

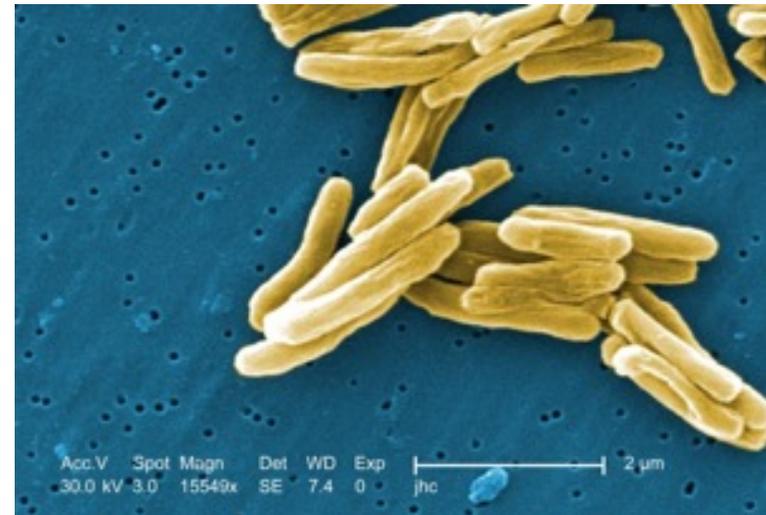
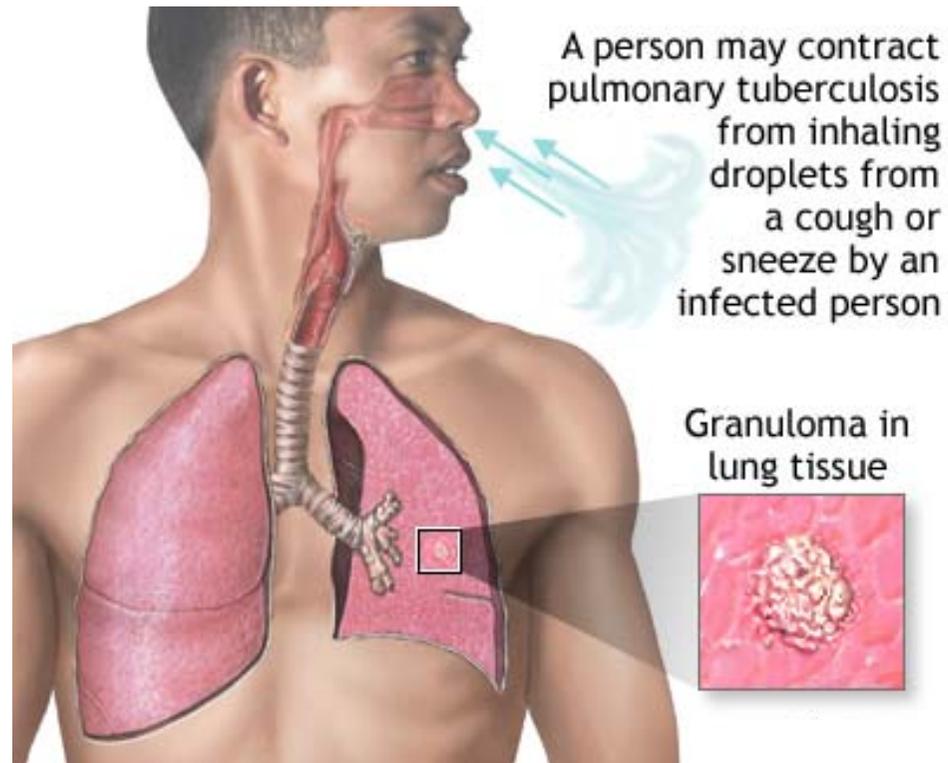
TUBERCULOSIS in CHILDREN

WHAT IS TUBERCULOSIS?



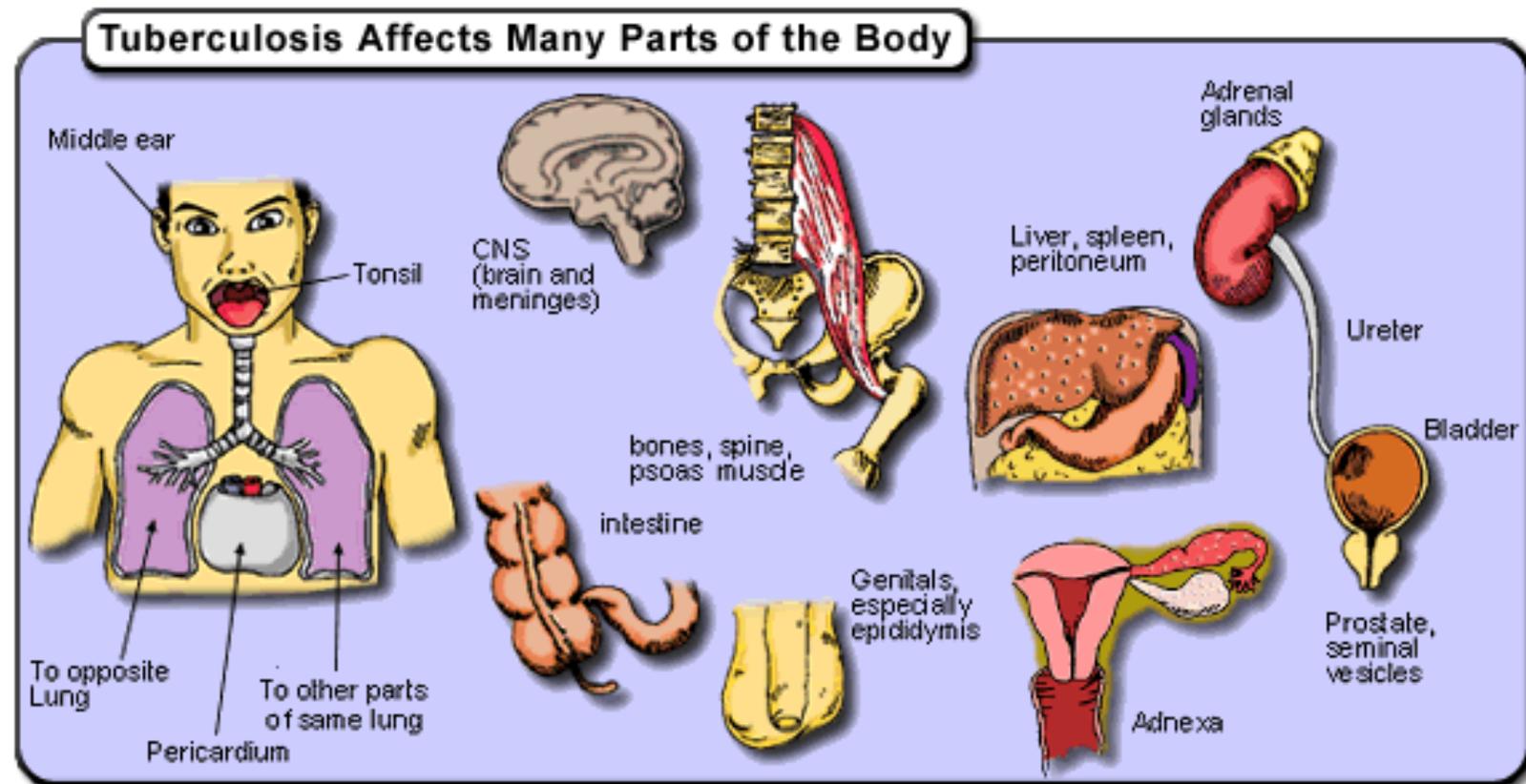
- Tuberculosis, or TB, is an infectious bacterial disease caused by **Mycobacterium tuberculosis**, which most commonly affects the lungs.
- It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease.

Tuberculosis

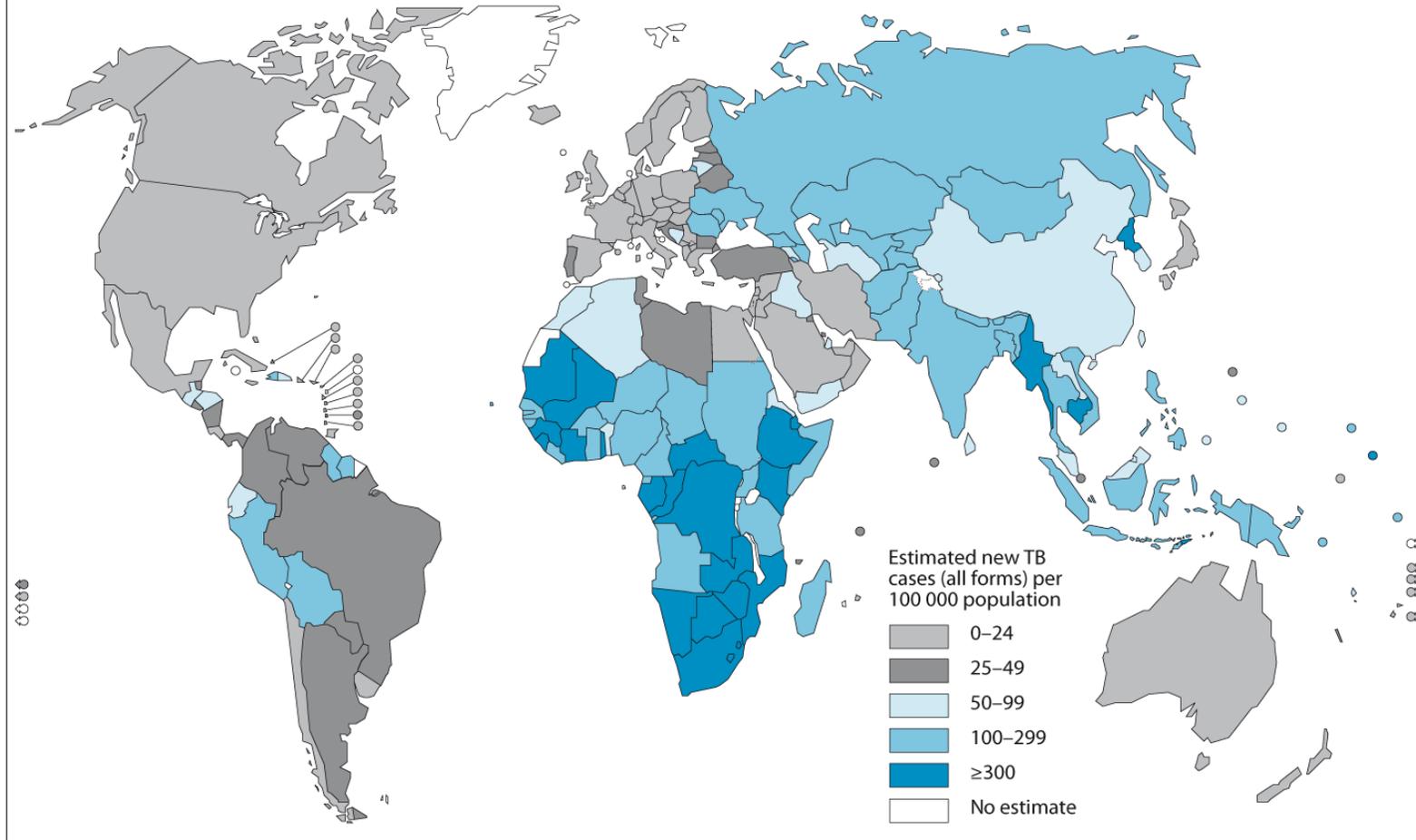


If not treated, each person with active TB can infect on average 10 to 15 people a year.

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.

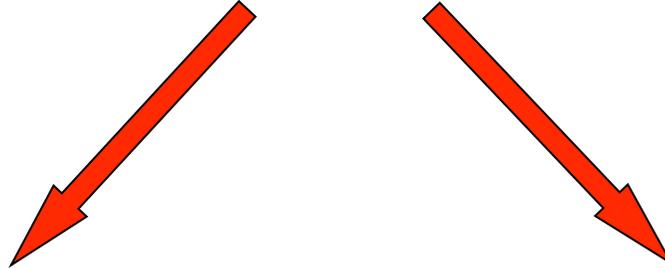
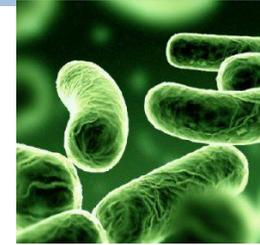
TB in children



- 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

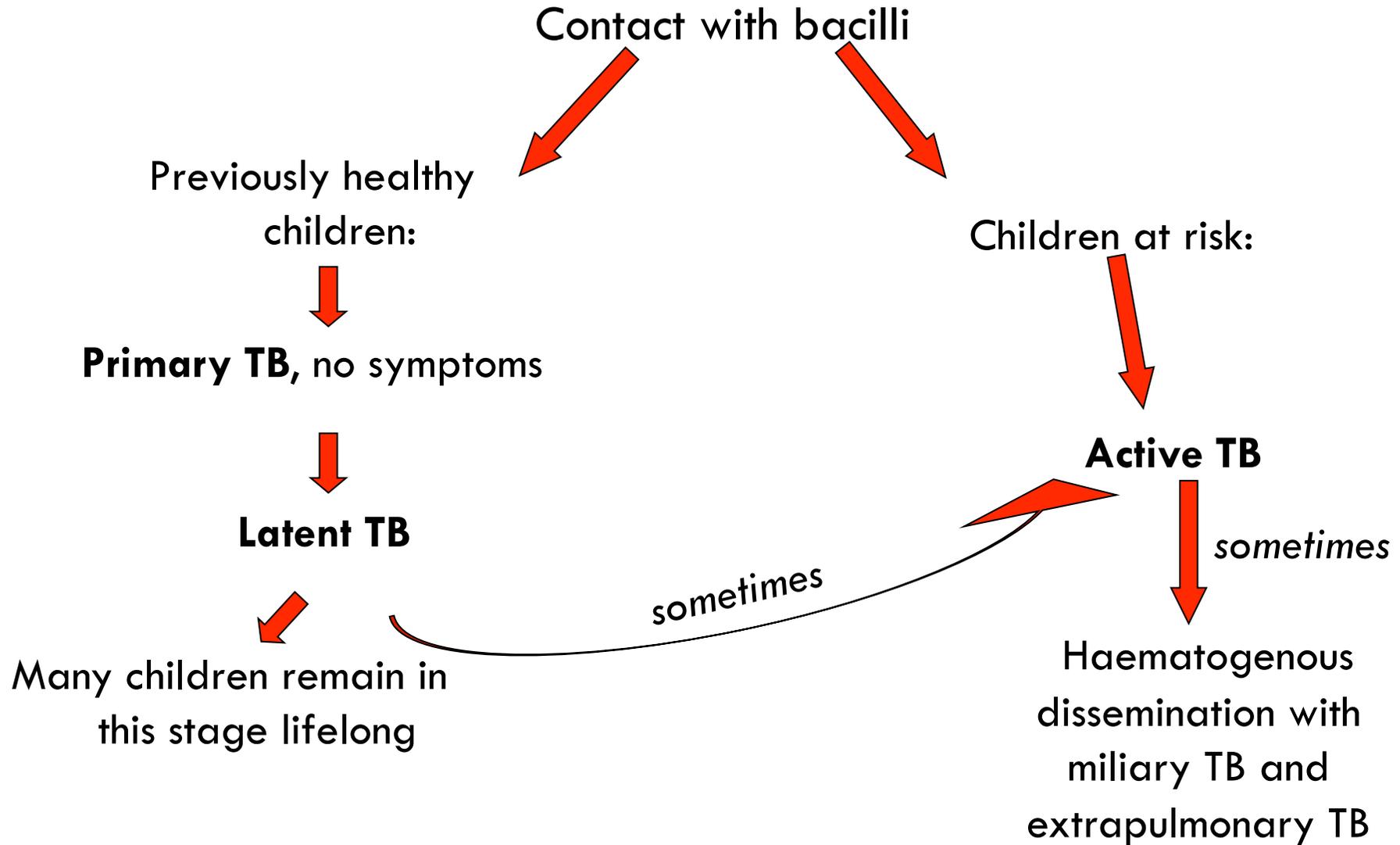
TB history: latent versus active disease



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)



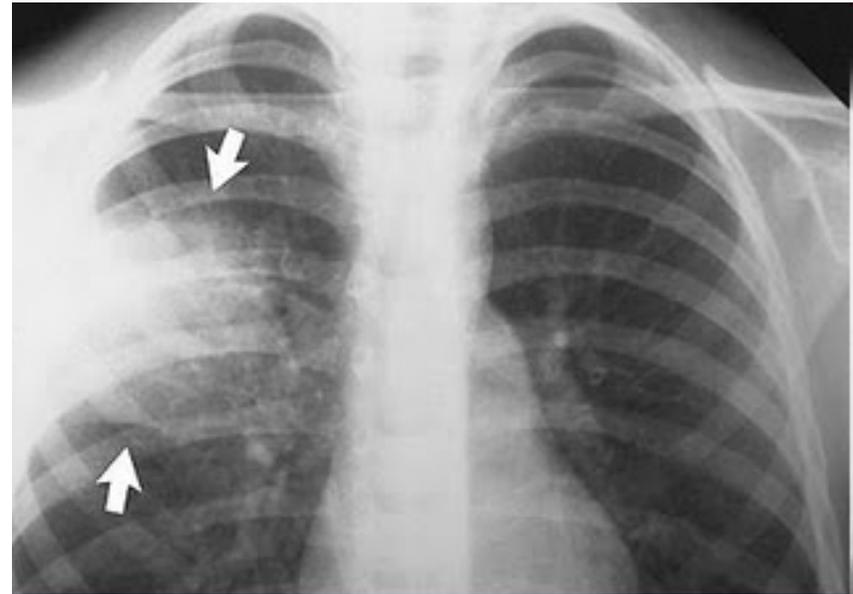
- Pay attention!
 - A positive TST indicates that patient has had a contact with TB bacilli and then his immune system is able to react to TB antigens. This contact could be occurred in any moment of patient's life
 - A positive TST, then, does not indicate that patient has necessarily active TB
 - Previous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



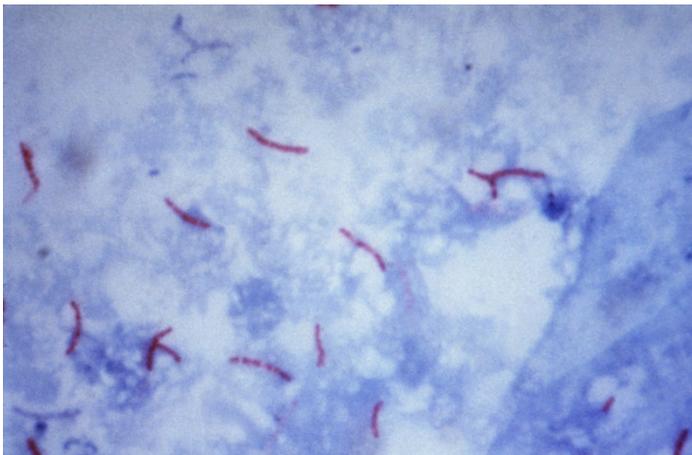
- Pulmonary TB
 - Children > 6 aa: sputum
 - Children < 6 aa: gastric aspiration (early morning)

- 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



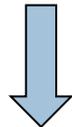
- The ultimate goal is to achieve sterilization of the TB lesion
- Patients should assume therapy for long period (6 months or more)
- Strict adherence is required
- The regimen always should consist of multiple drugs
- Very important: patient's strict **contacts** should be identified and treated if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

- 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