



**MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE**

DEPARTMENT OF PEDIATRICS

Lecture № 14

TUBERCULOSIS

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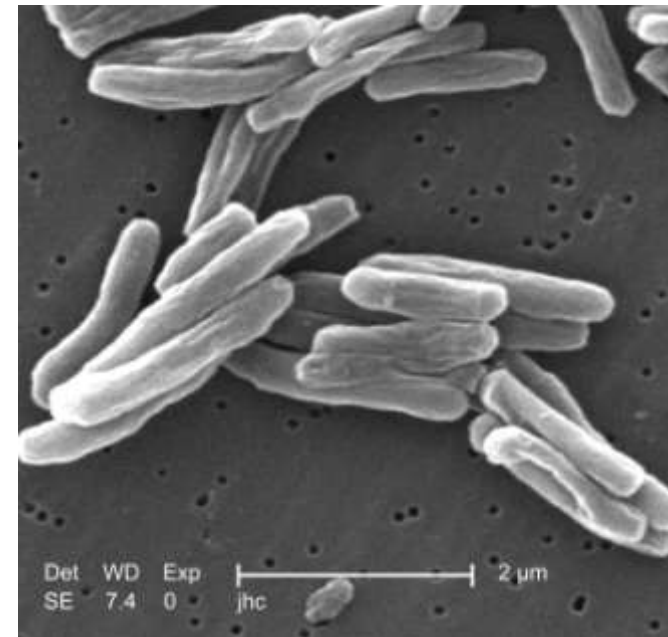
TUBERCULOSIS

Mono- ethiological disease
with multiple clinical features
and chronic type of inflammation



ETIOLOGY

- Mycobacterium tuberculosis - R. Koch 1882 :G pos. bacterium, 1.5-4 mcm, Zill - Nelson red colored
- Stationary, non capsules and spores forming bacteria
- Types : Typus humanus, bovinus, avium
- Obligative aerob
- Long reproduction- over 20 hours
- Stable in acids and detergents



EPIDEMIOLOGY

- In 1945 Bulgarian incidence of TB : 595/100 000
- In 1990 : 25/100 000
- In 1996 in Bulgaria incidence of TB increases to 40/100 000 and among children from 8/100 000 to 19/100 000 in 1996
- Reasons : lack of chemoprophylactic , lack of early diagnostic, non - treated adults with TB, poor feeding, poor hygiene, narcotics, AIDS, etc.



PATHOGENESIS OF TB

- M.tuberculosis contamination : aerogenic way, stomach and intestines, aero-lymphogenic way, skin, trough the placenta
- Contagious index : 20%, only 5 % develop TB disease
- For children:
 - respiratory way
 - aero- lymphogenic way
 - intestinal way
 - skin
- TB source: sick people and animals: sputum, urine sample, puss, milk, excretions



PATHOGENESIS OF TB

1. **Virulent (latent) TB infection:** infection with *M. tuberculosis*, no morphologic changes, positive Mantoux
2. **TB disease :** positive Mantoux and morphologic changes

Distribution of TB: near by, bronchial way, **lymphogenic way, hematogenic way**
(last two play major role in childhood)



ACTIVE TB AND LATENT TB

	Active TB	Latent TB
Signs and symptoms	+	-
Tuberculin skin test	+	+
Blood test	+	+
Sputum	+	-
Chest X-ray	+	-
Treatment	+	+
Transmission	+	+



TB

1. Primary tuberculosis :

- lympho-hematogenic way
- No immune information
- Tendency for generalization
- Organization with calcium into the caseous focus

2. Secondary tuberculosis

- Bronchial way
- Immunocompetent organism
- Local inflammation, cavernae, destruction, mainly pulmonary forms



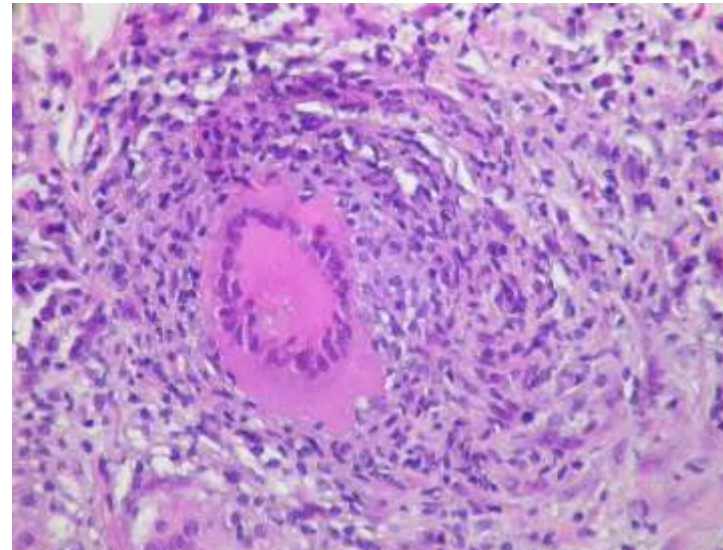
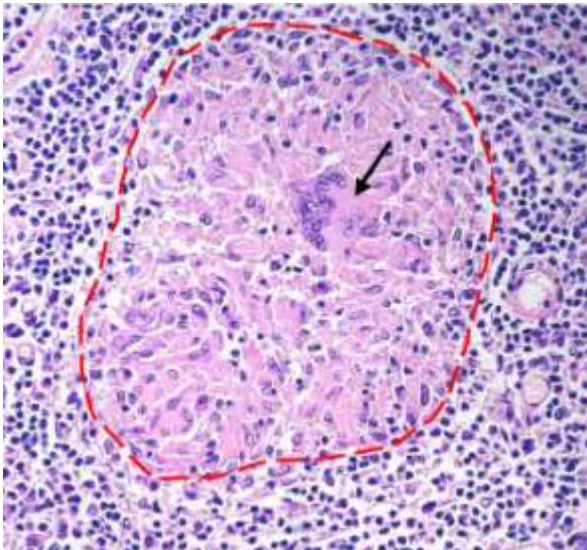
TB CLASSIFICATION OF TURBAN AND GERHARD

1. TB intoxication in children and adolescents
2. TB of respiratory system
 - a/primary forms
 - b/secondary forms
3. Extrapulmonary tuberculosis:
 - ❖ TB of the brain
 - ❖ TB of intestines
 - ❖ TB of bones and joints
 - ❖ TB of the skin
 - ❖ TB of peripheral lymph nodes
 - ❖ TB of urinary tract
 - ❖ TB of eyes
 - ❖ Other forms of TB



TB — PATHOMORPHOLOGICAL CHANGES

- **Tuberculum** (primary caseom)- typical structure : central necrosis, epithelial cells, macrophages, lymphocytes, giant cells “Pirogov - Langhans”
- When **healing**: collagen, fibroblast cells, calcium
- When **liquefying** : proteolysis : central necrosis and caverna formation with oval forms and 3 zones: necrosis and caseosa, granulation tissue, fibrosis



PPD TEST – MANTOUX TEST

The test performing is in order to investigate TB sensitivity

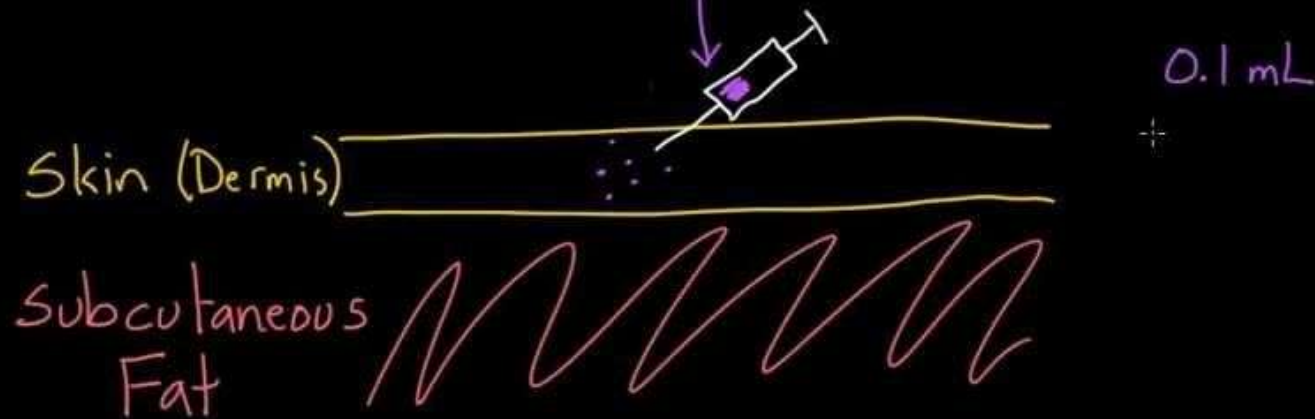
- PPD tuberculin contains antigen bioproducts of *M. tuberculosis*
- Allergic reaction of type 4 with cellular immune response : macrophages, Th1, immunocytes
- Time for sensibilization 4-8 weeks
- 0.1 ml intradermal PPD tuberculin, 72 hour interval - reassessment
- Quantitative measurements : Negative : 0-5 mm, normal 6-14 mm, positive : over 15 mm
- Qualitative measurements : infiltration, induration, surface, color, lymphangitis, lymphadenitis, duration, pigmentation, desquamation, etc.



Mantoux Test = PPD = TST

Purified
(TB) Protein
Derivative

Tuberculin
Skin
Test



"Bubble"



BCG VACCINE

- Alive lyophilizate of BCG bacteria
- Invented by Calmette and Guerin in 1921
- Bulgaria has its one strain :374A1 with 5-7 year immunity coverage
- Primary vaccination : after birth all children up to 48 hour, revaccination 7-11-17 years with PPD test
- BCG vaccine is applied in dose 0.1 ml intradermal left shoulder
- Side effects : local : abscesses, lymphadenitis, osteitis , and general effects



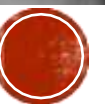
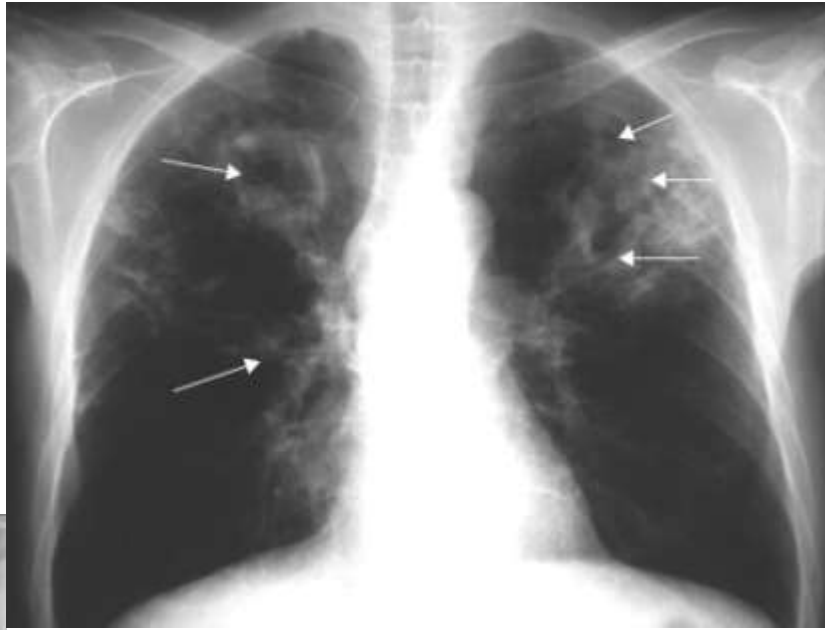
PRIMARY FORMS OF TB

1. Primary TB complex

- Classical form of TB disease: 60% in upper lobes, mainly right lung
- **90%** aerogenic way, **10%** - intestinal way : primary intestinal complex
- Triade: **primary pulmonary affect + lymphadenitis+ lymphangitis**
- Evolution of the primary focus: healing or progression
- Complication with hematogenous forms, TB meningitis, extra-pulmonary forms



TB



CLINICAL FEATURES

- Intoxication syndrome : fever, sub febrile temperature, headache, failure to thrive, poor appetite, sweetening
- Loosing weight
- Cough
- No physical changes or diminished breathing sounds
- Diagnosis : anamnesis+epidemiology+physical examination+CBC, differential count+positive Mantoux test+ X - ray of the chest, ADA test
- Treatment : 8-12 months, healing with calcification



PRIMARY FORMS OF TB

2. TB of tracheo - bronchial lymph nodes

- Most typical form for TB in childhood, more than **70%** of all forms
- Mainly : paratracheal, bifurcation, bronchial and broncho- pulmonal lymph nodes
- Main form for extrapulmonary forms
- Two types :
 - ❑ **Tumorous form**
 - ❑ **Infiltrative form**



CLINICAL FINDINGS

- Flu- like syndrome with fever, dry cough, expiratory dyspnea, dysphonia, , dysphagia, atelectasis , etc.
- Asthma - like syndrome with wheezing and recurrent cough
- CBC, differential count - normal
- Mantoux test - positive
- ADA, QuantiFERON test
- X - ray of the chest , tomogram
- Complications : atelectasis, hypoventilation, pleuritis, fistula between the bronchus and the lymph node, TB of trachea and larynx, pneumonia caseosa, hematogenic dissemination, all forms of extrapulmonary TB start from this form
- Treatment is over an year



HEMATOGENIC FORMS (HF) OF TB

- These are primary forms of TB with one - stage or multiple - stage dissemination into the lungs
- They are significantly decreased due to BCG vaccine
- Incidence is **1.08%**
- HF can be primary dissemination or reactivation of secondary forms
- Main focus : intra-thoracic lymph nodes and lympho - hematogenic way
- 5 types of HF TB infection :



A. ACUTE TB SEPSIS

- Sepsis of Landousi
- Immunocompromised infants
- Generalized infection, alteration, typhus - like clinical symptoms : high fever, adynamia, dyspepsia, headache, bronchial obstruction, tachycardia, hepatosplenomegaly
- Elevated ERS, leukopenia, neutrophilia, Eo-penia
- Pulmonary infiltrates on X- ray
- Poor prognosis
- Mantoux test could be negative - anergia



B. ACUTE MILIARY TUBERCULOSIS

- One- stage dissemination of TB infection
- Immunosuppression
- All organs and tissues are infiltrated with miliar tuberculi 1-2 mm in interstitial tissue
- Clinical symptoms : intoxication, fever, dry cough, tachypnea, cyanosis, wheezy crackles
- Lymphopenia, monocytosis, albuminuria
- Negative Mantoux quite often
- X - ray : hyperinflation of the lungs, miliar infiltration apico- caudal “ star sky”



MILIARY TB



C. TB MENINGITIS

- Etiology: hematogenic way from pulmonary forms of TB or from the liquor
- Basal meningitis and vasculitis with sero- fibrinous exudate with yellow color
- Clinical evolution: - **prodromal period** (viral disease symptoms, behavioral deviations, headache, fever, bradycardia, problems with accommodation) - 1-2 weeks
- **Meningial syndrome period**: persistent headache, fontan vomiting , skin hyperesthesia, bradycardia, seizures, ataxia, neck rigidity, pathological reflexes, opisthotonos, clonic muscle contractions, paralysis of n.oculomotorius, abducens, vagus and facialis.

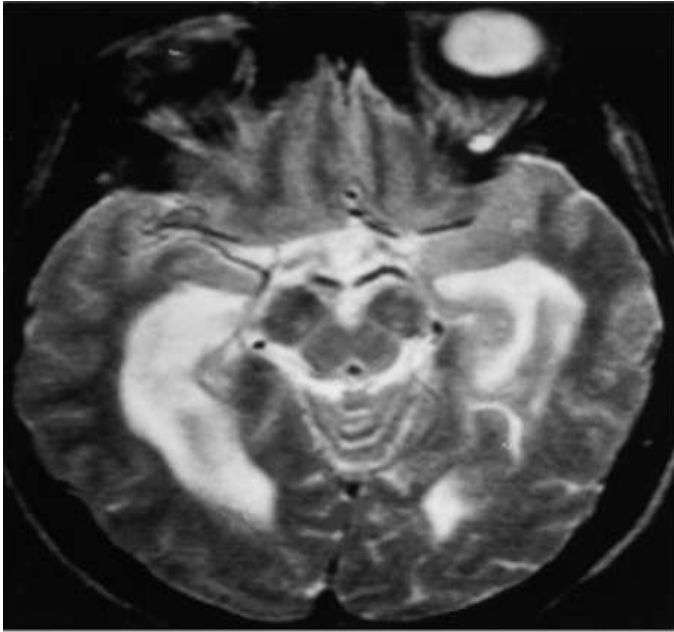


TB MENINGITIS

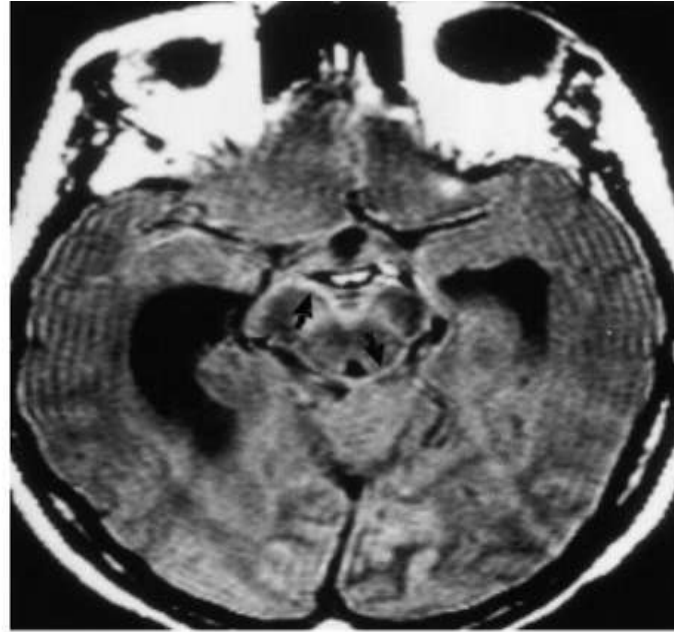
- **Sopor and coma period** : bulbar symptoms, thermoregulation instability, paralyzes of the extremities, death
- KAT : external hydrocephaly
- Anergic Mantoux test

Diagnosis : liquor diagnostic : high pressure of the liquor, pure liquor with xanthochromia, fibrin net, cellular - protein dissociation: slightly increased protein (0.8-1.5 g/l) , hypoglycorrhachia and hypochlororrhachy, lymphocytes, cells 100-1000 mm³

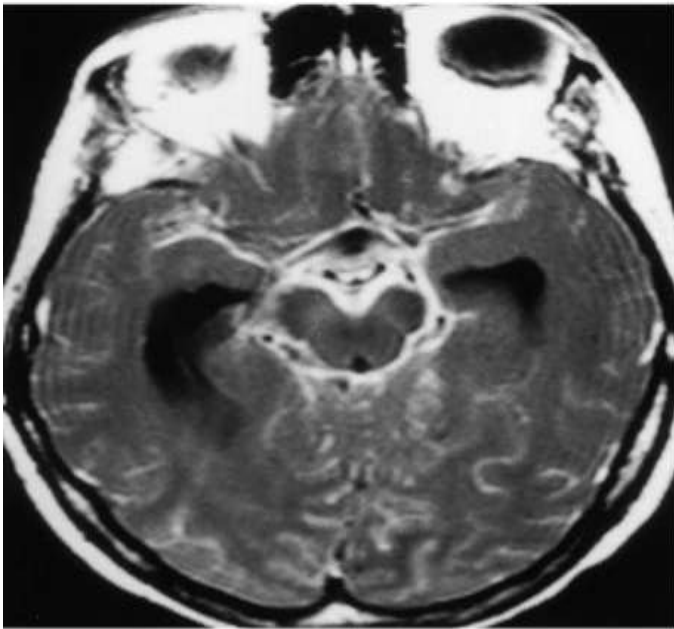




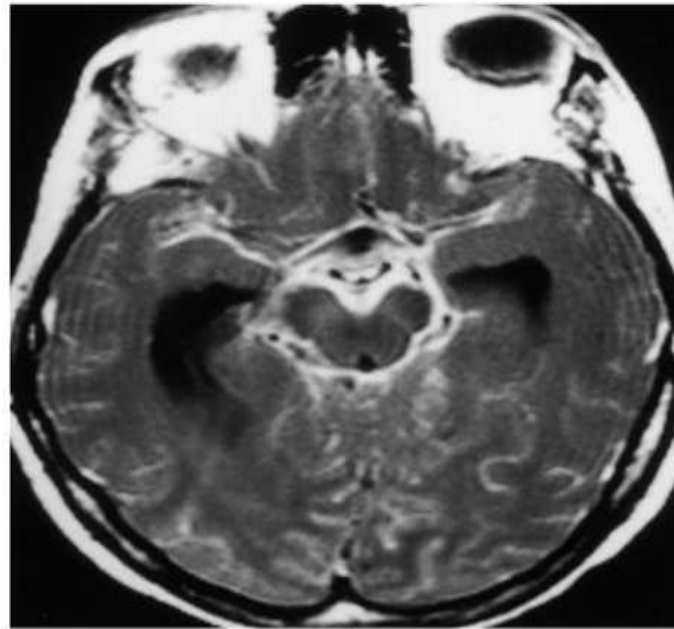
(a)



(b)



(c)



(d)



D. SUBACUTE HEMATOGENIC - DISSEMINATED TB (SHDTB)

- Important is the **duration** of the process and the **character** of the foci
- Multi - stage infiltration of the lungs in short intervals, with intermittent improvement and worsening
- Apico- caudal way of infiltration, symmetry, interval of exacerbation 1 month
- Wave course with fatigue, poor appetite, insomnia, sweatening, dry non - productive cough, cyanosis.
- X - ray diagnosis : spotty shadows with different diameter, same intensity, confluence. Emphysema, cavernae.



E. CHRONIC HEMATOGENIC DISSEMINATING TB

- In case of multi-resistant TB strains
- Multi - stage dissemination, interval of more than 2 months
- Polymorphysm of the changes : exudative changes, cavernae, calcifications, fibrosis
- Symmetrical lung changes, cortico- pleural localization, mainly in the lung apex, emphysema, cavernae, sclerosis, cor pulmonale
- Chronic intoxication, cough, hemoptoe
- X- ray : shadows with different caliber and intensity, pleuritis, pericarditis, etc.



SECONDARY FORMS OF TB

1. Focal TB
2. Infiltrative TB
3. Tuberculum
4. Cavernous TB of the lungs
5. Pneumonia caseosa
6. Fibrous - cavernous TB of the lungs
7. Cirrhosis of the lungs
8. TB pleuritis
9. Other forms of the TB of the air ways



TREATMENT OF TB

The treatment is in two phases:

1. **Intensive phase:** 3-4 medications, 2 months, till no bacteria are detected
2. **Persistent phase :** 3-9 months, 2 medications



ANTI TUBERCULAR DRUGS

FRIST LINE AGENTS

- ✓ ISONIAZID(H)
- ✓ RIFAMPICIN(R)
- ✓ PYRAZINAMIDE(Z)
- ✓ ETHAMBUTOL(E)
- ✓ STREPTOMYCIN(S)

SECOND LINE AGENTS

- *Aminoglycosides
 - KANAMYCIN
 - AMIKACIN
- *Macrolides
 - AZITHROMYCIN
 - CLARITHROMYCIN
- *Fluoro quinolones
 - LEVOFLOXACIN
 - MOXIFLOXACIN
- *PARA AMINO SALICYLIC ACID
- *BEDAQUILINE
- *CYCLOSERINE
- *ETHIONAMIDES
- *CAPREOMYCIN
- *THIACETAMIDE



MEDICATIONS:

1. Streptomycin

- Aminoglycoside antibiotic, broad spectrum, extracellular bacteria
- No passing haemato-encephal barrier, only in case of meningitis : penetrance of the brain is improving
- Ototoxicity, nephrotoxicity, cytopenia, allergy, transitory bleeding
- 20 mg/kg/daily i.m. once a day
- 1-3 months
- Audiometry



MEDICATIONS:

2. Rimicid (Isoniazid)

- Extracellular bacteria
- Passing well hemato- encephalic membrane
- Side effects: vertigo, nausea, hepatotoxicity, agranulocytosis
- Dose : 5-10 mg/kg twice a day after food orally
- Maximal dose 400 mg
- Duration of treatment 12-15 month +Vit B 6



MEDICATIONS:

3. Tubocin(Rifampicin)

- Antibiotic from rifampicin group
- Passing hemato - encephalic barrier
- Side effects :orange /red color of the urine, sweat, feces, tears and flam, skin itchiness, hepatotoxicity, anemia, thrombocytopenia
- Dose: 10 mg/kg once a day on an empty stomach, morning time
- Duration: 6-9 months



MEDICATIONS:

4. Pyrazinamid

- Effective in intracellular conditions : cavities, caverna
- Side effects : headache, nausea, myalgia, hepatotoxicity, hyperuricemia, anemia, thrombocytopenia
- Dose: 25-30 mg/kg twice a day orally
- Duration : 3-5 months

5. Etambutol

- 20-25 mg/kg twice a day orally, after the second month: 15 mg/kg , duration : 6-9 months
- Side effects: neuritis n.opticus + vit.A



MEDICATIONS:

6. Corticosteroids :

- In case of serositis, in case of some disseminated forms and TB meningitis

7. Anti- seizures medications

8. Diet - hypercaloric, reach of proteins

Vitamins and immunostimulators

1 phase : 4 tuberculostatics :

Rifampicin+Isoniazid+Ethambutol+Pyrazinamid+Streptomycin

2 phase : 2 tuberculostatics

Other medications: Ethionamide, Kanamycin, Cycloserin, Ofloxacin, etc.



**Thank you
for
your attention !**

