
6.3 Neuroglia

Glia reacts very prominently towards many CNS diseases. The neuroglial cells have **supportive and nutritional functions**.

1. **Astrocytes**, having many fiber branches, serve as supportive cells. The nutritional function of astrocytes is enabled by the fact that part of its branches is situated on the endothelial cells that form the wall of the capillaries (known as vascular ped). From this site they acquire the nutritional substances and transport them to the nerve cells. Upon neuronal injury the astrocytes together with the microglial cells phagocytose the detritus and the products of digestion and form the so called glial scar. They are less vulnerable than the neurons. They share in the formation of scar in a way that they produce and increase the fibrin formation, later on the cells with atrophy and there will be the formation of a thick fibrinous network. This process is called **gliosis**. Gliosis accompanies many diseases and it is analogous with scar formation. The collagen scar forms in CNS only upon the injury to mesodermal structures such as for e.g. the vascular tissue.
2. **Oligodendrocytes** are small cells with short branches. They perform mainly nutritional functions in relation to neurons. It is mainly seen during neuronal injury. Upon neuronal injury the number of oligodendrocytes increases, and cells become enlarged. The whole process is known as satellitosis.

The microglial cells are part of the mononuclear phagocytic system. Their reaction is best seen upon tissue necrosis, around the infarct. The activated large foamy cells phagocytose lipids, haemosiderin, and others. They are very different from the small inactive microglial cells. According to the shape and type of phagocytosed material those cells are variably marked as: lipophages, foamy cells or so the called gitter cells.

6.4 The basic etiopathogenetic factors in the nervous system disturbances

The etiopathogenic factors, that cause nervous system diseases, are classified depending on many conditions. One of the basic classifications is a classification into two groups: (1) **intrinsic** and (2) **extrinsic ones**. Although this is a general and very wide division, it is not possible to enclose all the diseases within the mentioned groups because both **the groups are interchanged and interconnected** with each other.

Diseases of the nervous system from **the etiopathogenetical** point of view are divided into three groups:

1. diseases with mainly intrinsic causes,
2. diseases with mainly extrinsic causes,
3. diseases with mixed or possibly unknown etiology.

6.4.1 Diseases with mainly intrinsic causes

An important subgroup of this group are **the genetically conditioned diseases**. Changes of **the chromosomal number** are very often associated with developmental disorders of the nervous system, for e.g. trisomy of the 21st chromosome – Down syndrome). **Down syndrome** is characterized by a prominently slow mental development, with the typical mongoloid expression of the face (sometimes marked as mongolism) and brachiocephaly.

Another cause might be changes of **the chromosomal structures**, and hence their abnormality (2) for e.g. changes in sequence of the DNA on the short arm of chromosome the 4th are the cause of **Huntington chorea**, that is manifested by choreatic movements with the consequent loss of intellect. As a differentiation from the Parkinson disease the amount of dopamine in the basal ganglia is higher.

The 3rd group of the genetically conditioned diseases is composed of many diseases in which the injury of disturbance of function is not localized.

To this group we may count the **metabolic disturbances, the neuromuscular diseases and some neuropathies**:

1. group of the congenital disturbances of the aminoacid metabolism:

- **phenylketonurea** – an increased phenylalanin level in the blood due to the absence of phenylalanin hydroxylase, The low phenylalanin content in a child nutrition can prevent oligophrenia in the first years of life.
- **maple sirup disease** – a higher blood leucin concentration as well as isoleucin and valin is caused by the deficient decarboxylation, a disease ends up lethaly in the first years of life with sighs of de cerebration rigidity,
- **mental retardation** is accompanied with another aminoacid metabolism disturbance – cystationinurea, citrulinurea, hyperprolinemia, hydroxyprolinemia, hyperglycinemia etc.

2. Lipid metabolism disturbances

Generalized gangliosidosis – gangliosides are cumulated due to the absence of specific galactosidase. The disease is typically manifested by the psychomotor disturbances, hepatosplenomegaly due to foamy cells and skeletal deformity. The disease can have two forms and both are fatal.

Tay-Sachs amaurotic familiar idiocity – due to the accumulation of gangliosides in the neurons, this ganglioside side can not be metabolised. The disease is manifested by psychomotor retardation and disturbance of vision.

The disease have a progressive course with blindness and idiocity and ends by death 3–4 years later.

Glycosphingo-lipidosis (Fabry syndrome). There is an X-chromosomal hereditary disease, during which ceramid is cumulated. Skin dark red lesions are very characteristic. During the attacks there is severe neuralgia.

Gaucher disease – cerebrocyte tezaurism with many form types. There is the acute neuropathic form during the first months of life, when a progressive loss of neurons takes place, disturbance of motor function, and idiocity. In the chronic form of the disease there are neurological signs.

Leucodystrophy (Krabbe disease) – is the disturbance of ceramid metabolism. The brain white matter degenerates very quickly, myelin is lost and is substituted by globoid cells. The disease starts in the 3–6 month by an increased muscular stimulation. After blindness and some serious neuronal disturbances and loss of function the disease ends by exitus within two years. An experimental model of this disease in dogs is known by now. This disease is identical in its cause and course.

Sphingomyelin lipidosis (Niemann-Pick disease) – is an autosomal recessive disease, in which lysosomal sphingomyelinase enzyme is absent. This enzyme function is to degrade sphingomyelin. Sphingomyelin then cumulates in the foam cells of the reticuloendothelial system. During the acute neuropathic form of the disease we might notice loss of motor and intellectual function in the children. Treatment is yet unknown.

3. Disturbances of sacharide metabolism

These disturbances are known under the name **glycogenosis**. The diseases during which an increases amount of a normal or atypical glycogen is stored in the cells belong to this group. The cause is either a high synthesis or a disturbance of its break down. There are many types of glycogenosis:

Gierke disease – glucose 6-phosphatase deficiency,

Pompe disease – a generalized glycogenosis, that is also manifested with neuromuscular form with hyporeflexia, language abnormalities as well as some disturbance of swallowing and muscular hypotonia.

Cori disease – is a limiting dextrinosis and it is a relatively rare disease.

McArdle disease being a deficiency of the muscle phosphorylation, during ischemia the muscle activity is lower, and no lactate is formed during work. The symptoms of this disease are prominent tiredness, and painful muscular spasms.

Galactosemia – is an aotosomal recessive disease with nutritional disturbances and mental retardation. By controlling the diet we might prevent the occurrence of nervous system injury.

In **gargoylism** there is a metabolic disorder of mucopolysacharides, during which heparansulphate and dermatansulphate accumulate in the central nervous system with the consequent disturbance of its function. The name of this disease comes from the gotic statues and is named as water spout which patients

looked very much like. In all these disorders it is very important to prevent hypoglycemia.

Other disease – and mainly those that belong to the group of degenerative diseases, that we describe elsewhere in this chapter we suggest the hereditary factor to play the most important role (for e.g. **Wilson disease** – hepatolenticular degeneration with damage of the basal ganglia, **Friedreich ataxia** – that affect the cerebellum and medulla oblongata), some rare disease are **the familiar spastic paraplegia, hereditary cerebellar ataxia** with spasticity and other diseases.

6.4.2 Diseases mainly die to extrinsic causative agents

The most common cause is the mechanical damage of the nervous system at different levels. Upon an accident there might be cut, tear, or compression of the nervous tissue. According to the mechanism of injury trauma is commonly combined with hemorrhage, and edema that always worsen the result of trauma. A special group consist of so called birth trauma, that are usually associated with hypoxia. Hypoxia belongs to the basic etiopathogenetic factors of nervous system injury. The sensitivity of the nervous tissue to hypoxia is variable. The most sensitive to hypoxia are the phylogenetically younger and the functionally higher specialized neurons (cerebral cortex, centers with high metabolism, interneurons, where ischemia produces disconnection signs). Even nutritional disturbances can predispose to CNS damage. If there is a deficiency of the energetic substrates and mainly during development (marasmus) or protein deficiency (kwashiorkor), there will occur a long term affection of the CNS, and mainly some defects of the intellectual functions.

For the normal CNS development in man it is necessary to provide an adequate **sensory stimulation**, adequate social and emotional suggestions. During the child development this sensory stimulation is equally necessary as the adequate nutrition. The deficiency of stimuli in the sensory and emotional area leads to the retardation of the intellectual development, personality abnormalities and emotional disturbances.

Many **toxic substances** have unfavorable effect on the CNS. These are mainly some metal (lead – encephalopathies with spasms and hemiplegia with

coma, mercury – narrowing the vision field, ataxia, tremor, psychological changes, and extrapyramidal symptoms, thallium – affects vision till blindness, spasms, delirium, and death, manganese – signs of the Parkinson disease, arsenic – polyneuritis, encephalitis, and neuritis of the optic n.).

Disturbances of the nervous system is also caused by inappropriate use (and mainly overdosing) of some pharmaceuticals. Upon a long use of barbiturates, psychopharmaceuticals, antihistaminics ataxia might occur, as well as lethargy desorientation, and memory changes.

Antibiotics and chemotherapeutics mainly affect the sensory functions (for e.g. streptomycine has the affinity to the vestibulocochlear system). Some stimulants might evoke convulsive states.

An important cause of nervous system damage at the time being is **the drug dependence**. The most common drug dependence is to alcohol. Chronic intoxication is characterized by spasms, polyneuritis, cerebellar degeneration, personality decomposition, and Korsakoff's psychosis, that apart of the mentioned is manifested by desorientation, confabulation and memory loss. Due to the effect of alcohol there might be degeneration of the other parts of the CNS and even myelin degeneration.

CNS infection can be divided according to the causative agent into many groups (**pyogenic meningitis, nonpyogenic meningitis – serous meningitis, parasitic diseases, viral diseases**). Pyogenic meningitis is most commonly caused by meningococci and staphylococci. The nonpyogenic meningitis are usually viral in origin but also due to mycosis or tuberculosis and syphilitic infection. Thank to the antibiotic therapy the prognosis of the mentioned diseases today is much better than previously. **Vaccination** could eradicate acute viral polomyelitis (Heine-Medine disease). Meanwhile there is a special group of diseases known as the infection with slow viruses (meaning infection with slow course). From the human diseases it is mainly **the subacute sclerosing encephalitis, Creutzfeld-Jacob disease and kuru** – a disease of Melanesian population. In the last years the acquired immune deficiency syndrom (AIDS) is spreading, and upon brain affection with this disease there will be encephalopathy with the gradual desintegration of the intellectual functions and personality and a progressing atrophy and brain tissue degeneration that ends lethally. The CNS due to its

high affinity to the virus (nearly 80% compared with the leucocytes) is threatened with direct viral invasion, but also an indirect invasion upon the failure of self-defence immunological mechanisms against other infections.

6.4.3 Diseases with mixed or unknown etiology

The diseases that belong to this group are those diseases of medical interest not merely because of the therapeutic – preventive point of view but also due to their scientific research value. Upon the manifestation of nervous system disease the main cause never is an individual isolated cause of that disease. There is always a multifactorial conditioned state. In many diseases the decisive factors remain unknown. Diseases that belong to this group can be further subdivided into three subgroups: **CNS tumors, neuroimmunological diseases and neurodegenerative diseases** of the CNS.

Tumors of the CNS develop either directly in the nerve tissues (primary tumors), or they originate from other tissues (secondary, metastatic tumors).

Even in case of tumors we suppose the presence of an inborn predisposition, that are activated due to the effect of the outside environment and mainly the blastogenic effects. The question of the chemical or viral origin of these tumors remain still unsolved. During childhood as well as during adulthood the most common tumors are **gliomas** (about 88% of the affected children and 50% of adults). In children there is commonly **craniopharyngeoma** (4%) and **teratoma** (3%). In older people there is often **meningiomas** (20%), **metastases** (10–20%) and **tumors of the neural sheaths** (10%).

The neuroimmunological diseases of the CNS form till now a nonhomogenous group of diseases, that have a common manifestation and immunological basis. **Multiple sclerosis** most probably belongs to this group of diseases (with a high content of gammaglobulins in the cerebrospinal fluid), and **myasthenia gravis** that is a defect in nerve impulse transmission at the neuromuscular junction. Antibodies against the brain tissue were described even in **Alzheimer disease** (a disturbed cholinergic neurotransmission).

The degenerative diseases of the CNS might have many etiopathogenic causes. Their causes might be vascular changes, nutritional disturbances, neuroin-

fection, but demyelination might be a secondary change resulting from the destruction of the nervous system. Some **unclear etiology** is for e.g. that of **senile dementia**, degenerative changes of the cerebellum, or progressive subcortical encephalopathy. Compared to the previous diseases **Parkinson syndrome (paralysis agitans)** has got a well known etiology and mainly what concerns the neurotransmission and dopaminergic mechanism in the nigra strata. Neuroinfections as well as poisoning, arteriosclerosis and other factors might be triggering factors yet the direct mechanism of the substantia nigra destruction remain unclear.

6.5 Some syndromes occurring upon the injury of the nervous system

To the extrinsic causes of nervous system injury we might commonly add **trauma, accidents, the effect of mechanical power**. Because of the fact that all the medullary nerves are mixed (they contain the afferent sensitive, and efferent motor fibers), upon their injury there will be a result so called **peripheral nerve syndrome**, that commences disturbance of sensation as well as motor disturbances. Upon the destruction of the anterior horn (that contains motor fibers) there will be plegia and upon the destruction of the posterior horn (that contains only the sensitive nerve fibers) the result will be loss of sensation (hyposthesia or anaesthesia, yet if the lesion concerns the afferent fibers in the affected horns, there might be hyperesthesia).

Upon **the lesion of spinal cord or brain** the condition is more complicated by **bleeding** (haemorrhage), an **increased pressure** in the closed cranial system or the closed spinal canal, **edema** and other lesions (degenerative changes) of the nerve tissue. The neurological finding is characterized according to the level and the localisation of the CNS injury: we divide them into **spinal syndromes** (for e.g. the transversal separation of the spinal cord syndrome – with motility and sensation loss according to the level of lesion,