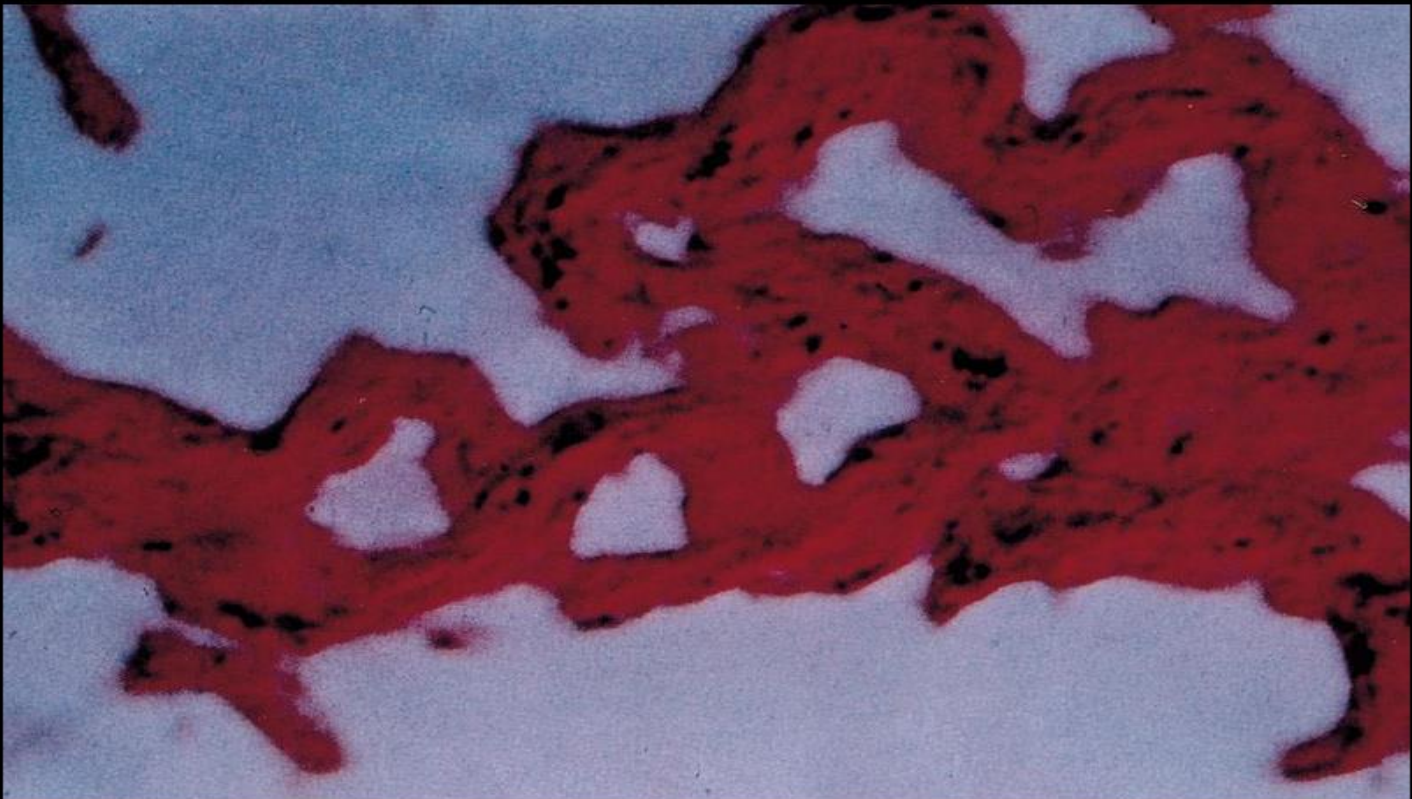


Tuberculosis

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Ziehl-Neelsen stain of 'cords' of *Mycobacterium tuberculosis* isolated from a broth culture. Tubercle bacilli aggregate end to end and side to side to form serpentine cords, especially in broth cultures.



TUBERCULOSIS

Etiology:

The most important causative agent of tuberculosis (TB) is **Mycobacterium tuberculosis**. - together with *M. bovis*, *M. africanum* and *M. microti*, form the 'M. tuberculosis complex', which is a group within the genus *Mycobacterium*. This genus also includes many different nontuberculous mycobacteria (NTM), of which *M. leprae* and *M. avium* are best known.

M. tuberculosis is typically a slightly curved or straight rod-shaped microbe. Its length is 2–5 µm and the generation time ranges from 12–24 hours. The bacterium is aerobic and non-spore forming ¹

The source of infection

Humans are the main source for *M. tuberculosis* and *M. africanum*. For *M. bovis*, cattle are the most important host. Cases of TB can occur sporadically in monkeys and some other mammals.

Route of transmission

Transmission of TB is aerogenic. After coughing, sneezing, speaking or singing, infected sputum droplets can dry and form into droplet nuclei of approximately 6–18 µm. These droplet nuclei can float in the air for a longer period and penetrate into the alveoli of the host after inhalation. In moist warm air, the droplet nuclei can survive for hours

Susceptibility

Susceptibility to TB is general. The highest susceptibility is in early childhood (under 4 years of age), puberty and in pregnant women. A higher risk of TB development exists in immunodeficient states, silicosis, diabetes, alcoholics, malign diseases, and in the sick with immunosuppressive treatment and HIV.

Preventive measures: is the foundation for effective TB control programmes. Preventive measures focusing on the early diagnosis and immediate effective treatment of people with contagious TB is therefore essential.

The vaccine currently available is the BCG-vaccine (Bacille Calmette Guérin). This is a live, weakened strain of *M. bovis*. It mainly gives protection against severe forms of the disease, like meningitis TB and miliary TB, in children under five years of age.

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Clinical features and diagnosis

Tuberculosis is a general chronic infectious disease mainly affecting the respiratory tract. In approximately 10 % of cases it has extrapulmonary localization.

The disease manifestations can be classed as **primary** and **postprimary**.

- **Primary TB infection** is characterized by **development of a primary complex** formed by a specific inflammation at the point of entry of BK (Koch's bacillus), peribronchial lymphangiitis and a specific inflammation of a regional lymphnode. A prevalent part of the primary complexes is **localized in the lungs**. An extrapulmonary primary complex usually develops due to a deglutition BK infection. Primary TB infection manifests through nonspecific symptoms and clears spontaneously. Calcification of the residual foci occurs during the further course of TB. Mycobacteria may persist there up to several decades and cause **endogenic reactivation of TB**. Only in about 10 % of infected individuals does the so-called postprimary TB develop in the course of life. **The primary infection confers cellular immunity**, its manifestation is a late-type tuberculin hypersensitivity (PPD).

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- **Postprimary TB** - all forms of tuberculosis which develop in primarily infected persons, i.e. in humans who had a positive tuberculin reaction prior to the disease. The spread of BK occurs by **preformed airways**, aspiration of the metastases, and sputum expectoration (larynx TB). The spread may occur by a **lymphatic route** when the agent surpasses the lymphatic barrier and reaches the blood. Dissemination into other organs occurs (e.g., bones, cerebral matter, joints, kidneys).
- The symptomatology of tuberculosis is varied depending on the scope of affection. In about 1/3 of cases the disease is long-term asymptomatic.


Infection with *M. tuberculosis* is asymptomatic. The symptoms that occur when TB disease develops are usually not very specific. Often there are complaints of tiredness, listlessness, loss of weight, sub-febrile body temperature and night sweating.

In the case of **pulmonary TB**, usually a cough has been present for weeks or even months, possibly accompanied by haemoptysis.

Localisation **in the vertebral column** (spondylitis tuberculosa) can, apart from back pain, also present itself as an abscess with vertebral collapse.

Lymphadenitis tuberculosa usually presents itself by painless lymph node enlargement in the neck.

Blood in the urine (haematuria) can present as the only symptom of **TB of the kidney**.



In cases of co-infection with HIV, the clinical presentation can be less typical. This atypical presentation is usually seen in a more advanced stage of the HIV infection and is the result of impaired cellular immunity.

HIV-infected patients show disseminated forms of TB relatively often.

M. tuberculosis can develop resistance to drugs by spontaneous chromosomal mutations.

When a case of active TB is not correctly treated, it can result in multidrug-resistant (MDR) TB and extensively drug-resistant (XDR) TB.

MDR TB is defined as TB bacteria that are resistant to at least isoniazid and rifampicin.

XDR TB means that, in addition to isoniazid and rifampicin, the TB bacteria are resistant to any fluoroquinolone and at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin)⁴.

In general, in patients with a positive Ziehl-Neelson slide and/or positive culture of their sputum, the start of coughing complaints is considered **to be the start of the period of infectiousness.**

- **The incubation period** (between infection and the first signs of illness) varies between eight weeks to a lifetime.

The greatest chance of progressing to disease is within the first two years after infection, with half of all cases of disease occurring within five years of the original infection. However, a lifelong risk of progression to disease remains for all those people with 'dormant' organisms. People in whom infection progresses to disease are only a minority of all infected persons.

People with latent TB infection are never infectious.

The risk of transmission in cases of active TB is determined by patient factors and the type of contact made with their surroundings.

The level of contagiousness of TB patients depends on:

- the concentration of bacteria in the sputum,
- the severity of the cough and
- the coughing hygiene practiced by the patient.

In general, the closer and/or more frequent the contact, the higher the chance of transmission.

Characteristics of the place of contact may also play an important role (e.g. size of the room, ventilation). Usually, intimate contacts (household) are at the highest risk of being infected.

PREVENTION

The vaccine currently available is the BCG-vaccine (Bacille Calmette Guérin). This is a live, weakened strain of *M. bovis*.

It mainly gives protection against severe forms of the disease, like meningitis TB and military TB, in children under five years of age.

- The World Health Organization (WHO) advises BCG-vaccination for all newborns in countries with a high incidence of TB within the framework of the Expanded Program of Immunization (EPI).
- Within the EU, the policy on BCG-vaccination varies between countries. Low incidence countries commonly vaccinate only persons with an increased risk of TB; for example, children whose parents come from high incidence countries and who travel regularly to their home country²

PREVENTION

- BCG-vaccination should not be given to the immunosuppressed (e.g. HIV, leukaemia, chemotherapy) due to the increased risk for complications. Also, BCG-vaccination during pregnancy should be avoided, even though no harmful effects on the foetus have been observed¹⁶.
- Practising cough hygiene will decrease the spread of all types of infections that are spread through the air.

PREVENTION

- Preventing the transmission of the disease is the foundation for effective TB control programmes.
- Preventive measures focusing **on the early diagnosis and immediate effective treatment** of people with contagious TB is therefore essential. Many factors have been shown to be associated with a delay in diagnosis including old age, low education/awareness, poverty, negative sputum smear, extrapulmonary TB, female sex and a history of immigration¹⁷.
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- Passive case finding is defined as the detection of TB cases among patients attending healthcare facilities because they have symptoms. Active case finding focuses on the screening of high-risk groups (immigrants, drug addicts, homeless people and prisoners) for TB. It aims to identify and treat TB cases at an early stage and to provide preventive treatment to those at the highest risk for developing active TB.