

1

## **PRIMARY TUBERCULOSIS**

2

TB is infectious disease with a long period between infection and disease.

After contact with the MBT probability of infection depends on the properties of the pathogen and host's susceptibility  
The first years after infection

3,4

The risk of disease depends on a number of factors.

Puberty

Reinfection MBT

HIV infection

Comorbidities

Corticosteroids and immunosuppressive therapy.

### **Primary infection**

Primary infection occurs in people who have not had any previous exposure to tubercle bacilli. Droplet nuclei, which are inhaled into the lungs, are so small that they avoid the mucociliary defences of the bronchi and lodge in the terminal alveoli of the lungs. Infection begins with multiplication of tubercle bacilli in the lungs. The resulting lesion is the Ghon focus. Lymphatics drain the bacilli to the hilar lymph nodes. The Ghon focus and related hilar lymphadenopathy form the primary complex. Bacilli may spread in the blood from the primary complex throughout the body. The immune response (delayed hypersensitivity and cellular immunity) develops about 4–6 weeks after the primary infection. The size of the infecting dose of bacilli and the strength of the immune response determine what happens next. In most cases, the immune response stops the multiplication of bacilli. However, a few dormant bacilli may persist. A positive tuberculin skin test would be the only evidence of infection. In a few cases the immune response is not strong enough to prevent multiplication of bacilli, and disease occurs within a few months.

### **Post-primary TB**

Post-primary TB occurs after a latent period of months or years following primary infection. It may occur either by reactivation of the dormant tubercle bacilli acquired from a primary infection or by reinfection. Reactivation means that dormant bacilli persisting in tissues for months or years after primary infection start to multiply. This may be in response to a trigger, such as weakening of the immune system by HIV infection. Reinfection means a repeat infection in a person who has previously had a primary infection.

The immune response of the patient results in a pathological lesion that is characteristically localized, often with extensive tissue destruction and cavitation. Post-primary TB usually affects the lungs but can involve any part of the body. The characteristic features of post-primary TB are the following: extensive lung destruction with cavitation; positive sputum smear; upper lobe involvement; usually no intrathoracic lymphadenopathy. Patients with these lesions are the main transmitters of infection in the community.

фильм

**5**

The cumulative risk of disease for the first 5 years is 5-10%, and 5% throughout life. One is likely to be infected by contact with the MBT+ microscopic in 8-10 times higher than the MBT + culture, at 16-20 times higher than with the MBT-

**6**

### **Tuberculosis in children.**

Each year become ill 1.3 million children, 450,000 children die before the age of 15 years.

**Progressive primary TB. Common and extra pulmonary symptoms (erythema nodosum, pharyngitis, joint inflammation phlyctenular conjunctivitis). Primary infectious complex (tuberculous mediastinal lymphadenitis and endobronchial tuberculosis). Progressive primary pulmonary tuberculosis. Reactivated pulmonary disease.**

The incidence and prevalence of pediatric tuberculosis (TB) worldwide varies significantly according to the burden of the disease in different countries. It has been estimated that 3.1 million children under 15 years of age are infected with TB worldwide. According to the World Health Organization (WHO), children with TB represent 10 % to 20 % of all TB cases. The majority of these cases occur in lowincome countries where the prevalence of HIV-infection is high. According to WHO reports, India, China, Pakistan, the Philippines, Thailand, Indonesia, Bangladesh, and the Democratic Republic of the Congo account for nearly 75 % of all cases of pediatric TB. Furthermore, it has also been reported that TB is responsible in Sub-Saharan countries for between 7% and 16% of all episodes of acute pneumonia in HIV-infected children, and for approximately one fifth of all deaths in children presenting with acute pneumonia.

**7**

Tuberculosis in children is difficult to diagnose, even in its pulmonary form; children rarely produce sputum, so sputum smear examination can therefore not be used to obtain bacteriological proof, which is the cornerstone of diagnosis in adults. It is therefore diagnosed using a systematic approach whereby a number of clinical signs are interpreted.

## **8**

Risk factors of childhood TB are following:

- epidemiology (contact with TB patients, infection acquisition)
- biomedical (weighed premorbid background, defects BCG vaccination, hyperergic TST)
- socioeconomic (adverse living conditions)

## **9**

The basic points for childhood TB are following:

- TB is not a congenital disease
- Children infected with TB from adults
- This is a disease of the whole body
- Primary infection - high risk, but the disease may not be apparent for many years
- TB is the most dangerous for young children
- Adequate protection is BCG-vaccination
- TB can be cured

## **10**

TB disease in children is usually primary TB. Post-primary TB may occur in adults following reactivation of dormant TB bacilli acquired in childhood. The age when a child is infected determines the pattern of primary disease. Pulmonary disease in young children is closely linked to pathology of the mediastinal nodes. This is lymphobronchial TB, which results in a wide spectrum of segmental lesions. These lesions may also be found in adults, but are unusual. Young children (i.e. less than 5 years of age) are particularly susceptible to severe forms of disseminated disease following primary infection. These severe forms include miliary TB and extrapulmonary forms of TB, e.g. meningitis.

Tuberculosis disease presents in various clinical forms:

- primary pulmonary tuberculosis;
- acute disseminated tuberculosis: meningitis and miliary tuberculosis;
- post-primary pulmonary tuberculosis;
- extrapulmonary tuberculosis.

## **11**

### **Clinical approach to childhood TB includes:**

- Careful history taking (TB contact, risk factors, symptoms of the disease)
- Physical examination (based on age)
- TST
- microbiological examination
- X-ray examination

## **12**

LTBI is the presence of *M. tuberculosis* organisms (tubercle bacilli) without symptoms or radiographic evidence of TB disease.

LTBI is characterized with

- TST or QFT positivity
- Negative chest radiograph
- No symptoms or physical findings suggestive of TB disease

Active TB disease is characterized with

- TST or QFT usually positive
- Chest radiograph may be abnormal
- Symptoms may include one or more of the following: fever, cough, night sweats, weight loss, fatigue, hemoptysis, decreased appetite
- Respiratory specimens may be smear or culture positive

## **13**

### **Primary pulmonary tuberculosis**

The diagnosis of TB is particularly difficult in children because, under the age of 6–8 years, children with TB rarely cough up sputum. The readily available usual test for adults and older children with PTB is sputum smear microscopy. However, there is no such “gold standard” test for the majority of children with TB. Young children usually swallow their sputum. Gastric suction and laryngeal swabs are generally not useful. This means that bacteriological confirmation is usually not possible. The diagnosis of TB in children is therefore nearly always presumptive.

There are no specific features on clinical examination that can confirm that the presenting illness is due to TB. Respiratory symptoms and disease are extremely common in childhood, particularly before 5 years of age. In most cases of suspected TB, the child has been treated with a broad-spectrum antibiotic, with no clinical response.

## **14**

Always look for three important clues to TB in children:

1) Contact with an adult or older child with smear-positive PTB. It is usually possible to identify the source of infection. This is most often the child's mother or another female carer, such as an aunt, grandmother or older sister. They are the ones who spend most time with young children. Adult cases of PTB are occasionally diagnosed when a child presents with suspected TB.

2) Failure to thrive or weight loss (growth faltering). This is a good indicator of chronic disease in children and TB may be the cause. It is not specific and may also be due to poor nutrition, persistent or recurrent diarrhoea or HIV infection.

3) Respiratory symptoms such as cough lasting for more than three weeks in a child who has received a course of broad-spectrum antibiotics.

Primary infection is asymptomatic in the majority of cases, and goes unnoticed. This is termed infection and must be distinguished from disease. In 10% of cases primary infection has clinical manifestations and presents with certain symptoms and radiographic abnormalities. Generalized symptoms are often subtle: slight fever, loss of weight, apathy and listlessness can attract the attention of the parents. Sometimes the symptoms are more obvious (e.g. a high fever of 39–40°C and profound lethargy), and alert the parents to the fact that something is wrong.

## 15

Mucocutaneous manifestations, although infrequent, are highly characteristic:

Erythema nodosum appears in the form of painful nodules on the shins, sometimes on the backs of the arms and rarely on the front, in two to three bursts. They are painful, red, raised lesions that may turn purple and take on the appearance of a bruise;

Phlyctenular conjunctivitis begins with generalized pain and irritation in one eye accompanied by watering and photophobia. On examination, grey or yellow lesions can be observed where the cornea joins the white of the eye; a number of blood vessels enter the lesions, giving an appearance of vascular engorgement of the conjunctiva. Each lesion persists for about a week, then disappears, to be replaced by others. In severe cases the cornea may ulcerate.

## 16

Radiological signs of primary pulmonary tuberculosis are characteristic. On postero-anterior and lateral radiography, the following may be observed:

- typical primary complex, the most frequent manifestation, consists of a small area of infiltration at any location in the lung parenchyma, accompanied by unilateral mediastinal lymphadenopathy. The infiltration forms when the bacilli are first

inhaled (as a defence reaction around the location at which the bacilli first deposit); it is characteristically small (3 to 10mm in diameter). This nodular shadow is sometimes surrounded by a lighter, less dense shadow with irregular edges. On lateral X-ray, mediastinal lymphadenopathy appears as a rounded or oval latero-tracheal or hilar shadow.

- in some cases, isolated mediastinal lymphadenopathy may occur without any visible changes in the pulmonary parenchyma;
- occasionally, primary infection lesions may present as segmental (or lobar) consolidation associated with mediastinal lymphadenopathy. This is shadowing of a discrete area (usually right middle lobe, or lingula on the left), with clear margins and no bronchial markings, caused by compression of the (usually) middle lobe bronchus. It can mask the infiltration and even part of the causal lymphadenopathy.

### **17-21**

The course of primary tuberculosis is usually benign, whether or not the child is treated, and most children recover completely without sequelae. They may, however, subsequently develop active tuberculosis (reactivate) after a period of quiescence.

### **22**

**Local complications of primary tuberculosis**, while unusual, are well recognized:

fistulation of the lymph node into the bronchi: the lymph node swells and erodes into the bronchus (usually between the 4th and 7th month of development). This can be a serious event for small infants, where the caseous material can create acute bronchial obstruction; in older children it usually causes cough;

the formation of a primary tuberculous cavity at the site of infiltration is a more unusual complication.

In both cases the child is usually incapable of producing sputum, but if a sample of bronchial or gastric aspiration is obtained, acid-fast bacilli can be recovered from smear microscopy.

*Delayed local complications can result from the sequelae. Without treatment, lymphadenopathy can compress a lobar or segmental bronchus, creating breathing difficulties. Bronchiectasis may develop in the poorly ventilated area of the lung, creating bronchial superinfections and repeated episodes of haemoptysis. The most characteristic feature of this type of sequelae is “hilar disease” or “right middle lobe syndrome”: atelectasis, hilar calcification and recurrent haemoptysis. Antero-posterior and lateral X-ray will show systematic, very dense retractile shadowing, with concave edges, with some clear images and hilar calcifications in the centre.*

## 23

### **Acute forms of tuberculosis**

These are early complications of primary infection (within 2–10 months). Caused by the dissemination of bacilli from the primary infection through the bloodstream, they can occur at all ages, but do so most often in very young children (<2 years of age), particularly if they have not been vaccinated with BCG. They are serious, and are often fatal if diagnosed late.

#### **Miliary disease.**

Disseminated tuberculosis is a form of the disease that affects many sites in the body simultaneously and is not limited to the lungs.

This is generalized, massive infection characterized by diffusion throughout the organism, of very small nodular elements («millet seeds»). It can occur immediately after primary infection or during reactivation of a latent site. Its onset may be either insidious or abrupt, depending on the bacillary load and/or the host immune situation, with unvaccinated infants, elderly and immunodeficient patients being the most susceptible.

Clinical manifestations are nonspecific and protean, depending on the predominant site of involvement. The clinical picture is completed in one to two weeks. Fever, night sweats, anorexia, weakness, and weight loss are presenting symptoms in the majority of cases. At times patients have a cough and other respiratory symptoms due to pulmonary involvement as well as abdominal symptoms. Physical findings include hepatomegaly, splenomegaly, and lymphadenopathy. Eye examination may reveal choroidal tubercles, which are pathognomonic of miliary tuberculosis, in up to 30% of cases. Meningismus occurs in <10% of cases.

## 24

A high index of suspicion is required for the diagnosis of miliary tuberculosis. Frequently, chest radiography reveals a miliary reticulonodular pattern, although no radiographic abnormality may be evident early in the course and among HIV-infected patients. Other radiologic findings include large infiltrates, interstitial infiltrates (especially in HIV-infected patients), and pleural effusion.

Sputum smear microscopy is negative in 80% of cases.

Various hematologic abnormalities may be seen, including anemia with leukopenia, lymphopenia, neutrophilic leukocytosis and leukemoid reactions, and polycythemia. Disseminated intravascular coagulation has been reported. Elevation of alkaline phosphatase levels and other abnormal values in liver function tests are detected in patients with severe hepatic involvement.



The TST may be negative in up to half of cases, but reactivity may be restored during chemotherapy.

Bronchoalveolar lavage and transbronchial biopsy are more likely to provide bacteriologic confirmation, and granulomas are evident in liver or bone-marrow biopsy specimens from many patients.

If it goes unrecognized, miliary tuberculosis is lethal; with proper early treatment, however, it is amenable to cure.