

1.8 Cystic fibrosis (of the lungs)

It is an inherited disorder, which has the character of a multisystemic disease. Its essence resides in abnormal function of exocrine glands. Almost every patient with this disorder develops a chronic progressive disease of the respiratory system which is the most frequent cause of the morbidity and mortality in patients with cystic fibrosis. Besides the pulmonary manifestation pancreatic dysfunction, hepatobiliary and urogenital disturbances can occur in cystic fibrosis.

The "cystic fibrosis gene" is localized on the long arm of chromosome 7. The genetic defect causes a disturbance in secretion of chloride ions. Under physiological conditions the channels for the chloride ions on the luminal side of epithelial cells are closed. When the channels are open, chloride ions enter the lumina of the glands. In this manner a concentration gradient is produced *attracting* water into the lumen. **The disorder of secretory cells concerns the release of chloride into the secretion.** In the ductal (draining) part of the glands the reabsorption of chloride from the secretion is simultaneously decreased. The anomalous secretion of glands in the airways, but also in other organs, contains an inadequate amount of water. The physical qualities of the mucous secretion and the secretion of other glands are changed. That leads to an uncontrollable secretion of macromolecular substances (glycoproteins and other substances). The "*cleansing*" function of the secretion is disturbed. These changes determine the development of clinical manifestation (Fig. 1.3).

In the early post-natal period gastrointestinal disorders dominate. In the newborn children the inspissated meconium can evoke the symptoms of intraluminal obstruction. Respiratory symptoms – cough and repeated respiratory infections dominate later. A chronic pansinusitis can be present secondary to stagnation of secretion in the paranasal sinuses. Respiratory infections in these patients last longer than expected. The cough is more intense at night and in the morning. The sputum is usually viscous and purulent. The X-ray examination reveals hyperin-

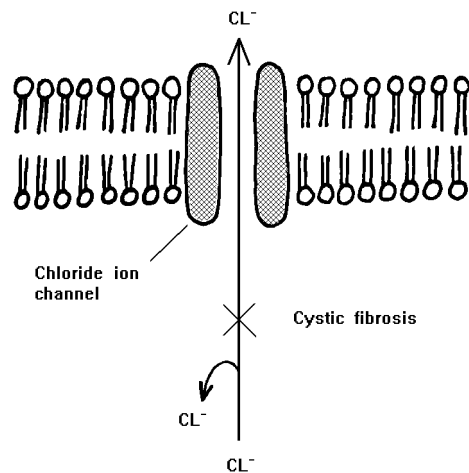


Figure 1.3: Disturbed transport of Cl^- ions in cystic fibrosis

flation of the lungs. Often bronchitis is present and bronchiectasis develops. The altered secretion causes an obstruction of small airways, resulting in atelectasis of the lung tissue. The oxygenation in the organism is impaired and pulmonary hypertension develops. Besides, in some patients hyperreactivity of the airways can be observed.

Patients with cystic fibrosis have an evident disturbance of pancreatic exocrine function. It is usually present in 95 per cent of patients. It leads to malabsorption, steatorrhoea, deficiency of fat-soluble vitamins and B_{12} vitamin (protein intrinsic factor does not release the vitamin B_{12} because it cannot be hydrolyzed by proteases and this situation results in megaloblastic anaemia). Sometimes biliary cirrhosis of the liver occurs, probably because of bile stagnation due to its increased viscosity.

The sweat glands in the skin are anatomically unchanged. Just the analysis of sweat can show different concentrations of sodium and chloride, which are usually increased. **The main problems of the patients** originate in the respiratory system. Unexpected complications occur during respiratory infections. Bronchiectasis can develop quickly. Atelectasis can occur in any area of the lungs. In young patients the atelectatic part of lungs can reexpand and refill with air. In other cases spontaneous pneumothorax can appear, especially during the development

of bullous emphysema. As the disease progresses hypoxaemia and pulmonary hypertension develop. Cor pulmonale appears in all patients. The therapy is symptomatic and the prognosis obscure.

1.9 Interstitial lung diseases

Interstitial lung diseases are defined as a group of conditions with a common sign of diffuse inflammatory alterations in the terminal parts of lungs and airways. The term of interstitial lung diseases refers especially to the fact, that the **interstitium of alveolar walls is thickened in consequence of fibrotic changes.** Changes of the epithelial cells in alveoli and terminal bronchioles are present, as well as alterations of the capillary endothelial cells in the alveolar walls, and in the lung parenchyma. Interstitial diseases can progress slowly, as long as the alveolar-capillary units become gradually destroyed and *irreversibly lost*. The condition can lead to respiratory failure which ends lethally. Interstitial lung diseases have an inexpressive clinical symptomatology. Dyspnoea during physical effort and an unproductive cough can occur. An expressive clinical manifestation does not occur usually before the respiratory surface of lungs becomes really reduced.

Disorders appearing during interstitial lung diseases are caused by the inflammatory reaction which is induced by activation of *inflammatory cells*, accumulated in alveolar walls.

Terminal bronchioles and alveoli with the capillaries and venules form together mutually cooperating functional pulmonary units. The walls of alveoli consist of a single layer of epithelial cells situated on a thin basement membrane. 95 per cent of these cells are epithelial cells of type I. The remaining 5 per cent are the cells of type II, producing surfactant – a complex substance which prevents the collapse of alveoli by reducing the surface tension. Under the thin basement membrane there is the interstitium which contains mesenchymal cells and the supporting tissue consisting of collagen, elastic fibres, proteoglycans and several glycoproteins. The pulmonary capillaries are in very close contact to alveoli. The

basement membrane of capillaries is very often in immediate vicinity to the basement membrane of the alveolar walls which is lined on its other side with epithelial cells of type I. Here are the sites where the gas exchange takes place. In intact lungs the thickness of alveolar walls is 5–10 μm . **In interstitial diseases the wall of alveoli is several times thicker** at the expense of the alveolar space. In the first type, the alveolar walls can deform in consequence of *inflammatory cell* accumulation in interstitium. This condition results in the derangement of alveolar wall *architecture*. These changes are reversible. They can be repaired after elimination of material participating in the inflammatory process. In the second type there are fibrotic changes. This type occurs in idiopathic pulmonary fibrosis or frequently when the pathogenic factor is present in the inhaled air. The epithelial cells of type I are destroyed and they are replaced by cuboid cells being, in fact, the proliferated cells of type II. The cells from terminal bronchioles also migrate into the alveoli. Simultaneously, the capillary endothelial cells are destroyed. In the interstitium oedema and proliferation of mesenchymal cells producing collagen occur. The interstitium undergoes fibrotic changes. A very aggressive form develops when the accumulated material from interstitium enters the alveoli through their destroyed alveolar basement membranes. This material is connected with the alveolar walls and forms a picture of intraalveolar fibrosis. Such type of alterations has an especially bad prognosis.

According to the etiologic factor, two groups of interstitial lung diseases can be distinguished. The first one includes diseases where the etiologic factor is not exactly defined, or it is complex. The second group includes interstitial lung diseases where the etiologic factor is represented by pathogenic particles or noxious gases present in the inhaled air.

Inflammatory changes that are the cause of destroyed alveolar walls are mediated by inflammatory – immunity cells accumulated in the lung parenchyma. The inflammatory process is localized especially in the alveoli (therefore it is called alveolitis), but also in the alveolar walls, in small bronchioles and sometimes also in the pulmonary vessels. The troubles of patients result from the disturbed gas exchange and from the destroyed alveolar-capillary units of the lungs. It is not always clear, how the inflammatory reaction in the alveoli is initiated. In the