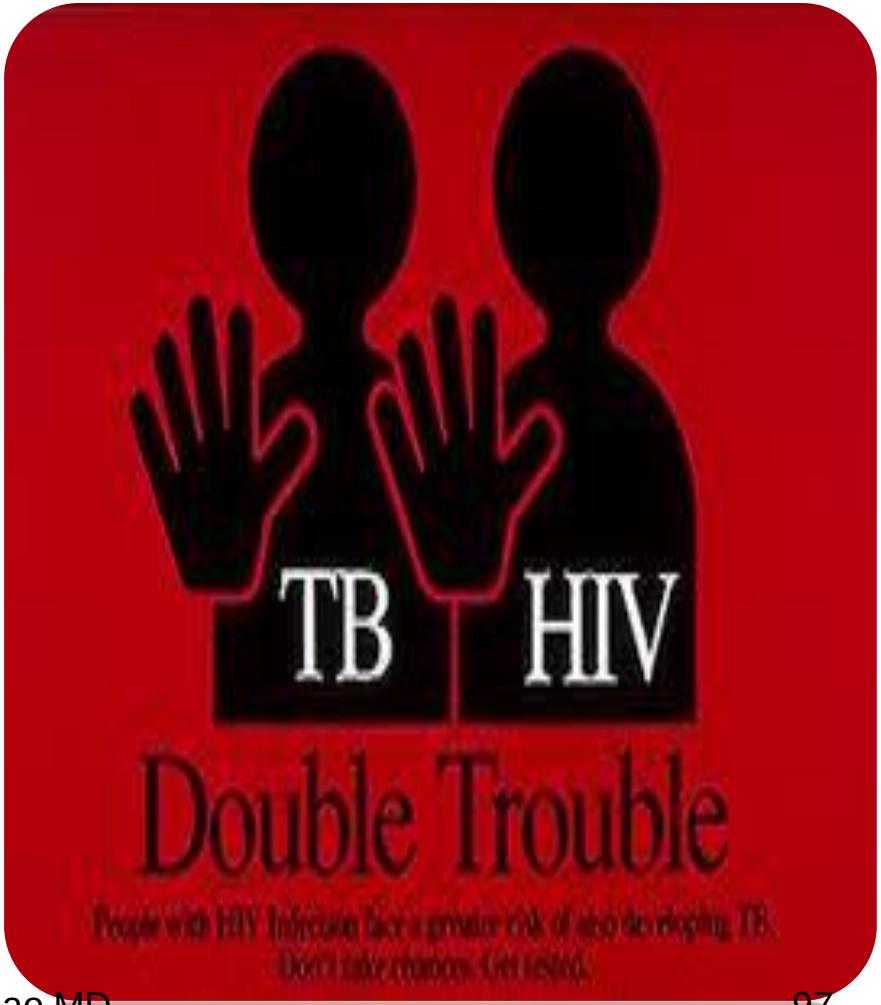
In spite of several scientific, and molecular advances Microscopy in Tuberculosis continues to be back bone in Diagnosis.

Epidemiology

- An ancient disease, called as white plague
- 1/3 of the world population is infected
- 2 billion infected
- Each year 9 lakhs to 1 million are infected
- Poor nations phase the burnt of the disease.
- In developing world > 4o% of the population is effected
- 15 million suffer the disease
- 3 million are highly infective.

Tuberculosis and HIV infection

- HIV association has become a threat to the developed countries too
- HIV association will lead to rapid spread of tuberculosis

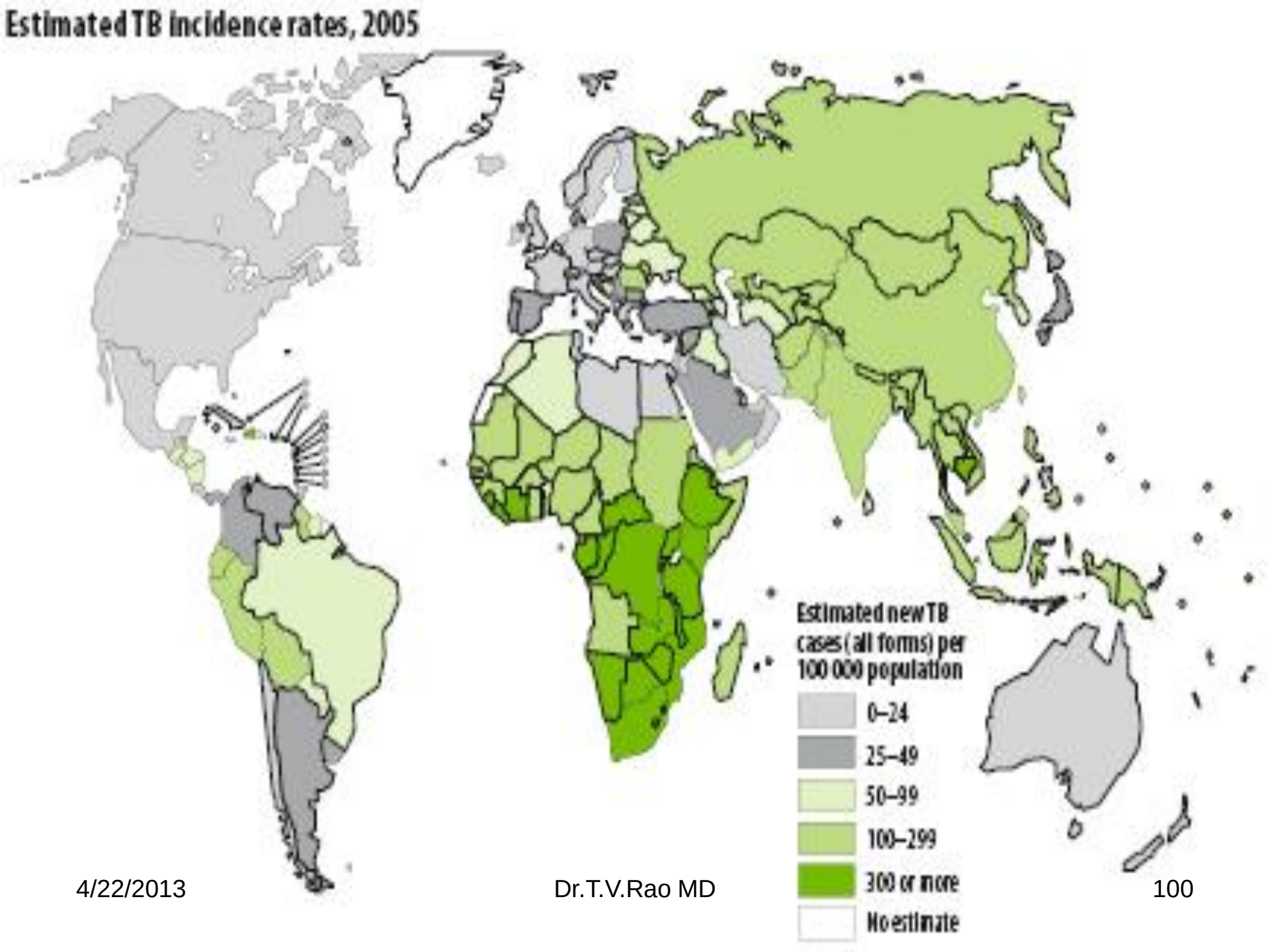


HIV Considerations

- HIV is the strongest risk factor for progression to active disease
- HIV kills $CD4^+$ T Helper cells which normally inhibit *M. tuberculosis*
- HIV interferes with PPD skin test
- Protease inhibitors interfere with rifampin

MDR tuberculosis

- Multidrug resistant tuberculosis has become a global threat.
- In 1993 WHO declared Tuberculosis a Global emergency
- Animals shed the bacilli in Milk, human's get infected after drinking the unsterilised Milk
- Pasteurization has reduced the incidence of Bovine tuberculosis.


Estimated TB incidence rates, 2005
Estimated new TB cases (all forms) per 100 000 population
0–24
25–49
50–99
100–299
300 or more
No estimate

Some one infected every Second

- Someone in the world is newly infected with TB bacilli every second.
- Overall, one-third of the world's population is currently infected with the TB bacillus.
- 5-10% of people who are infected with TB bacilli (but who are not infected with HIV) become sick or infectious at some time during their life. People with HIV and TB infection are much more likely to develop TB.

TB as a Worldwide Public Health Issue

- World population ~ 6 billion
- ~ 1in 3 people in world infected
- ~ 9.4 million new cases of active TB/year
- 1.7 million deaths/year
- US population 280 million
- ~ 3-5% infected
- ~ 11,000 cases/year
- ~ 5-7% mortality

Treatment for TB Disease

- TB disease is treated with medicine to kill the TB germs
- Usually, the treatment will last for 6-9 months
- TB disease can be cured if the medicine is taken as prescribed, even after you no longer feel sick

Treatment of pulmonary TB

- NB of compliance (helps cure pt & prevents spread of resistance)
- Before tx baseline FBC, LFTs (incl alt), RP
- Isoniazid, rifampicin & pyrazinamide all hepatotoxic
- Test colour vision (Ishihara chart) & acuity (Snellen chart) before & after tx (ethambutol may cause (reversible) ocular toxicity
- TB treated in 2 phases – initial phase using at least 3-4 drugs & continuation phase using 2 drugs in fully sensitive cases

First-Line Anti-TB Drugs (1)

Essential Drug (abbreviation)	Recommended Daily Dose in mg/kg body weight (range)
Isoniazid (H)	*Adults*: 5 mg (4-6) kg/d, 300mg/d maximum *Children*: 10-15 mg/kg/d, 300 mg/d maximum
Rifampicin (R)	*Adults*: 10 mg (8-12), 600mg/d maximum *Children*: 10-20 mg/kg/d, 600 mg/d maximum

First-Line Anti-TB Drugs (2)

Essential Drug (abbreviation)	Recommended Daily Dose in mg/kg body weight (range)
Pyrazinamide (Z)	25 mg (20-30), 2000 mg/d maximum
Ethambutol (E)	*Adults*: 15 mg (15-25), 1600 mg/d maximum *Children*: 20 mg/kg (range 15-25 mg/kg) daily
Streptomycin (S)	15 mg (12-18) Maximum for <40 years = 1g Maximum for ≥ 40 years = 0.75g

Modern TB Chemotherapy

- INH – kills rapidly growing organisms (early bactericidal activity)
- INH and RMP protect each other from development of resistance
- Rifampicin and pyrazinamide kill slowly growing organisms
  - Sterilizing activity

Source: Combs D et al., Ann Intern Med., 1990.

Beginning in New era in Treatment

DOTS

- The technical strategy for DOTS was developed by Dr. Karel Styblo in the 1980s, primarily in Tanzania. In 1989, the World Health Organization and the World Bank began investigating the potential expansion of this strategy. In July 1990, the World Bank, under Richard Bumgarner's direction, invited Dr. Styblo and WHO to design a TB control project for China. By the end of 1991, this pilot project was achieving phenomenal results, more than doubling cure rates among TB patients. China soon extended this project to cover half the country.

DOTS

- DOTS (directly observed treatment, short-course), is the name given to the World Health Organization-recommended tuberculosis control strategy that combines five components:
- Government commitment (including both political will at all levels, and establishing a centralized and prioritized system of TB monitoring, recording and training)

DOTS helps in ……

- Case detection by sputum smear microscopy

Standardized treatment regimen directly observed by a healthcare worker or community health worker for at least the first two months

- A regular drug supply
- A standardized recording and reporting system that allows assessment of treatment results

RNTCP and DOTS India

- The DOTS strategy along with the other components of the Stop TB strategy, implemented under the Revised National Tuberculosis Control Programme (RNTCP) in India, is a comprehensive package for TB control.

India's success with DOTS

- The Revised National Tuberculosis Control Programme (RNTCP), based on the DOTS strategy, began as a pilot in 1993 and was launched as a national programme in 1997. Rapid RNTCP expansion began in late 1998. By the end of 2000, 30%of the country's population was covered, and by the end of 2002, 50%of the country's population was covered under the RNTCP. By the end of 2003, 778 million population was covered, and at the end of year 2004 the coverage reached to 997 million. By December 2005, around 97% (about 1080 million) of the population had been covered, and the entire country was covered under DOTS by 24th March 2006.

Stop –TB
Use DOTS

MDR TB

- MDRTB refers to strains of the bacterium which are proven in a laboratory to be resistant to the two most active anti-TB drugs, isoniazid and rifampicin. Treatment of MDRTB is extremely expensive, toxic, arduous, and often unsuccessful.

DOTS prevents MDR- TB

- DOTS has been proven to prevent the emergence of MDRTB, and also to reverse the incidence of MDRTB where it has emerged. MDRTB is a tragedy for individual patients and a symptom of poor TB management. The best way to confront this challenge is to improve TB treatment and implement **DOTS.**

BCG vaccine

- BCG is live attenuated strain derived from M. bovis → stimulates development of hypersensitivity to M. tuberculosis
- Within 2-4wks swelling at injection site, progresses to papule about 10mm diam & heals in 6-12 wks
- BCG recommended if immunisation not previously carried out & neg for tuberculoprotein hypersensitivity
  - Infants in area of TB incidence > 40/100,000
  - Infants with parent/grandparent born in country with incidence of TB >40/100,000
  - Contacts of pts with active pulmonary TB
  - Health care staff
  - Veterinary staff
  - Prison staff
  - If intending to stay for >1 mth in country with high incidence TB

Do not Forget

- **Programme Created by Dr.T.V.Rao MD for Medical and paramedical Students in the Developing World**
- Email
- doctortvrao@gmail.com