

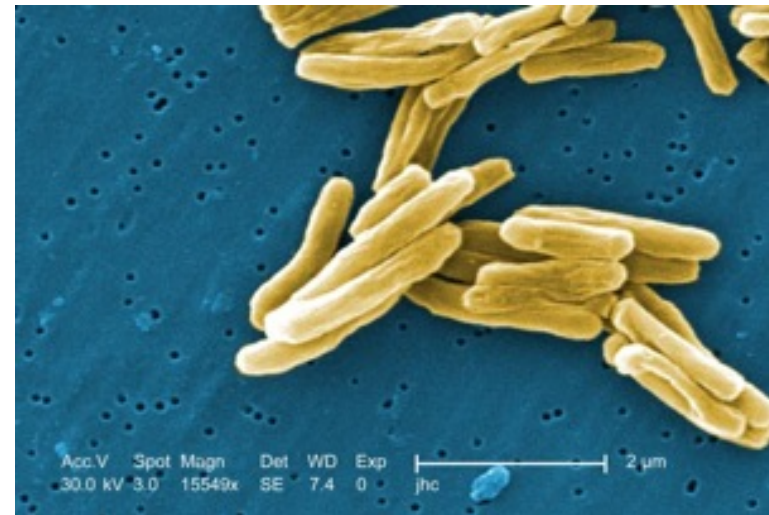
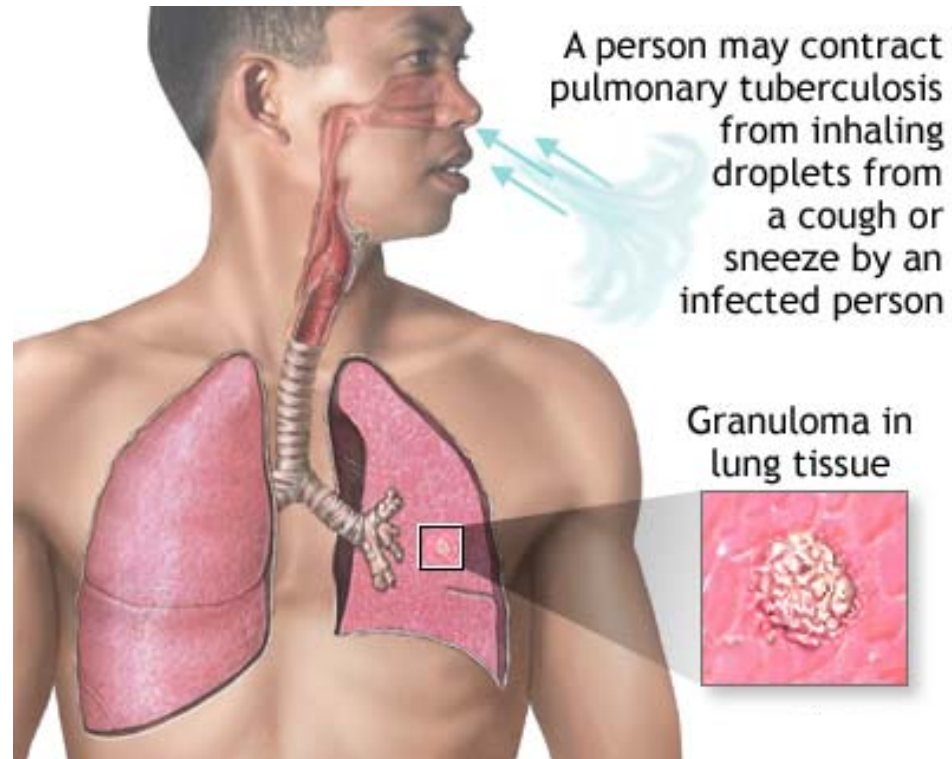
# TUBERCULOSIS in CHILDREN

# WHAT IS TUBERCULOSIS?



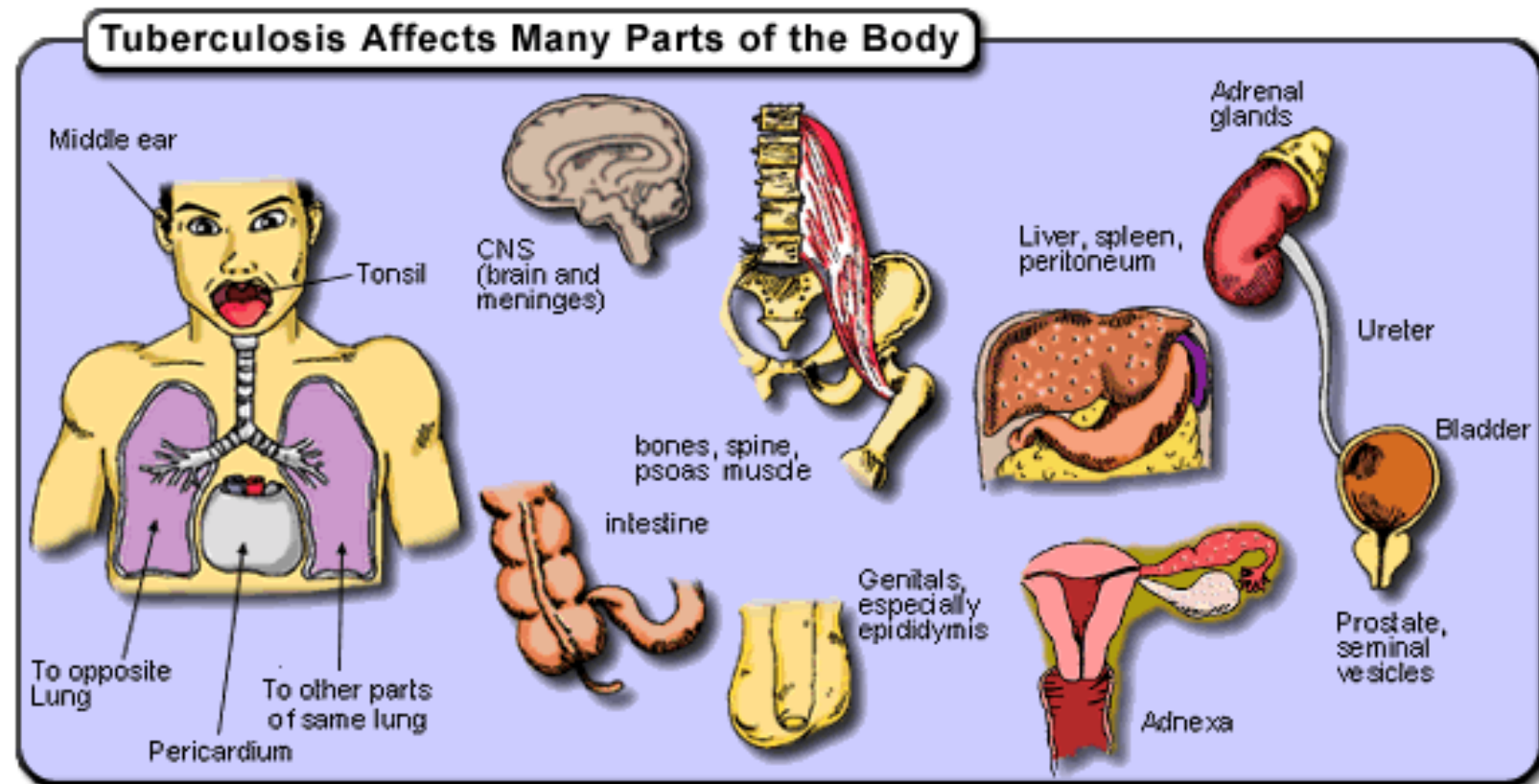
- Tuberculosis, or TB, is an infectious bacterial disease caused by **Mycobacterium tuberculosis**, which most commonly affects the lungs.
- It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease.

# Tuberculosis

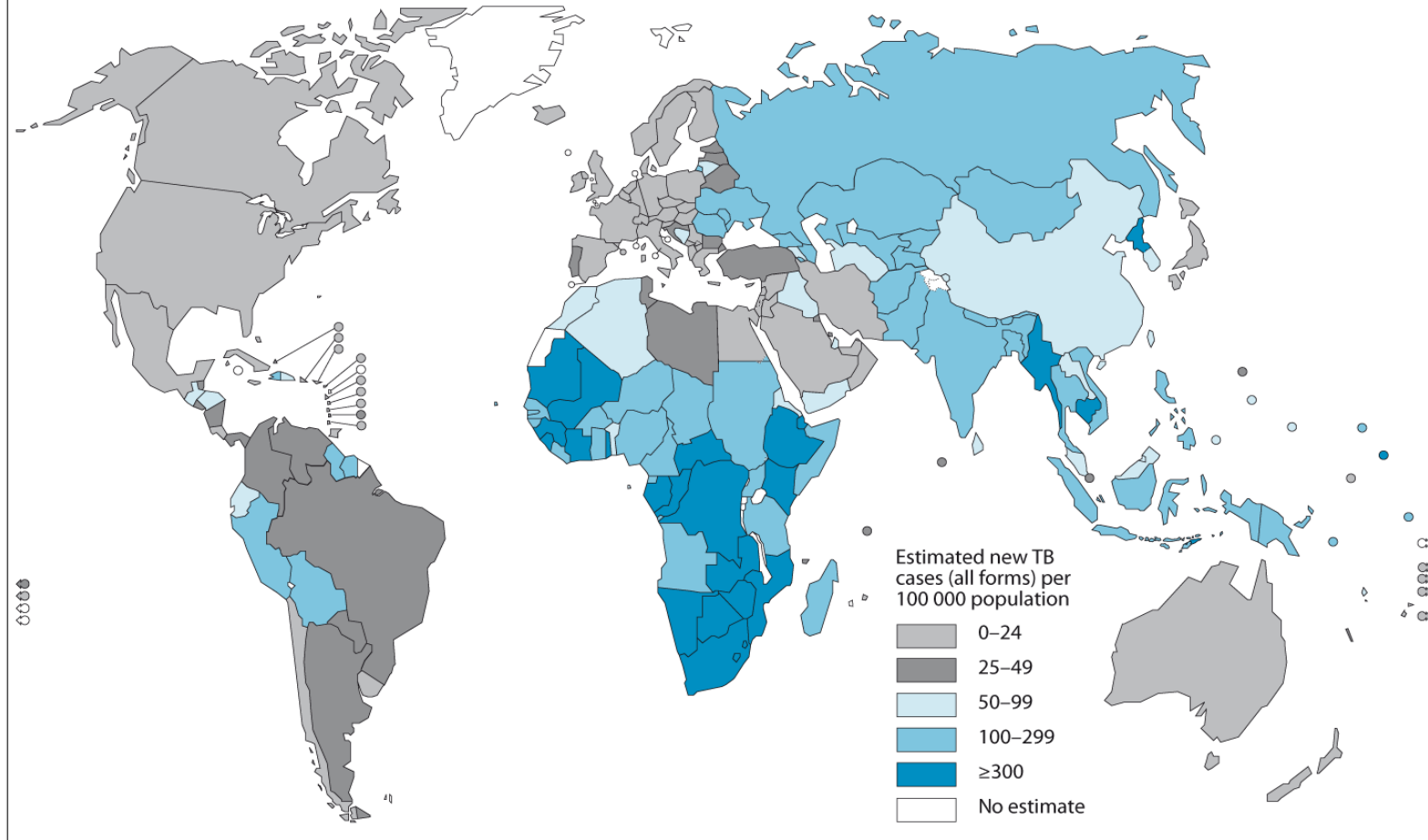


If not treated, each person with active TB can infect on average 10 to 15 people a year.

# Tuberculosis: other manifestations



## Estimated TB incidence rates, by country, 2009



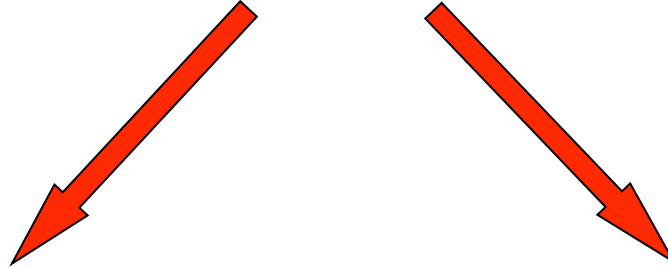
Over 250,000 children develop TB and 100,000 children will continue to die each year from TB.

# TB in children



- A child usually gets TB infection from being exposed to a sputum-positive adult
  
- Children at higher risk to develop disease symptoms and signs:
  - Below ten years of age
  - HIV infected (higher risk of meningeal and other severe forms)
  - Other infectious or non infectious comorbidities
  - Malnourished

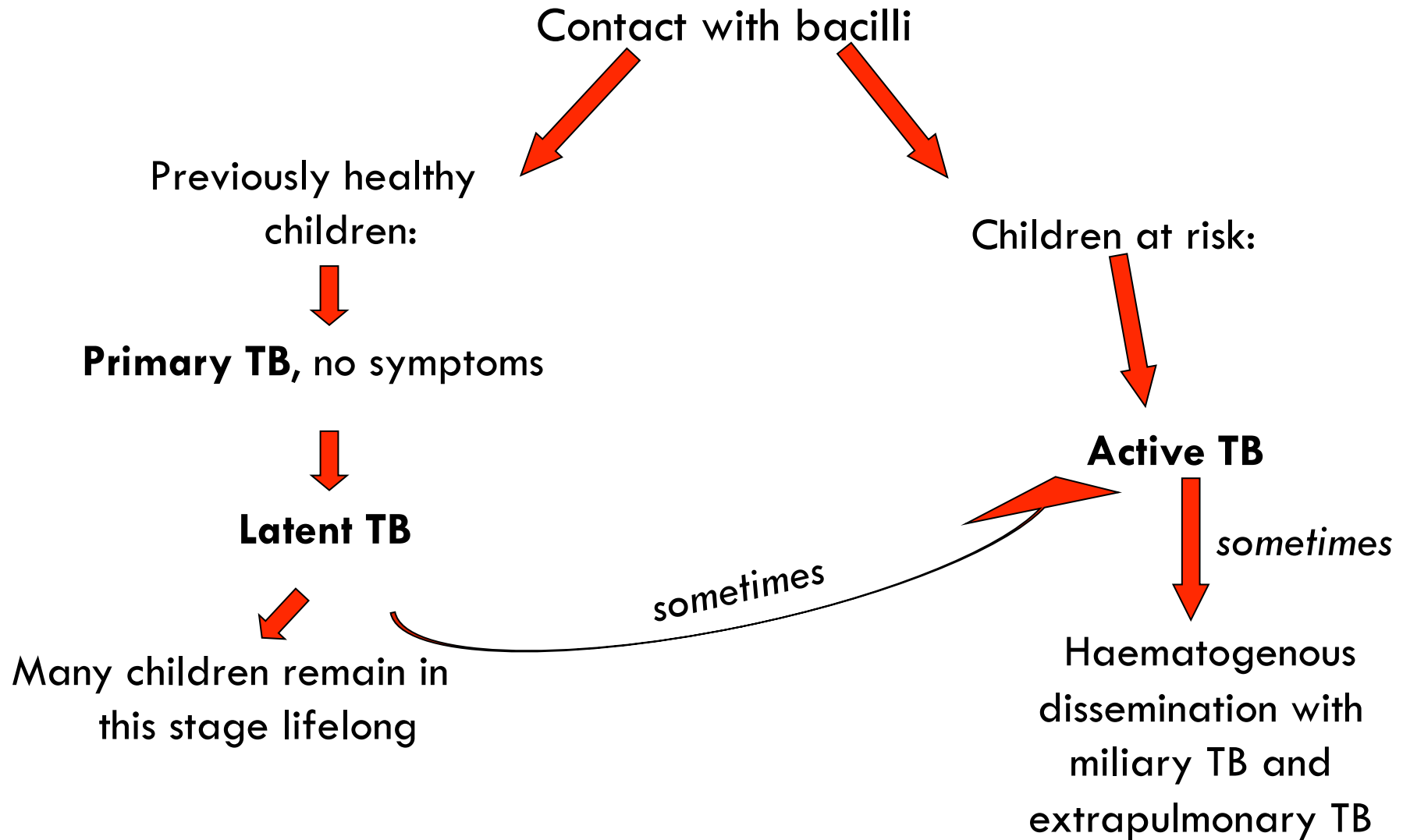
# TB history: latent versus active disease



Healthy people infected with *M.tuberculosis* usually do not develop active disease. However they host bacteria in non-active form (**latent disease**) and in 5-10% of cases will develop **active disease** in the future

People at risk (already ill, HIV +, malnourished...) may develop **active disease**, sometimes in military pattern

# TB history





# TB in children: principal features

- Fever
  - ▣ Frequently less than 101-102 F°
  - ▣ Frequently higher at evening
  - ▣ Frequently associated with night sweating
  
- Weight loss or failure to gain weight
  
- And...
  - ▣ Cough (with or without sputum) since more than 2 weeks
  - ▣ Painless, soft, enlarging lymph nodes
  - ▣ Abdominal pain
  - ▣ Meningeal signs (nuchal stiffness, altered mental status or, in younger children: bulging fontanelle, paradoxical irritability, high-pitched cry, hypotonia)

# Suspect TB in a child... (1)



- **Who is ill, with a history of contact with a suspect or confirmed case of pulmonary TB;**
- Who does not return to normal health after measles or whooping cough;
- With loss of weight, cough, fever who does not respond to antibiotic therapy for acute respiratory disease;

# Suspect TB in a child... (2)



- With abdominal swelling, hard painless mass and free fluid;
- With painless firm or soft swelling in a group of superficial lymph nodes;
- With signs suggesting meningitis or disease in the central nervous system.

# How to confirm TB diagnosis?



- Carefull anamnesis
  - ▣ Contact with TB cases
  - ▣ Fever and its characteristics
  - ▣ Weight loss or failure to gain weight
  - ▣ Features of current disease...
- General and segmental physical examination
- Other studies:
  - ▣ Blood tests
  - ▣ Tuberculin skin test (TST)
  - ▣ Chest X-rays
  - ▣ Sputum or other specimen analysis

# Blood tests



- Blood count, not so useful for diagnosis, but it may show anemia
- Bio-chemistries, including at least AST, ALT, alkaline phosphatase, uric acid, serum creatinine
- ESR (Erythrocyte Sedimentation Rate)
- HIV serology

# Tuberculin skin test (TST)

- 5 tuberculin units of purified protein derivative (PPD) should be injected intradermally into the volar aspect of the forearm using a fine needle
- Result should be evaluated 48-72 hours later
- Exam is positive if a papule appears
- Measure the amount of induration and not erythema



# Tuberculin skin test (TST)

- Consider the test as positive if induration is:
  - ▣ > 15 mm
  - ▣ > 10 mm in children at higher risk to develop severe TB (malnourished, history of BCG vaccination...)
  - ▣ > 5 mm in children with
    - a close contact with known or suspected contagious cases of TB
    - HIV infection
    - Chest X-rays consistent with active tuberculosis

# Tuberculin skin test (TST)



- Pay attention!
  - A positive TST indicates that patient has had a contact with TB bacilli and then his immune system is able to react to TB antigens. This contact could be occurred in any moment of patient's life
  - A positive TST, then, does not indicate that patient has necessarily active TB
  - Previous BCG vaccination cause TST positivity

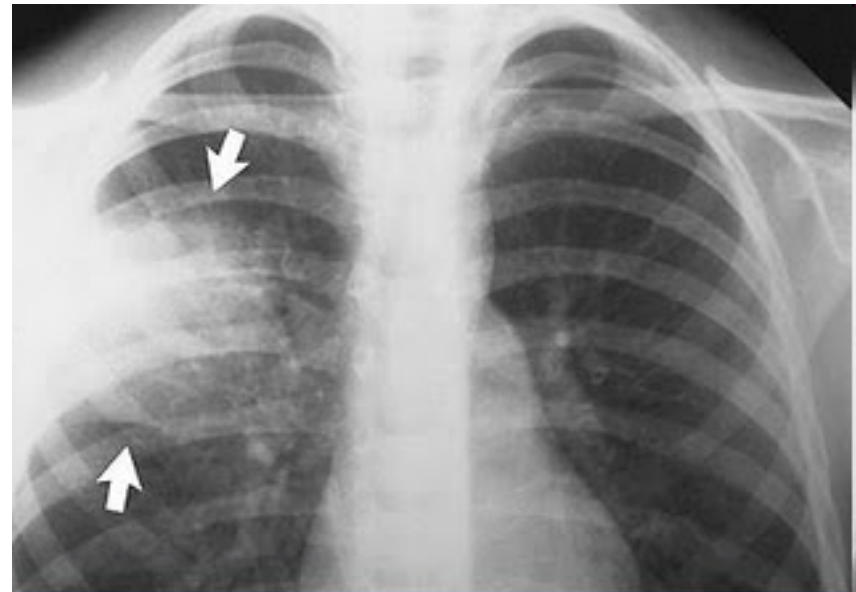


# Tuberculin skin test (TST)

- Positive TST and other clinical/  
lab features of active TB → Active tuberculosis
- Positive TST without other  
clinical/lab features of active  
TB → Latent/past  
Tuberculosis
- Negative TST → No tuberculosis

# Chest x-rays

- Parenchymal opacity
- Cavitary lesion
- Pleural effusion
- Nodal enlargement
- Calcifications (older lesions)



- Upper-lobe involvement is typical. In addition other pulmonary segments - namely, the apical or posterior segments of the upper lobe or the superior segment of a lower lobe – are frequently involved

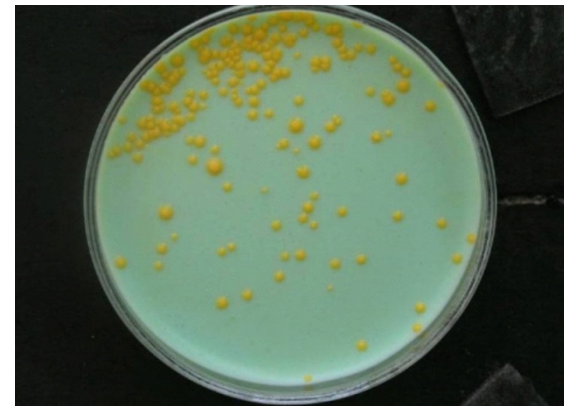
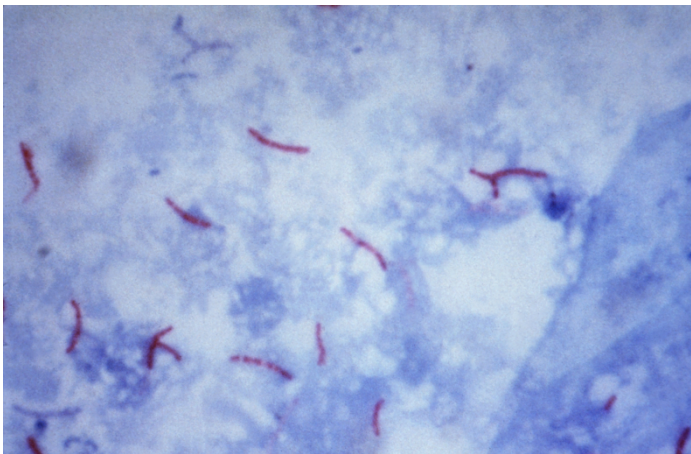
# Specimen collection for analysis



- Pulmonary TB
  - Children > 6 aa: sputum
  - Children < 6 aa: gastric aspiration (early morning)
  
- Other form of TB
  - Liquor
  - Urine
  - Surgical specimen (whole node in lymphnodal disease)
  
- All types of specimens must be collected in a sterile holder!

# Specimen collection for analysis

- Direct bacterioscopic examination after staining for acid-fast bacilli (*Ziehl Neelsen* staining method) may provide preliminary confirmation
- Culture of specimen to identify *Mycobacteria* growth is the definitive method to detect bacilli



# Diagnosis: special concerns in pediatric population



- Younger children are not able to complain their symptoms
- Often TB is associated with poor socio-economic status with no access to health system
- Difficulties in collecting appropriate sputum sample
- Chest X-rays often do not help in diagnosis

# Therapy: overview



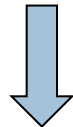
- The ultimate goal is to achieve sterilization of the TB lesion
- Patients should assume therapy for long period (6 months or more)
- Strict adherence is required
- The regimen always should consist of multiple drugs
- Very important: patient's strict **contacts** should be identified and treated if necessary!

# Therapy: the resistances

- *M. tuberculosis* is able to develop the ability to escape antibiotics activity (antibiotic resistance)
- Resistances develop if:
  - ▣ A single drug is used
  - ▣ Compliance is not good

To avoid resistance patients should...

Use a multiple drugs regimen



Many antibiotics work together

Take tablets every day in the right dose (good adherence)



All antibiotics have always the right concentration

# Therapy: the drugs available

- First line drugs: less toxicity and greater efficacy
  - Rifampin
  - Isoniazid
  - Pyrazinamide
  - Ethambutol
  - Streptomycin
  
- Second line drugs: to use in case of resistance to first line agents
  - Fluoroquinolones (Ciprofloxacin, Levofloxacin, Moxifloxacin, Ofloxacin)
  - Kanamycin
  - Capreomycin
  - Cycloserine
  - Ethionamide
  - PAS
  - Linezolid



# Therapy: pulmonary TB

## □ Pulmonary TB

### □ **Rifampin** 10 mg/kg daily for **6 months**

- Formulation: 150, 300, 450 and 600 mg tablets; syrup; iv. Tablets and syrup should be ingested in morning time at least 30 minutes before eating

### □ **Isoniazid** 10 mg/kg (max 300 mg/day) daily for **6 months**

- Formulation: 200 mg tablets, iv

### □ **Pyrazinamide** 15-30 mg/kg divided in three doses for **2 months**

- Formulation: 500 mg tablets

### □ **Ethambutol** 15-25 mg/kg divided in two or three doses for **2 months**

# Therapy: extrapulmonary TB

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- Lymphonodal TB: same as pulmonary TB
- Genitourinary TB: same as pulmonary TB
- Bone and joint disease: 2 months with 4 drugs, then 10 months with Rifampin and Isoniazid
- Meningeal disease: 2 months with 4 drugs, then 10 months with Rifampin and Isoniazid
- Miliary disease: 2 months with 4 drugs, then 10 months with Rifampin and Isoniazid

# During anti-TB treatment monitor



- GOT and GPT every 2-4 weeks
- Uric acid every 4 weeks
- ESR every 4 weeks

# Special issues in African context



- Use of *Directly observed therapy* (DOT) to improve adherence
- Use of drug co-formulations, whenever possible (fixed doses are difficult to be used in children)
- Use of new regimens which do not require daily drug assumption
- Strict control of patient's contact, to stop transmission chain

# WHO *Stop TB strategy*

- 2006-2015 program, articulated in 6 points:
  - Pursue high-quality DOTs expansion and enhancement by ensuring adequate case detection
  - Address TB/HIV co infection, contain MDR- and XDR-TB and other challenges
  - Contribute to health system strengthening that would increase access to TB diagnostic and treatments services
  - Engage all care providers in the provision of TB diagnostic and treatment services
  - Empower people and communities with TB
  - Enable and promote research