

## **SECONDARY PULMONARY TUBERCULOSIS.**

In an adult, pulmonary tuberculosis may arise in a number of ways.

Progression of a primary lung infection in a person who has never previously been infected (previously tuberculin negative). In progressive primary tuberculosis in adults, the mid and lower parts of the lung are involved more frequently than the upper lung zones.

Progression of lung lesions comes from the blood spread of bacilli, which normally occurs after a primary lesion. These bacilli may end up in the lung as in other organs (Figure 3.1). If there are many bacilli and defences are poor, disseminated tuberculosis results. If there are only a few bacilli and defences are good, the bacilli may be killed. In between, lesions may start at one or both apices of the lung and later spread to other areas. This is an uncommon way for adult tuberculosis to develop.

Reactivation of an earlier primary infection, perhaps years after a childhood infection by TB (Figure 3.2a-d). The patient's defences may have kept the lesion under control in childhood, but lowering of the patient's defences (e.g. by malnutrition, pregnancy, parturition or other diseases) may allow the TB to become active and spread the disease. In post-primary tuberculosis, the lesion is often in the apex or upper zone of the lung. The lung lesion is often more obvious than the lymph node enlargement, which you may not be able to detect on an X-ray. This is a common way for tuberculosis to develop in adults.

Reactivation of an old post-primary lesion that had been partially healed.

Re-infection may happen in persons previously infected with tuberculosis and progress to disease.

## **CLINICAL ASPECTS**

### **Pulmonary TB in adults**

The most frequent form of presentation of tuberculosis is disease that affects the lungs (pulmonary tuberculosis), while less frequent forms may affect any part of the body (extra-pulmonary tuberculosis) or present as acute disseminated tuberculosis.

#### ***Symptoms***

The most important symptoms in the diagnosis of PTB are the following:

- cough for more than 2 or 3 weeks;
- sputum production;
- weight loss.

Over 90% of patients with sputum smear-positive PTB develop a cough soon after disease onset. However, cough is not specific to PTB. Cough is common in smokers and in patients with acute upper or lower respiratory tract infection. Most acute respiratory infections resolve within 3 weeks. Therefore a patient with a cough for more than 2 or 3 weeks is a PTB suspect and must submit sputum samples for diagnostic microscopy.

Patients with PTB may also have other symptoms. These may be respiratory or constitutional (general or systemic).

***Respiratory:*** chest pain, hemoptysis, breathlessness.

***Constitutional:*** fever, night sweats, tiredness, loss of appetite, secondary amenorrhoea.

### ***Physical signs***

The physical signs in patients with PTB are nonspecific. They do not help to distinguish PTB from other chest diseases. There may be general signs, such as fever, tachycardia (fast pulse rate) and finger clubbing. Chest signs (heard through a stethoscope) may include crackles, wheezes, bronchial breathing and amphoric breathing. There are often no abnormal signs in the chest.

The first screening test for PTB suspects is sputum smear microscopy. In most cases of sputum smear-positive PTB a CXR is not necessary. In a few cases, a CXR may be necessary; the indications are as follows:

- a) suspected complications in a breathless patient, needing specific treatment, e.g. pneumothorax, pericardial effusion or pleural effusion (note that a positive sputum smear is rare in pericardial effusion and pleural effusion);
- b) frequent or severe haemoptysis (to exclude bronchiectasis or aspergilloma);
- c) only 1 sputum smear positive out of 3 (in this case, an abnormal CXR is a necessary additional criterion for the diagnosis of sputum smear-positive PTB).

For practical purposes, a normal chest X-ray excludes tuberculosis. Very rarely, however, endobronchial tuberculosis or disease hidden by the mediastinum or diaphragm may look like a normal chest X-ray.

The following X-ray shadows are strongly suggest of tuberculosis:

upper lobe infiltrates or bilateral infiltrates

upper zone patchy or nodular shadows (on one or both sides)

cavitation

pulmonary fibrosis and shrinkage

oval or round solitary shadow

diffuse small nodular shadows (miliary tuberculosis)

If you suspect tuberculosis from the X-ray but the sputum is negative, give a non-tuberculosis antibiotic for 7-10 days then obtain another X-ray. Shadows of an acute pneumonia will show improvement.

**Acute progressive pulmonary TB. Risk factors of acute TB progression, course and prognosis.**

Acute progressing TB disease is severe pulmonary affection which can be various by pathogenesis. It develops in predisposed patients with immunodeficiency and other risk factors. Clinical signs of phthisis are rapid onset, severe intoxication, hectic consumption, leanness and cachexia, extensive lung lesion and often TB generalization which predicts lethality. Fatal prognosis in spite of intensive treatment is typical for acute progressing TB disease.

Risk factors of acute TB progressing:

1. drug resistance of MBT
2. HIV infection
3. severe side effects of anti-TB drugs which make impossible adequate treatment application
4. concomitant diseases such as diabetes, immunosuppression of various genesis, alcoholic debilitation, poor nutrition, etc.

Earlier described miliary tuberculosis is an acute TB form which is highly specific for primary progressing and HIV associated tuberculosis. That is characterized by a wide hematogenous dissemination throughout the entire body (rare in an individual organ) and by the tiny size of the lesions (1–5 mm). The second one is caseous pneumonia which develops in predominated patients but without favorable conditions for hematogenous generalization.

Caseous pneumonia is an acute progressing TB form in which tubercles are not prominent, but with a diffuse extensive cellular infiltration that undergoes caseation that affects large areas of lung.

The symptoms of caseous pneumonia are determined by extension and intensity of inflammation. The disease starts acutely with hectic fever (40-41° C in the evening and normal or even lower in the morning), sometime fever may become permanently high or low in terminal stage. Acute adinamia, weight loss, profuse sweating, dyspnoea, chest pain, coughing with voluminous sputum are specific in such patients. Hemoptysis often occurs from eroded vessels. Profuse lung hemorrhage leading to asphyxia can become a reason of fulminant death. X-ray visualizes massive, of the whole lobe or more, infiltration with giant cavities. Lesion spreads fast and often

involves the whole lung. Bilateral total affection is not rare. Sputum is smear positive and the patients are highly contagious. Blood analysis shows ESR increasing and leucocytosis with toxic granulation. Lymphocytopenia frequently occurs which predicts unfavorable prognosis. In majority of cases patients' predisposition and acute progressing risk factors determine impossibility of curing and lethality rate in patients with caseous pneumonia is predictably high. If case is effectively cured cavities acquire fibrotic walls and caseous pneumonia transforms to chronic caverns. In little portion of cases if advanced fibrosis and cirrhotic transformation predominate TB inflammation can gradually lose the activeness which may be followed by getting completely recovered.

**Tuberculoma – pathogenesis, histopathology and clinical aspects. Radiographic features and verification methods. Course and prognosis. Indication for surgical treatment.**

The lung tuberculoma – a special form of secondary tuberculosis, characterized by the development of lung dense caseous focus rounded form, separated from the surrounding tissue by a fibrous capsule.

The source of tuberculoma formation basically two forms of lung tuberculosis are served: infiltrative and focus. Besides tuberculoma could be formed from cavernous lung tuberculosis by means of filling of cavity with caseous masses.

Types of tuberculoma:

- 1) infiltrative-pneumonic tuberculoma – encapsulated quite fresh focus of caseous pneumonia;
- 2) caseoma is like the next step in the evolution of delimited caseous focus (desintegration, compaction, calcification, resorption);
- 3) filled cavity - pseudo-tuberculoma.

Variants of the tuberculoma aggravation;

- 1) development of the perifocal inflammation;
- 2) cavitation – discharge of the caseous masses from a cavity, through draining bronchus.

The term lung tuberculoma unites aetiologically various capsulated caseous focuses more than 1 cm in diameter cavities.

Tuberculoma can be single or multiple. Distinguished small tuberculoma (up to 2 cm in diameter), average (2 — 4 cm) and large (more than 4 cm in a diameter).

Three clinical variants of tuberculoma course are allocated:

1) progressing, described by occurrence at any stage of illness of disintegration, perifocal inflammation around tuberculoma, bronchogenic dissemination in surrounded lung tissue;

2) stable — absence of tuberculoma rentgenological changes or rare aggravations without signs of tuberculoma progressing;

3) regressing tuberculoma is characterized, by slow reduction in its size with the subsequent focus or group of focuses formation on its place, and of the field of indurations or combination of these changes.

The proportion tuberculoma among all forms of lung tuberculosis make 6 — 10 %. It is explained that large infiltrative pneumonic processes under influence of treatment and the increase of a host resistance becoming limited, are condensed, losing the aggravated course. Process recovers not completely, the precisely outlined dense formations remain in the places of infiltrations.

Clinical signs. As tuberculoma in itself is a parameter of high body resistance, frequently patients with this form of lung tuberculosis easy reveal casually, at fluorography examinations, routine examinations, at presence of other diseases. Practically the patients do not show complaints. At tuberculoma usually symptoms of intoxication, peculiar to tuberculosis: weakness, weight loss, sweating, cough, raise of temperature are absent. There are periods of expectoration of a big amount of sputum with inclusion of caseous grains.

At physical examination of the patient any pathological signs in lungs often usually are not presented. The crackles are listened only at massive inflammation with widespread infiltrative changes around tuberculoma or its disintegration.

X-ray image of tuberculoma looks like rounded shadow with precise contours. Inside of the shadow circle form of enlightenment, boundary localized could be observed due to disintegration. Sometimes there are perifocal inflammation and small amount of bronchogenic focuses, and also calcification sites. Calcinated lymphatic nodes could be revealed In lungs roots. For tuberculema localization in II, I and VI segments are typical, more often in lateral position. The focuses could be revealed around tuberculoma, insignificant fibrosis, pleural deposits. Frequently tuberculoma is connected with visceral pleura by gentle bars.

The picture of blood without peculiarities, sometimes at acute stages moderate acceleration of ESR observed.

Mycobacterium tuberculosis is not found in sputum at stable course of tuberculoma, but at presence of disintegration bacilli expectoration meets if there is connection with drainage bronchus.

At the background of chemotherapy the tuberculoma is regressing or proceeding chronically without any aggravations among the 80% of patients.

If in tuberculoma the disintegration is long kept and the patient continues to expectorate MBT, and prolong therapy does not give desirable results, the surgery intervention is recommended.

Surgical treatment. Usually operation is made with the minimal removal of lung tissue — segmenal resection. The surgical treatment is shown also in cases, when there is no certainty that the patient ill with tuberculosis and it is difficult to distinguish tubercular tuberculoma from other lung diseases.

### **CHRONIC TB DISEASE. DRUG RESISTANT TUBERCULOSIS. TUBERCULOSIS COMPLICATIONS.**

The tuberculous granuloma gradually develops into a fibrous tubercle. Collagenous fibres invade the tuberculous focus, which is enclosed in a fibrous shell with fibroblasts and lymphocytes, forming a fibro-caseating granuloma that is then transformed into a fully fibrous tubercle. This focus can become entirely calcified. Chronic forms of TB disease develop as it lasts at least for 2 years which is enough for wide expressed lung fibrosis developing. The reasons for chronic forms occurring are following:

1. Late case-finding when the lung tissue is destructed and cavities have a rigid fibrotic wall due to which it cannot get cured
2. Primary drug resistance of MBT which can be the reason of treatment fail
3. Secondary drug resistance developing as a result of incorrect treatment application (especially if it is uncontrolled by medical stuff)
4. Patient's non-adherence to the treatment.

Chronic forms develop as a result of undulate progression of TB inflammation. Cavernous tuberculosis is intermediate form between infiltrative tuberculosis with lung tissue disintegration and chronic forms of pulmonary tuberculosis. This form is characterized by the presence of a thin-walled cavity without perifocal infiltration. The lung cavities have an external fibrotic capsule and contain undischarged caseous masses. X-ray examination shows a round cavity with a thin wall and which usually localizes in subclavicular area. The scarring and fibrous tissue is forming at long existence of a cavity so it becomes to be rigid. MBT and elastic fibres are found in sputum but the portion of patients may become smear-negative or for detection of MBT not only bacterioscopy, but culture method is necessary.



As a cavity exists longer than 2 years the sclerosis of surrounding tissue highly progresses which is specific for chronic pulmonary TB disease. Irregular change of progression and remission is representative for fibrous-cavernous pulmonary tuberculosis. Fibrotic cavity has a thick three-layered wall – the inner layer consists of caseous masses, the middle layer is performed by tubercular granulation tissue and the external layer of a cavity wall consists of the rigid fibrosis. The process can be unilateral and bilateral with one or many cavities. Focuses of bronchogenic dissemination are usual for chronic forms. High concentration of MBT which is often resistant to anti-TB drugs is specific. These patients represent the most epidemiologically dangerous contingent being the sources of TB infection in population.

If lung cirrhosis predominates (cirrhotic tuberculosis) then the concentration of MBT is not high and it may often not be found in sputum by bacterioscopy but only by culture method. Such cases can be stable and possible to get cured by long treatment courses.

For chronic TB forms the high frequency of pulmonary and non-pulmonary complications is specific, such as respiratory failure, haemophthysis, spontaneous pneumothorax, systemic amiloidosis and so on. Healing in such patients is often impossible especially in MDR-TB cases, and cachexia accompanied by different complications becomes the reason of lethal outcome.

Drug resistance in tuberculosis is the result of selection of resistant mutants in the bacterial population, due to killing of susceptible bacilli by anti-TB drugs. The problem is greatly exacerbated by inadequate treatment such as direct or indirect monotherapy, resulting from intake of a single anti-TB drug or from intake of several drugs with suboptimal concentrations. Susceptible bacilli are killed rapidly and resistant mutants are then able to multiply. Mycobacterium tuberculosis has the ability to undergo spontaneous, slow but constant mutation, resulting in resistant mutant organisms. This natural phenomenon is genetically determined and varies from drug to drug.

As with other infectious diseases, from staphylococcal infections to malaria, pathogens have almost invariably developed resistance to the drugs used to treat them. Tuberculosis is no exception: strains resistant to streptomycin were identified within months of the start of use, in the mid 1940s, of this first antituberculosis drug. Indeed, the emergence of drug resistance was the primary reason that therapy for TB evolved to include treatment with more than one drug for up to 18 to 24 months – the standard

of care for over two decades. The advent of rifampicin in the early 1970s permitted a drastic reduction in the duration of therapy to six months while the efficacy of treatment improved. But in the mid-1990s, most countries participating in a global survey of anti-TB drug resistance registered cases of MDR-TB.

The main reason for the development of drug resistance is inadequate therapy.

### **Types of drug resistance.**

**Primary resistance** is due to infection with a resistant strain, originating from a patient who has acquired resistance as a result of inadequate treatment. Thus the patient with primary resistance to a drug has never taken this drug in the past, but the original source of infection must have done so.

**Acquired (secondary) resistance** occurs when a patient is exposed to a single drug through failure of the programme to ensure adherence to treatment, or because of selective drug intake, irregular drug supply, poor drug quality, inappropriate prescription, or, rarely, erratic absorption of medications. The growth of bacilli susceptible to that drug is suppressed, but multiplication of resistant organisms continues.

A «natural» **drug-resistant** strain is a wild strain that is resistant to a particular drug without ever having been in contact with it: neither the patient with naturally resistant bacilli nor the source of infection has received treatment with that drug in the past. This type of drug resistance is of little practical importance.

**Multidrug-resistant tuberculosis (MDR-TB)**, defined as TB caused by organisms that are resistant to isoniazid and rifampicin, two first-line anti-TB drugs. It can occur primarily (a patient infected by someone with MDR-TB) or secondarily (poor prior therapy). In most cases, resistance followed erratic treatments. MBT+ TB patients with resistant bacilli are as contagious as those infected by sensitive bacilli.

**Mono or poly-drug resistance (PDR)** – resistance to at least isoniazid or rifampicin but not both simultaneously or another first-line drugs. These patterns of resistance require adapted regimen in order to prevent possible evolution to MDR-TB under standard regimen

**Extensive drug-resistant TB (XDR-TB)**, defined as MDR-TB that is resistant as well to any one of the fluoroquinolones and to at least one of three injectable second-line drugs (amikacin, capreomycin or kanamycin), has heightened this threat. XDR-TB has been identified in all regions of the world since 2006. Treatment outcomes are significantly worse in XDR-TB patients than in MDR-TB patients.



Outbreaks of XDR-TB in populations with high prevalence of HIV have caused alarmingly high mortality rates.

**Hemoptysis** is coughing up of blood from the respiratory tract. Massive hemoptysis is production of  $\geq 600$  mL of blood within 24 h.

Most of the lung's blood (95%) circulates through low-pressure pulmonary arteries and ends up in the pulmonary capillary bed, where gas is exchanged. About 5% of the blood supply circulates through high-pressure bronchial arteries, which originate at the aorta and supply major airways and supporting structures. In haemoptysis, the blood generally arises from this bronchial circulation, except when pulmonary arteries are damaged by trauma, by erosion of a granulomatous or calcified lymph node or tumor, or, rarely, by pulmonary arterial catheterization or when pulmonary capillaries are affected by inflammation.

Physical examination: Vital signs are reviewed for fever, tachycardia, tachypnea, and low O<sub>2</sub> saturation. Constitutional signs (e.g., cachexia) and level of patient distress (e.g., accessory muscle use, pursed lip breathing, agitation, decreased level of consciousness) should also be noted.

A full lung examination is done, particularly including adequacy of air entry and exit, symmetry of breath sounds, and presence of crackles, rhonchi, stridor, and wheezing. Signs of consolidation (e.g., egophony, dullness to percussion) should be sought. The cervical and supraclavicular areas should be inspected and palpated for lymphadenopathy (suggesting cancer or TB).

Neck veins should be inspected for distention, and the legs and presacral area should be palpated for pitting edema (suggesting heart failure). Heart sounds should be auscultated with notation of any extra heart sounds or murmur that might support a diagnosis of heart failure and elevated pulmonary pressure.

The abdominal examination should focus on signs of hepatic congestion or masses, which could suggest either cancer or hematemesis from potential esophageal varices.

The skin and mucous membranes should be examined for ecchymosis, petechiae, telangiectasia, gingivitis, or evidence of bleeding from the oral or nasal mucosa.

If the patient can reproduce hemoptysis during examination, the color and amount of blood should be noted.

The following findings are of particular concern:

- Massive hemoptysis
- Back pain

- Presence of a pulmonary artery catheter or tracheostomy
- Malaise, weight loss, or fatigue
- Extensive smoking history
- Dyspnea at rest during examination or absent or decreased breath sounds

## **Treatment**

Massive hemoptysis. Initial treatment of massive hemoptysis has two objectives:

- Prevent aspiration of blood into the uninvolved lung (which can cause asphyxiation)
- Prevent exsanguination from ongoing bleeding

It can be difficult to protect the uninvolved lung because it is often initially unclear which side is bleeding. Once the bleeding side is identified, strategies include positioning the patient with the bleeding lung in a dependent position and selectively intubating the uninvolved lung and/or obstructing the bronchus going to the bleeding lung.

Prevention of exsanguination involves reversal of any bleeding diathesis and direct efforts to stop the bleeding. Clotting deficiencies can be reversed with fresh frozen plasma and factor-specific or platelet transfusions. Laser therapy, cauterization, or direct injection with epinephrine or vasopressin can be done bronchoscopically.

Massive hemoptysis is one of the few indications for rigid (as opposed to flexible) bronchoscopy, which provides control of the airway, allows for a larger field of view than flexible bronchoscopy, allows better suctioning, and is more suited to therapeutic interventions, such as laser therapy.

Embolization via bronchial artery angiography is becoming the preferred method with which to stop massive hemoptysis, with reported success rates of up to 90%. Emergency surgery is indicated for massive hemoptysis not controlled by rigid bronchoscopy or embolization and is generally considered a last resort.

## **Spontaneous pneumothorax.**

Air is not normally present between the visceral and parietal pleural surfaces. However, air can be introduced into the pleural space by a break in the surface of either pleural membrane, thus creating a pneumothorax.

A pneumothorax can result from a break in the parietal pleura (e.g., from trauma, needle or catheter insertion) or in the visceral pleura (e.g., from rupture of a subpleural air pocket, necrosis of lung adjacent to the pleura).

Intrapleural pressure is normally negative (less than atmospheric pressure) because of inward lung and outward chest wall recoil. In pneumothorax, air enters the pleural space from outside the chest or from the lung itself via mediastinal tissue planes or direct pleural perforation. Intrapleural pressure increases, and lung volume decreases.

Tension pneumothorax is a pneumothorax causing a progressive rise in intrapleural pressure to levels that become positive throughout the respiratory cycle and collapses the lung, shifts the mediastinum, and impairs venous return to the heart. Air continues to get into the pleural space but cannot exit. Without appropriate treatment, the impaired venous return can cause systemic hypotension and respiratory and cardiac arrest (pulseless electrical activity) within minutes.

### **Symptoms and Signs**

Small pneumothorax is occasionally asymptomatic. Symptoms of pneumothorax include dyspnea and pleuritic chest pain. Dyspnea may be sudden or gradual in onset depending on the rate of development and size of the pneumothorax. Pain can simulate pericarditis, pneumonia, pleuritis, pulmonary embolism, musculoskeletal injury (when referred to the shoulder), or an intra-abdominal process (when referred to the abdomen). Pain can also simulate cardiac ischemia, although typically the pain of cardiac ischemia is not pleuritic.

Physical findings classically consist of absent tactile fremitus, hyperresonance to percussion, and decreased breath sounds on the affected side. If the pneumothorax is large, the affected side may be enlarged with the trachea visibly shifted to the opposite side. With tension pneumothorax, hypotension can occur.

### **Diagnosis**

The diagnosis is suspected in stable patients with dyspnea or pleuritic chest pain and is confirmed with upright inspiratory chest x-ray. Radiolucent air and the absence of lung markings juxtaposed between a shrunken lobe or lung and the parietal pleura are diagnostic of pneumothorax. Tracheal deviation and mediastinal shift occur with large pneumothoraces.

### **Treatment**

- Immediate needle decompression for tension pneumothorax[
- Observation and follow-up x-ray for small, asymptomatic, primary spontaneous pneumothorax[
- Catheter aspiration for large or symptomatic primary spontaneous pneumothorax
- Tube thoracostomy for secondary and traumatic pneumothorax[

