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TREATMENT OF PULMONARY TB-PATIENTS

The aim of treatment

- The aims of treating tuberculosis in adults are:

 to eliminate the clinical features of tuberculosis;

 promote a stable healing of the tubercular lesions;

 restoration of the working capacity and social status of the patient.

- The goal in treating tuberculosis in children

 to cure without any residual changes or with minimal changes.

The complex treatment of pulmonary tuberculosis patients includes:

- antimycobacterial therapy

- pathogenetic treatment

- colapsotherapy and surgical methods of treatment

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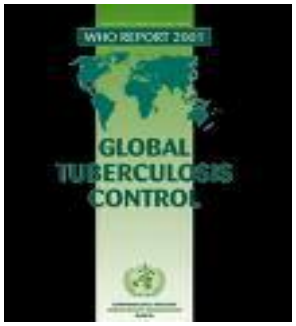

- symptomatic therapy

Principles of treatment of patient with tuberculosis

1. **Complexity is combination** of specific and non-specific, as well as surgical treatment. Specific therapy includes etiotropic therapy, which is intake of anti-tubercular medication; non-specific therapy includes following hygienic and dietetic regimen, as well as prescription of pathogenic and symptomatic medication.

2. **Combination** of treatment is using of no less then 4 medications at the beginning of treatment of all patients with bacterial seeding. Combined therapy prevents MBT drug resistance and increase effectiveness of anti-tubercular medications. Besides different medication acts on different structures of microbial cell. Combination of etiotropic medications promotes more complete reparation.

Principles of treatment of patient with tuberculosis

3. Biphasic treatment of tuberculosis**.** First intensive phase is aimed at depression of multiplication of MBT population, significant decrease of the latter and partial sterilization of the focus of specific infection. Patients are treated on an in-patient basis. Second phase (continued treatment) includes daily or intermittent antimicrobial therapy on inpatient basis, outpatient basis or in sanatorium aimed at clinical recovery of patient (stable cease of bacterial seeding; dissolution of infiltration, healing of destruction cavities) or at preparation for surgical treatment.

Principles of treatment of patient with tuberculosis

4. Individual treatment of patient with tuberculosis is based on results of evaluation of patient and close control over effectiveness of treatment. Thus sensitivity of cultured MBT to medication, individual sensitivity of patient to medication, concomitant pathology, age and weight of patient. According to WHO recommendations, patients with negative MBT cultures might not be hospitalized but might be given controlled chemotherapy on an outpatient basis.

Individual approach foresees changes into primary regimen of treatment. This may be necessary due to development of drug resistance to prescribed medications, little effect of therapy (continuing of bacterial seeding, slow dissolution of inflammatory alteration, absence of positive dynamics of the destruction cavity). Change of regimen might be due to change of medication or the way of their introduction.

Principles of treatment of patient with tuberculosis

5. Long-term and continued treatment, which should last for several (often 6-8) months. In caseation necrotic masses and in caverns with MBT there is obliteration of vessels with cheese-like necrosis or their destruction. Thus adequate concentrations of medications are not achieved in main focus of pathogen collection. One has to consider that involution of tubercular alterations starts soon but it takes long time for reparation to complete. Sometimes treatment lasts for several years.
Continued (regular) intake of medication decreases incidence of drug resistance and promotes effectiveness of treatment. Intermittent therapy first introduced in 1964-1966 is considered continued therapy (intake of antimycobacterial medications 2-3 times a week).

6. Staged treatment includes such stages as in-patient (day care), sanatorium, outpatient, and dispensary follow-up with courses of anti-relapse treatment. This provides succession of phthisiology service. From 1956 outpatient treatment plays significant role in foreign countries.

Principles of treatment of patient with tuberculosis

7. **Controlled chemotherapy** means that all medication should be taken in the presence of medical personnel, close relatives, social workers or volunteers. Purpose of controlled chemotherapy is to provide regular intake of antimycobacterial medications. It has been shown that up to 50% of treatment failure is associated with failure of patient to comply with prescribed treatment. Availability and adequate number of medication, fully informed patient about gravity of disease, the need for treatment and possible outcomes estimate quality of anti-tubercular service. Economizing on personnel training and lack of state support of realization of anti-tubercular programs lead to increase of expenses for fight with tuberculosis.

8. Treatment of tuberculosis should necessarily be free of charge, available and safe. Chemotherapy is aimed at one pathogen, Mycobacterium tuberculosis. Most important ***factor*** in choice of antimycobacterial therapy is sensitivity of Mycobacteria to antitubercular medication.

ANTITUBERCULAR DRUGS CLASSIFICATION (1)

Group I (A)- the most effective drugs	Group II (B)- the drugs of average effectiveness	Group III (C)- the least effective chemodrugs
Isoniazidum (H) (and its derivatives), **Rifampicinum (R)**	**Pyrazinamidum (Z)** **Kanamicini (K)** **Ethambutolum (E)** **Ethionamidum (Et)** **Cycloserinum (C)** **Florimycin (F)** **Ofloxacin (Of)**	**PAS (PAS)** **Thioacethazonum (T)**

ANTITUBERCULAR DRUGS CLASSIFICATION (2)

Antitubercular drugs of 1th line	Antitubercular drugs of 2th line	Others
Isoniazidum(H) Rifampicinum (R) Streptomycin (S) Pyrazinamidum (Z) Ethambutolum (E)	Amikacin (A) Kanamicini (K) Ethionamidum (Et) Prothionamidum(Pt) Cycloserinum (C) Ofloxacin (Of) Ciprofloxacin (Cf) Capreomycin (Cp) PAS	Rifabutinum (Rb) Clarythromycin (Cl) Amoxicillin/ Clavunat acid (Am) Florimycin (F) Phthivazidum (Ph) Flurenizid (Fl) Thioacethazonum (T)

ANTITUBERCULAR DRUGS CLASSIFICATION (3)

Group 1:
First-line oral agents

- Pyrazinamide (Z)
- Ethambutol (E)
- Rifampicinum (R)
- Isoniazidum (H)

Group 2:
Injectable agents

- Kanamycin (Km)
- Amikacin (Am)
- Capreomycin (Cm)
- Streptomycin (S)

ANTITUBERCULAR DRUGS CLASSIFICATION (3)

Group 3: Fluoroquinolones

- Levofloxacin (Lfx)
- Moxifloxacin (Mfx)
- Ofloxacin (Ofx)
- Gatifloxacin (Gfx)

Group 4: Oral bacteriostatic 2-line agents

- para-aminosalicylic acid (PAS)
- Cycloserine (Cs)
- Terizidone (Trz)
- Ethionamide (Et)
- Prothionamide (Pt)

ANTITUBERCULAR DRUGS CLASSIFICATION (3)

Group 5:

Agents with unclear role in treatment of drug resistant-TB

- Clofazimine (Cfz)
- Linezolid (Lzd)
- Amoxicillin/clavulanate (Amx/Clv)
- Thioacetazone (Thz)
- Imipenem/cilastatin (Ipm/Cln)
- high-dose Isoniazid (high-dose H)
- Clarithromycin (Clr)

Isoniazid (H)

Structure and general properties

- H is a pro-drug that requires processing by the bacterial catalase-peroxidase to become active.
- Once activated, it inhibits the biosynthesis of mycolic acids, which are essential components of the mycobacterial cell wall.
- This drug is bactericidal against metabolically active bacilli and bacteriostatic against resting bacilli.

Isoniazid (H)

Pharmacokinetics

- H is readily absorbed from the gastrointestinal tract or following intramuscular injections. Peak concentrations appear in blood between 1-2 hours after ingestion. It diffuses into all body tissues, including cerebrospinal fluid. The plasma half-life ranges from 1 to 6 hours.

- H is metabolized in the liver and the small intestine. Within the population, there are two groups of patients, depending on whether H is acetylated slowly or rapidly, a characteristic that is genetically determined. H and its metabolites are excreted in the urine.

Isoniazid (H)

Toxicity

- H is well tolerated at recommended doses, although slow acetylators can accumulate higher H concentrations and then have a higher risk of developing adverse effects.
- Neurological adverse reactions (A daily dose of 10 mg of pyridoxine hydrochloride is recommended to reduce neurotoxicity and to treat adverse effects caused by H).
- Transient increases in liver enzymes at the beginning of treatment, and sometimes hepatic damage.
- Hematological adverse effects
- Hypersensitivity reactions.

Rifampicin (R)

Structure and general properties

- R inhibits gene transcription, by interacting with the beta subunit of the ribonucleic acid polymerase enzyme.

- It is bactericidal against dividing mycobacteria and also has some activity against non-dividing bacilli. R is also active against a wide range of microorganisms, including staphylococci, Neisseria spp. Haemophilus influenza and Legionella spp.

Rifampicin (R)

Pharmacokinetics

- This drug is readily absorbed from the gastrointestinal tract (food may delay or decrease R absorption); within 2 to 4 hours after ingestion of a dose of 600 mg, peak plasma concentrations may reach 7-10 mg/L.
- It also can be given intravenously. In blood, R is bound to plasma proteins, and distributes into body tissues and fluids, including cerebrospinal fluid and breast milk, and crosses the placenta. The half-life of R ranges from 2 to 5 hours.
- R is metabolized in the liver, and excreted in the bile, feces and urine.

Rifampicin (R)

Toxicity

- R is well tolerated, although adverse effects may arise during intermittent therapy or when restarting an interrupted treatment.
- R will cause a red-orange coloration of body fluids such as urine, tears, saliva, sweat, sputum and feces; it may result in the coloration of soft contact lens.
- Increases in liver enzymes or hepatitis.
- Adverse effects also include diverse alterations in the gastrointestinal tract, skin, kidney and nervous system. It may also produce thrombocytopenia.

Ethambutol (E)

Structure and general properties

- E is only active against dividing mycobacteria, being bacteriostatic. Since E affects the biosynthesis of the cell wall, it has been suggested that it contributes towards increasing the susceptibility of M. tuberculosis to other drugs.

Ethambutol (E)

Pharmacokinetics

- E is given orally, as it is well absorbed in the gastrointestinal tract (and not affected significantly by food), although a part is excreted in the feces. After absorption, it is distributed in most tissues and diffuses into the cerebrospinal fluid and breast milk; it also crosses the placenta.

- Following a dose of 25 mg/kg body weight a peak concentration in serum is reached after 4 hours. The half-life is about 3 to 4 hours.

- Only a fraction of E is metabolized in the liver; the unchanged drug and its metabolites are excreted in the urine.

Ethambutol (E)

Toxicity

- E produces retrobulbar neuritis with a reduction in visual acuity, constriction of visual field, central or peripheral scotoma, and green-red color blindness. Usually, normal vision is recovered a few weeks after the end of the treatment, although in some cases, this recovery may not occur until some months after the completion of treatment. Consequently, E is contraindicated in patients with optic neuritis, and should be used with care in patients with visual disorders. E is not usually given to children under six years of age because of the difficulty in monitoring visual acuity.
- Other adverse effects include a reduction of urate excretion (hence producing gout), gastrointestinal disorders and hypersensitivity skin reactions.

Pyrazinamide (Z)

Structure and general properties

- Z is a bactericidal drug active only against M. tuberculosis, having no in vitro activity against other mycobacteria or any other microorganism. Susceptible strains have MICs of 20 mg/L at pH 5,6.
- It is active against persisting and non-dividing bacilli, even against those residing intracellular, being almost inactive at neutral pH.
- Z is a pro-drug that requires conversion into pyrazinoic acid to be effective; this is done by mycobacterial pyrazinamidases.

Pyrazinamide (Z)

Pharmacokinetics

- Z is given orally and is readily absorbed from the gastrointestinal tract.

- Serum concentrations reach a peak level of two hours after administration of a dose of 3 g. It is distributed in all body tissues and fluids, including the cerebrospinal fluid and breast milk. The half-life of Z is about 9-10 hours.

- Z is hydrolyzed in the liver, being converted to pyrazinoic acid, which is further hydroxylated and finally excreted in the urine.

Pyrazinamide (Z)

Toxicity

- Z is hepatotoxic in a dose-dependent manner. Following a daily dose of 3 g of PZA, 15 % of patients may develop liver alterations, such as transient increases in liver enzymes, hepatomegaly, splenomegaly and jaundice. Hepatitis has been reported in less than 3 % of cases.
- It may also produce hyperuricaemia, leading to attacks of gout. Therefore, it is contra-indicated in patients with liver damage, and it is advisable to test liver function before and regularly during treatment. It also should not be given to patients having a history of gout or hyperuricaemia.

Streptomycin (S)

Structure and general properties

- S, an antibiotic produced by some strains of Streptomyces griseous, was the first drug with antituberculosis activity to be discovered. It is mainly used in the treatment of TB (most M. tuberculosis strains are susceptible to 1-8 mg/L of streptomycin). It can also be used in the treatment of other bacterial infections such as those produced by Yersinia pestis, Francisella tularensis, and Brucella spp.

Streptomycin (S)

Pharmacokinetics

- S, like most aminoglycosides, is poorly absorbed from the gastrointestinal tract, and therefore it must be administered by intramuscular injection.
- The use of S has decreased, being relegated to the treatment of infections caused by drug-resistant strains.
- Two hours after an injection of 1 g S, drug levels in blood may reach up to 50 mg/L, where one third of it circulates bound to plasma proteins. The half-life for S is about 2,5 hours.
- S and the other aminoglycosides diffuse well into most extracellular fluids, maybe with the exception of the cerebrospinal fluid. Aminoglycosides also tend to accumulate in specific body tissues such as the kidneys. Streptomycin does not appear to be metabolized, and is excreted unchanged in the urine.

Streptomycin (S)

Toxicity

- Like most aminoglycosides, S has ototoxic effects affecting vestibular rather than auditory (cochlear) function, which manifest as dizziness and vertigo.
- It is less nephrotoxic than other aminoglycosides, although it may produce renal failure when administered with other nephrotoxic agents.
- Paresthesia, neurological symptoms such as peripheral neuropathies, optic neuritis and scotoma and hypersensitivity skin reactions have also been observed after S injections.

Other drugs against tuberculosis

Drugs in this group are interesting for one or more of the following features:

- widely used in the past but in our days its use has been relegated by the incorporation of more effective and/or less toxic drugs
- used when resistance to first-line antituberculosis drugs is suspected or confirmed and are usually denominated second-line drugs
- used when severe adverse effects to other antituberculosis drugs develop
- have been developed recently and, because of their usefulness for the treatment of TB, are potential first-line drugs that could be incorporated soon into standard (and maybe shorter) antituberculosis regimens
- allow intermittent doses, hence facilitating patient's adherence to antituberculosis treatment.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Bacteriologically confirmed case of TB**

A patient from whom a biological specimen is positive by smear microscopy culture or WHO-approved rapid diagnostic test (such as Xper MTB/RIF). All such cases should be notified, regardless of whether TB treatment is started.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Clinically diagnosed case of TB**

A patient who does not fulfill the criteria for bacteriologically confirmed TB but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Case of pulmonary TB**

Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Milliary TB is classified as pulmonary TB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitute a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Case of extrapulmonary TB**

Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **New case of TB**

A patient who has never been treated for TB or has taken anti-TB drugs for less than one month.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Previously treated case of TB**

A patient who has been treated for one month or more with anti-TB drugs in the past. Retreatment cases are further classified by the outcome of their most recent course of treatment into four categories.

1. ***Relapse patients*** have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).

2. ***Treatment after failure*** patients have previously been treated for TB and their most recent course of treatment failed i.e. they had a positive sputum smear or culture result at 5 month or later during treatment.

3. ***Treatment after loss to follow-up*** patients have previously been treated for TB and were declared 'lost to follow-up' at the end of their most recent course of treatment.

4. ***Other previously treated patients*** are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Case of multidrug-resistant TB (MDR-TB)**

TB that is resistant to two first-line drugs: isoniazid and rifampicin. For most patients diagnosed with MDR-TB, WHO recommends treatment for 20 months with a regimen that includes second-line anti-TB drugs.

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection

- **Case of rifampicin-resistant TB (Rif-TB)**

A patient with TB that is resistant to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether mono-resistance, multidrug resistance, poly-drug resistance or extensive drug resistance.

FOR ALL ***NEW CASES*** OF TB AND ***PREVIOUSLY TREATED CASES*** OF TB THE TREATMENT REGIMEN CONTAINING 4 FIRST-LINE DRUGS:

2HRZE/4HR

Treatment of mono- or poly-resistant non-multidrug-resistant tuberculosis

- These patients are relatively easy to treat and cure with a drug combination regimen of 9–12 months that includes R and three other drugs, including an Q. These three other drugs should be selected based on the rational categorization.
- The ideal treatment for a patient with H mono-resistance would be treatment length of 9 months with R+Q+E and the initial support of Z during the first 2 months.

Treatment of mono- or poly-resistant non-multidrug-resistant tuberculosis

- In Ukraine used the next regimen for **H-monoresistance** or **H+S** or **H+E** polyresistance:

2RZKmLfx10RZLfx.

- If there is **H+Z** polyresistance:

2REKmLfx10RELfx.

Treatment of mono- or poly-resistant non-multidrug-resistant tuberculosis

- A completely different situation exists in patients with ***R mono- and poly-resistance retaining susceptibility to H***. This situation is very rare because over 90 %–95 % of cases with R resistance are actually MDR-TB. Further, it must be remembered that while DST reliability for H is high, it is not 100 %. So, under field conditions, ***all R mono- or poly-resistant cases must be managed like MDR-TB patients,*** of course adding H for its potential helpful effect.

COMMON DRUG SIDE EFFECTS

	Most likely cause			Least likely cause
Hepatitis – ALT/AST predominant	Isoniazid	Pyrazinamide	Rifampicin	Ethambutol (very rare)
Hepatitis -cholestatic	Rifampicin			
Upper GIT symptoms	Rifampicin	Pyrazinamide	Isoniazid	Ethambutol
Arthralgia	Pyrazinamide	Rifampicin (flu like syn.)	Isoniazid (drug induced lupus)	Ethambutol
Hypersensitivity (fever plus rash plus other)	Isoniazid	Rifampicin	Pyrazinamide	Ethambutol

MANAGEMENT OF SIDE EFFECTS

Management of cutaneous reactions

- If a patient develops itching without a rash and there is no other obvious cause, the recommended approach is to try symptomatic treatment with antihistamines and skin moisturizing, and continue TB treatment while observing the patient closely. If a skin rash develops, however, all anti-TB drugs must be stopped.
- Once the reaction has resolved, anti-TB drugs are reintroduced one by one, starting with the drug least likely to be responsible for the reaction at a small challenge dose. The dose is gradually increased over 3 days.
- This procedure is repeated, adding in one drug at a time. A reaction after adding in a particular drug identifies that drug as the one responsible for the reaction.

MANAGEMENT OF SIDE EFFECTS

Management of drug-induced hepatitis

- If it is thought that the liver disease is caused by the anti-TB drugs, all drugs should be stopped. If the patient is severely ill with TB and it is considered unsafe to stop anti-TB treatment, a non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be started.
- If anti-TB treatment has been stopped, it is necessary to wait for liver function tests to revert to normal and clinical symptoms (nausea, abdominal pain) to resolve before reintroducing the anti-TB drugs. If the signs and symptoms do not resolve and the liver disease is severe, the non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be started (or continued) for a total of 18–24 months.

MANAGEMENT OF SIDE EFFECTS

Management of drug-induced hepatitis

- Once drug-induced hepatitis has resolved, the drugs are reintroduced one at a time.
- If symptoms recur or liver function tests become abnormal as the drugs are reintroduced, the last drug added should be stopped. Some advises starting with rifampicin because it is less likely than isoniazid or pyrazinamide to cause hepatotoxicity and is the most effective agent. After 3–7 days, isoniazid may be reintroduced. In patients who have experienced jaundice but tolerate the reintroduction of rifampicin and isoniazid, it is advisable to avoid pyrazinamide.

MANAGEMENT OF SIDE EFFECTS

Management of drug-induced hepatitis

- Alternative regimens depend on which drug is implicated as the cause of the hepatitis. If rifampicin is implicated, a suggested regimen without rifampicin is 2 months of isoniazid, ethambutol and streptomycin followed by 10 months of isoniazid and ethambutol.
- If isoniazid cannot be used, 6–9 months of rifampicin, pyrazinamide and ethambutol can be considered.
- If pyrazinamide is discontinued before the patient has completed the intensive phase, the total duration of isoniazid and rifampicin therapy may be extended to 9 months.
- If neither isoniazid nor rifampicin can be used, the non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be continued for a total of 18 – 24 months.

TREATMENT OF EXTRAPULMONARY TUBERCULOSIS

Bone and joint TB

- Standard course therapy

(5EHRZ, 4 HR) is sufficient in most cases where TB is known to be susceptible to first line drugs. The continuation phase is sometimes extended to 10 months but this regimen is not supported by published evidence unless infection is disseminated, treatment interruption or drug resistance is suspected or proven.

Central nervous system TB

- Standard treatment is extended to twelve months **(2EHRZ/10HR).** Adjunctive corticosteroids are usually recommended to prevent clinically dangerous paradoxical reactions.

SURGICAL TREATMENT

Absolute indications for surgery in TB treatment:

– a high probability of failure of medical therapy in MDR-TB patients (due to persistent cavitary disease and lung or lobar destruction) and massive haemoptysis or tension pneumothorax;

– persistent positivity of sputum-smear or sputum-culture despite adequate chemotherapy;

– a high risk of relapse (based on the drug-resistance profile and radiological findings);

– localized lesion;

– progression of TB despite adequate chemotherapy;

– repeated haemoptysis or secondary infection;

– localized disease amenable to resection;

– polyresistant and MDR-TB;

– absence of any radiological and/or bacteriological improvements during the initial three to four months of chemotherapy;

– allergic, toxic and mixed side-effects of drugs;

– chronic diseases of the gastrointestinal organs hindering effective chemotherapy.

SURGICAL TREATMENT

Emergency indications (that is, without surgery death is imminent and unavoidable) include:

– profuse lung haemorrhage

– tension spontaneous pneumothorax.

SURGICAL TREATMENT

Urgent indications include:

– irreversible TB progression, despite adequate anti-TB chemotherapy

– recurrent haemoptysis that cannot be stopped by other treatment methods.

SURGICAL TREATMENT

the majority of authors define the elective indications listed here:

– localized forms of cavitary TB with continuous M. tuberculosis excretion confirmed by bacteriological examination and DST after four to six months of supervised anti-TB chemotherapy;

– M/XDR-TB characterized by failure of anti-TB chemotherapy;

– complications and sequelae of the TB process (including M/XDR-TB), including:

- spontaneous pneumothorax and pyopneumothorax
- pleural empyema with or without bronchopleural fistula
- aspergilloma
- nodular-bronchial fistula
- broncholith
- pachypleuritis or pericarditis with respiratory and blood circulation insufficiency
- post-TB stenosis of trachea and large bronchi
- symptomatic and chronic post-TB bronchiectasis;
- other indications such as the elimination of complications of previous surgery.

Surgery should be seriously considered when:

- the disease is sufficiently localized to allow surgery;
- the remaining lung tissue around the resection margins is estimated to be free of TB;
- the patient's surgical risk level is acceptable, with sufficient pulmonary reserve to tolerate the resection.

In any case, irreversible pathomorphological changes in the affected lung(s) are a significant additional indication for surgery. In all cases, surgery is only indicated if it is possible to perform surgery (resection of the lung or other type of operation) without significant damage to the patient's lung function.

Types of operations

1. lung resections of different size

- wedge resection
- segmentectomy
- lobectomy and bilobectomy
- combined resection (lobectomy plus minor resection)
- pneumonectomy or pleuropneumonectomy
- lung resections with different correction methods of the haemithorax's volume.

2. **extrapleural thoracoplasty;**
3. **extrapleural pneumolysis;**
4. **thoracomyoplasty;**
5. **pleurectomy and decortications of the lung.**

6. Operations on the bronchi

- occlusion
- resection
- bronchoplasty
- re-amputation of the stump;

7. **thoracocentesis and thoracostomy (drainage of the pleural space);**
8. **artificial pneumothorax and pneumoperitoneum;**
9. **operations on both lungs.**

PATHOGENETIC TREATMENT OF TUBERCULOSIS

It is aimed at solving the following tasks:

1. Decreasing exudative pneumonic phenomena in a lesion nidus, speeding up its resolution and healing with minimum residual changes;
2. Correction of metabolic processes and disfunctions of various organs and systems disturbed by tuberculous intoxication and antimycobacterial drugs;
3. Strengthening of feebly-expressed inflammatory reactions and stimulation of repairing processes.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

The following methods of rational therapy are applied to realize these tasks:

I. Common means of pathogenetic therapy, which include:

1. Hygienic-dietary regimen, which from strict bed care widens to spare diet, training and to labour adaptation regimen;

2. Rational high calory and vitaminized diet (No 11 diet according to Peuzner);

3. Physical metods: aero-, helio-, hydrotherapy, climatotherapy;

4. Psychotherapy and autogenous training;

5. Means of metabolic detoxication and correction, in particular protein and water- electrolytic metabolism; oxidation-reduction processes, acidicalkaline equilibrium, regulation of hemodynamics and diuresis.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

The following methods of rational therapy are applied to realize these tasks:

II. Immunocorrecting therapy. It is performed after studying the function of T-lymphocytes system (cell immunity), B-lymphocytes (humoral immunity), unspecific defence factors. Among immunocorrectors the following drugs are used: thymalin, tactivin, sodium nucleinat, splenin, levamisol or decaris, interferon, Glutoxim.

Of unmedicamental treating methods for immunocorrection and as antiinflammatory methods enterosorption, hemosorption, speleotherapy, magnetotherapy, laser-therapy etc. are applied.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

Laser Therapy

This has also been tried as an adjunct to chemotherapy in some countries such as Russia for the treatment of drug resistant TB. This is effective in multicavitary disease with heavy bacterial loads particularly when there is an increased chance of failure of medical treatment. It is thought to have a role in the rapid killing of bacteria, increases and improves penetration of antitubercular drugs in walled off lesions and helps in early closure of cavities and is of proven benefit in tracheal and bronchial stenosis due to endobronchial growth. It also reduces the trauma of surgery and post-operative complications.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

Gene Therapy

The decoding of the human genome provides another fascinating aspect in the future therapeutic intervention of tuberculosis. By identifying resistance genes, it will be possible to detect drug resistance before start of therapy and also to develop drugs that target these specific genes, enabling us to considerably reduce the duration of therapy.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

Role of Steroids

The adjuvant use of corticosteroids in DR-TB patients has been shown not to increase mortality and can be beneficial in conditions such as severe respiratory insufficiency, severe drug induced rashes and central nervous system or pericardial involvement. Prednisone is commonly used, starting at approximately 1 mg/kg and gradually decreasing the dose to 10 mg per week when a long course is indicated.

Corticosteroids may also alleviate symptoms in patients with an exacerbation of obstructive pulmonary disease or when patient is in a very low general condition. In these cases, prednisone may be given in a short course, tapering over 1–2 weeks, starting at approximately 1 mg/kg and decreasing the dose by 5–10 mg per day. Injectable corticosteroids are often used initially when a more immediate response is needed.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

Other drugs

Inhibitors of proteolytic enzymes (Contrical 10000 in 200ml of the physiological solution of sodium chloride intravenously drop by drop once a day).

Stimulators of repairing processes and cavern healing.

PATHOGENETIC TREATMENT OF TUBERCULOSIS

Other drugs

The tracheobronchial tree sanation occupies one of the most prominent places in a complex treatment of respiratory organs tuberculosis patients. The sanative methods may be passive and active. To the former belong postural drainage, administering expectorants, to the latter ones – all methods that consist in aspiration of the tracheobronchial tree contents and immediate administration of medicines into it. With a view to increase sputum excretion the following preparations are applied: preparations stimulating expectoration on account of passive secretion of bronchial glands, decreasing sputum tenacity, increasing activity of twinkling epithelium and peristalsis of bronchioles.

Criteria of effectiveness in the treatment of tuberculosis patients are:

1) the disappearance of clinical and laboratory signs of tubercular inflammation;
2) the stable termination of MBT expectoration, confirmed by microscopic and cultural examinations;
3) the regression of radiographic signs of tuberculosis (focal, infiltrative, destructive);
4) the restoration of functional and work capacity.

THANK YOU FOR YOUR ATTENTION!