Tuberculosis (pneumology)

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This article has been translated from WikiSkripta; ready for the **editor's review**.

Tuberculosis (TB; *TBC in Czech*) encompasses all states of disease caused by the *Mycobacterium tuberculosis complex*

Epidemiology

- Tuberculosis is a specific infectious disease that had already existed in ancient Greece and well as in the Roman empire.
- Currently it is the most common lethal infectious disease in the world, about 20 million people are suffering from tuberculosis and about 3 million people die of it each year.
- Tuberculosis continues to be a disease related to social status.
- The most common *source* of the infection is a *person infected by tuberculosis*.
- The term "tuberculosis" was introduced in the year 1834 by Scholein, but its etiology was discovered by Robert Koch.

Etiology

- The human tuberculosis is caused by *Mycobacterium tuberculosis*, *Mycobacterium bovis* and *Mycobacterium africanum* – altogether they are called the *Mycobacterium tuberculosis complex*.
- *Mycobacterium tuberculosis* is an acidoresistant, alcaliresistant and alcoholresistant aerobic microbe that grows optimally in temperatures of 37–38 °C and has a long generation period, which necessitates cultivation on special culture media for 12 weeks.

Pathogenesis

- **Transmission of the disease** happens by *inhalation* (droplets). A transmission by *direct contact* (inoculation) and by alimentary means.
- The **entryway for the infection** is the respiratory system in 80–90 % of all cases.

Classification

- **Primáry tuberculosis** – appears after the first contact with mycobacterial infection. Under favorable circumstances, *Mycobacterium tuberculosis* enters the lungs, where it propagates and causes local exudative inflammatory reaction – **primary infect**. Within several hours, the *Mykobakterium tuberculosis* spreads by lymphatic means into regional lymph nodes which swell and along with the pulmonary inflammation they create the **primary tuberculous complex**.
    - Often the primary tuberculosis spreads from the tuberculous lymphadenitis, the "caseified" node perforates into the bronchus and allows the aspiratory spread of tuberculosis.
    - In 90% of all cases, the disease heals spontaneously as hypersensitivity to *tuberculin* appears.
- **Postprimary tuberculosis** – in persons already infected, affects the lungs most often.
    - A common form of postprimary tuberculosis is the Asmann-Redeker's early subclavicular infiltrate.
    - The infiltrate undergoes caseous necrosis after some time → spread of tuberculosis by aspiration.
    - It spreads further either directly into the surroundings, by expectoration or by the swallowing of sputum (tuberculous laryngitis, intestinal tuberculosis), by lymphatic vessels or by blood.
        - ***Exogenous infection*** (reinfection in 30 %) – by inhalation of new mycobacteria during contact with the diseased.
        - ***Endogenous reactivation*** of the primary tuberculosis while being weakened by malnourishment, pregnancy or by alcoholism.
        - Healing of lesions caused by postprimary tuberculosis is accompanied by the proliferation of collagenous ligament, scarring and by fibrotization of the pulmonary parenchyme.

Clinical manifestation

- Primary infection can progress without symptoms, in children it can rarely manifest by heightened temperature, loss of appetite and lowered activity.
- Postprimary tuberculosis can progress asymptomatically as well or accompanied by uncharacteristic sneaking problems manifesting as a flu-like illness
- Functional symptoms in most cases of TB manifest as notable tiredness, loss of appetite, loss of weight, lowered physical output, subfebrilia, night sweats, dry and later productive cough, mucoid or even mucopurulent sputum.
- Hemoptysis is an alarming symptom.

Diagnosis

  - Isolation of 'Mycobacterium tuberculosis *from various materials (in pulmonary infections we examine the **sputum**, the **aspirate** obtained by bronchoalveaolar lavage, the **gastric aspirate** and sometimes the **laryngeal swab** in persons that cannot expectorate).*
  - *Microscopic examination* after special staining (Ziehl-Neelsen), it is possible to prove acidoresistant bacilli within 24 hours.

- *Cultivation examination* on different media is evaluated after 3 weeks at earliest, then after 6 and 9 weeks. The result is negative only when the Mycobacteria do not grow on the media even after 12 weeks.

  - Polymerase chain reaction – PCR.
  - X-ray – local shadows in upper thirds of the lung fields, the translucency of caverns may be visible.
  - ***Mantoux II test*** positive (larger than 6 mm in 72 h), after intradermal application of 2 tuberculin units.
  - ***QuantiFERON (http://mikrobiologie.lf3.cuni.cz/mikrobiologie/bak/uceb/obsah/quantif/quantif.htm)*** *(link in Czech)*

Severe forms of tuberculosis

- **Miliary TB**

  Caused by the hematogenous spread of *mycobacteria* and affecting any organ (lungs, liver, meninges, spleen).
  The clinical manifestation is changeable. The disease has three forms:

    - ***typhous form*** – sudden septic state with tachycardia unresponsive to common antibiotics;
    - ***pneumonic form*** – shortness of breath, cyanosis, tachycardia, tachypnea;
    - ***meningitidic form*** – confusion, slurred speech, headache, meningeal symptoms.

  Diagnosis – ***chest x-ray*** – symmetrical spread of a shadow comprised of miliary loci (1 mm in diameter).

- **Tuberculous pneumonia**

  Begins suddenly, with shivers, fever, profound sweats, exhaustion and cough with purulent expectoration. Only the formation of a cavern, nonexistent effect of antibiotics and a cultivation differentiating it from usual bacterial pneumonia lead to the correct diagnosis.

Diagnosis of tuberculosis

- Is stated based on symptoms, the characteristic image on the chest x-ray and the proof of *mycobacteria*.
- ***Differential diagnosis***: it is necessary to consider any pulmonary disease, nonspecific pneumonia, bronchogenic cancer, sarcoidosis, pulmonary infarction, silicosis, Wegener's granulomatosis, …

Therapy

- **Sensitivity to antituberculotics**

  - ***Primary resistance*** – a strain resistant to a concrete drug in an otherwise sensitive mycobacterial species gained from the patient that has evidently never been treated with this drug before (1-2% in the CZ)).
  - ***Initial resistance*** is a combination of primary resistance and undiscovered gained resistance, in case we can not rule out or confirm an earlier usage of the antituberculotic drug.
  - ***Gained (secondary) resistance*** – originally a sensitive strain of *Mycobacterium* that has, during or after the treatment, become resistant to the drug that the patient had used for more than one month. Usually the result of an improper treatment.
  - ***Polyresistance*** (multiple drug resistance, MDR) is a name for a state where the tuberculous mycobacteria became resistant to multiple antituberculotics, to isoniazid and rifampicin at minimum. It is the most severe form of bacterial resistance which manifests due to the improper usage of the therapeutic regimen.

- **Antituberculotics**

Bactericidal – which kill the bacteria during cell division (nidrazid, rifampicin, streptomycin).
Sterilization effect – which kill the so-called "persister cells" (pyrazinamide, rifampicin).
Antituberculotics with bacteriostatic effect (ethambutol).

- ***Rifampicin*** (RMP, R)

  Most effective bactericidal antibiotic, administered per os before breakfast in the morning at a dose of 450-600 mg.
  It affects *Mycobacteria* with low metabolic activity.
  Colors saliva, sweat and urine orange.
  Side effects: hepatitis, thrombocytopenia with purpura, flu-like syndrome, allergy, kidney damage and digestion problems.

- ***Isoniazid*** (isonicotinic acid hydrazide, INH, H)

  Administered per os at a dose of 5mg/kg of weight in a daily manner.
  Effective and cheap bactericidal drug that affects both extra- and intracellular *Mycobacteria*.
  Administered as a preventive measure after contact with TB.
  Side effects: peripheral neuritis, hepatotoxicity and allergy.

- ***Streptomycin*** (STM, S)

  An aminoglycoside antibiotic, administered intramuscularly once a day at 0.75-7.0 g.
  Bactericidal to extracellularly located mycobacteria.
  Side effects: ototoxiticity and nephrotoxicity, allergic skin reactions.

- ***Pyrazinamid*** (PZA, Z)

  Administered per os at a dose of 1.5-2.0 g/day.
  Bactericidal effect to mycobacteria phagocytosed intracellularly.
  It is hepatotoxic and affects the tubular secretion of uric acid (hyperuricemia, gout).

- ***Ethambutol*** (EMB, E)

  Administered per os at a dose of 25 mg/kg of weight.
  Synthetically prepared antituberculotic with a mycobacteriostatic effect.
  A serious side effect is the manifestation of retrobulbar neuritis with disorders of sight and color vision.

Strategy of treatment

- Combined, prolonged and controlled as to prevent bacterial resistance.
- Using the combination of at least 3 drugs in a single morning dose under the control of the nursing staff.
- Hospital treatment (initial phase) is usually limited to 2 months, e.g. 2 months of the RHZ regimen, during which the infectiousness drops to minimum and eventually the drug interactions and side effects of the therapy are being considered. Following treatment (follow-up phase) is managed at a clinic either daily, e.g. 4 RH – 4 months of RH, or intermittently, e.g. 4 R3H3 – RH 3 times a week for 4 months.
- Minimum length of the treatment of bacteriologically proven TB is 6 months, 4 months if unproven.
- Dispensarization (a sum of measures which includes preventive methods, search and mandatory report, proper treatment, constant surveillance of health state and maintenance of the work ability).

Literature

- HOMOLKA, Jiří. *Vnitřní lékařství Svazek III.* first edition. nakladatelství Galen, 2001. 122 pp. pp. 60 – 71. ISBN 80-7262-131-9.