tack or brain edema. Status epilepticus rarely occur in other types of epilepsy (Jacksonian status epilepticus, status psychomotorius, and status petit mal).

6.12.4 Experimental epilepsy

Experimental epilepsy on animals is characterized as a motor reaction that is disproportional to the given situation. In psychological conditions the nervous stimuli that occur upon the stimulation of the nerve endings spread in a precisely defined tracts to subcortical and cortical areas in the CNS. In the place of the analyzor there will be stimulation that is bordered by inhibition. After processing the stimuly are conducted to afferent pathways and the result will be an organic cousative reaction – so called reflex. Any error in the interfunctioning processes of stimulation and inhibition in the brain leads to a non coordinated simultaneous spread of stimuli via many pathways in different directions, as a result of this, there will be an epileptic seizure.

An epileptic attack in animals could be evoked by:

- electric current (electroshock)
- pharmacological and metabolic substances (e.g. setting metabolic alcalosis in rabbits)
- focal brain damage (freezing of brain tissue in dogs, electrocoagulation of brain tissues in monkeys)
- audiogenic and photogenic stimuli (audiogenic epilepsy in rodents and photogenic epilepsy in monkeys).

The model of **audiogenic epilepsy** in rats demonstrates an epileptic seizure and the possibility of pharmacological alternation of the resulting functional state of the nervous system.

It is well known that the organism responds to unexpected or intensive sound by motor reaction. This is a phylogenic old unconditional orientation reaction, that predisposes the organism for flight or fight. A rat that lives in dark environment most of the time has a very developed auditory organs (the rat hears in the region between 22 Hz – 100 KHz). It is extermely sensitive to tones of high frequency and intensity. About 90 % of the infantile rats react to light by a marked motor restlessness, and some of them develop an epileptic attack even without pharmacological interaction upon auditory stimulus. The reason of this audioepileptogenic disposition in rats is yet unknown. It is interresting that upon extripation of the auditory and motor areas from the cerebral cortex, or even a complete decorticalisation can not prevent the occurens of audiogennic attack.

The manifestations of audiogenic epileptic attack in experimental animals are very much similar to the attack in human. Adversive syndrom of head and eye bulbs deviation to one side, with a simultaneous occurence of tonic and clonic spasms might occur in the grand mal type. Akinesis accompanies the petit mal form. This similarity of signs enables us to use animal models not marely for demonstration but also for the study of epileptic attacks.

6.13 Disturbances of the oxygen supply to the brain

An adequate supply of oxygenated blood to all parts of the nervous system is a condition for its normal function. The most sensitive parts of the nervous system to oxygen defficiency are the most specialized ones – especially the cerebral cortex. The blood supply of the brain comes via the common carotid artery and the internal carotid artery as well as the vertebral artery. Both supplied areas are interconnected via the posterior cerebral artery that will complete the circle of Willis. This is how the disturbances of blood supply can be compensated by one of these vessels. Those compensatory mechanisms are favourable mainly in the pathological conditions, they are more efficient in young age.

The cerebral circulation depends on many factors: **the perfusion pressure of the brain, blood viscosity, the characteristics of the cerebral blood field**.

The perfusion pressure is determined by the difference between the mean arterial and the intracranial pressure that represents the venous pressure and the interstitial pressure of the brain tissue. Upon a decrease of the arterial pressure, and hence an increase in the venous pressure (disturbed outflow, stasis) or upon an intracranial hypertension the blood supply is worsening.

Similar to the mentioned the increased **blood viscosity** that is manifested as a higher requirement for the cardiac function and a worse tissue perfusion, including the brain. When the blood viscosity is high (e.g. when the content of proteins is high, in cases of dehydration and blood concentration). The flow of blood is slower and the possibility of vascular obstraction (e.g. thrombosis).

The cerebral vascular field maintains a considerable ability for autoregulation of the blood flow. The basis of the autoregulation are changes of the pCO_2, H^+, and K^+ inside cells of the vascular smooth muscle. An increase of pCO_2 and a decrease of pO_2 lead to vasodilitation of the cerebral vascular field and hence the blood flow can be doubled. On the contrary a decrease of pCO_2 and an increase of pO_2 lead to vasoconstriction and here the flow is decreased. This autoregulatory ability is related to the state of the vascular smooth muscle and that is why it is disturbed in cases of arteriosclerotic changes and that is manifested by disturbances of the cerebral blood flow.

Cerebral hypoxia can be caused not only by low pO_2 due to low cerebral perfusion (**anoxia and ischemia**) but also due to other extracerebral extravasal or extracardial causes. One of those causes are **lower pO_2** in the inspired air. Anoxia caused by ischemia is moreover accompanied with disturbances of nutritional supply of the brain (mainly glucose) and metabolite conscription.

One of the most serious causes of brain damage is **the hypoxic (anoxic) syndrom and localized ischemia**.

6.13.1 Hypoxic syndrom

In cases of **hypoxic syndrom** the CNS function is disturbed in relation to whether it is acute disturbance of the blood supply, or a gradual slow decrease of cerebral tissue perfusion. **Acute hypoxia** occur either due to **external causes** (e.g. disturbed oxygen apparatus), or due to **internal causes** (e.g. ventricular fibrillation, heart failure, shock). A sudden cerebral hypoxia is manifested as loss of consciousness (syncopy). If the oxygen supply or vascular supply lasts for more than 5 min (according to the situation the time length might be shortened or lengthened for few min) there will be irreversible changes of the neurons (necrosis), its functional disturbance occur much earlier.

Cerebral ischemia may resulted from sudden drop of the blood pressure in systemic hypertention – we are talking about **a transient ischemic attack**, that can lead to a transient loss of cerebral function that lasts for about 24 hours. In more coplicated cases there might be vascular occlusion due to thrombocyte aggregation on the injured endothelial lining of the aterosclerotically changed vessels. A change in the thromboxan prostacyclin ratio plays an important role. More than 80 % of the vascular attacks are abstructive in type and only 20 % are vascular ruptures with haemorhage.

In cases of a gradual decrease of pO_2 (e.g. upon climbing up high attitudes, pulmonary edema, cerebral aterosclerosis) in the early stages there will be some psychological tiredness, disturbances of memory, lengthening the reaction time, and later loss of consciousness and spasms.

A continuous supply of oxygen and glucose to the brain,and to neurons is necessary because brain tissue can not form reserves of these substrates.

6.13.2 Localized ischemia

In **localized ischemia**, that might be caused by thrombosis or emboli of the cerebral vassels or their branches, vascular compression, brain edema, tumor pressure or haematoma there will be some localized necrosis (malacia) in the region supplied by the affected blood vessels. Reminding you that cerebral vessels are terminal and that is why an alternative supply via collaterals can not be provided.

When the oxygen supply to the brain is inadequate we have to realize its relationship with other systems. In the first place the determining factor is the cerebral blood flow and the oxygen content of the blood. The cerebral perfusion is determined by the cerebral perfusion pressure and the characteristics of the cerebral vascular system. The oxygen content of the blood depends on the Hb concentration and hence the blood ability to carry oxygen as well as the partial O_2 pressure. Cerebral hypoxia can result from conditions that cause hypotension (cardiac arrest, shock, heart failure etc.), increased intracranial pressure (edema, expansive pressures), vasoconstriction (aterosclerosis, emboli, malignant hypertension), as well as factors that affect the oxygen circulation in the organism (anemia, acute or chronic haemorhage, pulmonary diseases , chest diseases, that lead to the failure of ventilation).

According to the type of cerebral oxygen supply disorder there will be some localized changes that usually occure upon short lasting and mild decrease of pO_2, or generalized (diffuse) injury, that might be the result of a total disorder of oxygen supply to the brain. In this relation, it worths mentioning that similar neuronal injuries can also occur in acute hypoglicemia, and barbiturate or CO intoxication.

6.13.3 Hyperoxic syndrom

One of the disturbances of O_2 supply to the brain in which brain damage occur due to an increased pO_2 in the brain. It follows inhalation of pure O_2 under high pressure (e.g. upon treating CO poisoning). There might be syncopy, nausea, blurred vision, epileptic attack. The mechanism is unknown. We suppose that a high pO_2 results in vasoconstriction and lowering of glucose supply and hence a slower metabolite wash out that leads to the injury of nerve cells.

6.14 Cerebral infarction

The basic cause of **brain (cerebral) infraction is failure of oxygen supply to the brain** (as well as failure of glucose supply). The infarction is in the area supplied by a terminal vessel. The most common cause is a local disturbance of the blood flow via vessels (occlusion), yet it is very common that a central cardiovascular failure contributes to these disturbances of perfusion.The result will be necrosis of all tissues supplied by the terminal vessel.

The pathophysiology of the occurence of infarction can be summarized as follows:

risk factors – disturbance of perfusion – infarction (ischemia, necrosis).

As we already mentioned, there is commonly a local arterial occlusion or stenosis.

1. **Arterial occlusion** is usually caused by thrombosis on the atheromatous plaque or embolization (mostly cardiac – atrial fibrilation – endocarditis – intramural thrombus that follows myocardial infarction). Small infarcts can result from small emboli from the sloughed atheromatous plaques in the region of the internal carotid artery.

2. **Arterial stenosis**. Commonly occurs in cases of atheromatosis, because **atheroma** causes a turbulant blood flow in the area of narrowing and there will be some disturbance of the vascular anastomosis among the neighbouring areas and blood vessels. Despite of all that its not necessary that an atheromatous narrowing itself should always result in infarction. The infarction usually occurs when a central cardiovascular insufficiecy contributes to the narrowing. The cerebral infarction usually occurs upon lowering the blood pressure during sleep, or when the blood pressure decreases in cases of shock or myocardial infarction. One of the less common causes of the brain infarction is dissecting aneurism, arteritis and very rarely it could be caused by vascular spasm.

Hypertensive patients have **a higher risk to develop cerebral infarction**, that is indirectly caused by speeding up the development of arteriosclerotic changes and formation of **atheromas**. In these cases there will be formation of large and small cerebral infarctions, as well as dementia that is conditioned by arteriopathy. In cases of malignant hypertension there might occur the so called **hypertensive encephalopathy**. The pathomechanism of its occurence is a very fast raise of the blood pressure that consequently leads to disturbed cerebral circulatory autoregulation. There will be a focal dilitation of the small vessels, an injured endothelial lining and a disturbance of the integrity of vascular wall that leads to protein leak into the interstitial space (together with the erythrocytes),that might end up with **brain edema**. This condition is clinically manifested with some neurological signs, spasms, supor till coma. Papillary edema of the optic nerve is always a sign of an increased intracranial pressure.

The clinical picture differs according to the affected site. The injury might affect any area of the brain yet some areas and localities are more commonly involved. The most vulnerable area is the area of the so called end arterioles in those areas that lack collaterals. The cerebral cortex is relatively protected by a rich network of vascular collaterals. The injury is common to occur in the area of the medial cerebral artery and mainly the end arterioles