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Учреждение образования  
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии  
Обсуждено на заседании кафедры  
Протокол №7 от 30.08.2017

**МЕТОДИЧЕСКАЯ РАЗРАБОТКА**  
Для проведения занятия со студентами  
3 курса ФПСЗС, обучающихся на английском языке  
по патологической физиологии

Тема: **Патофизиология нервной системы**

Theme: **Pathophysiology of nervous system**

Время 3 ак. часа

**Actuality of the theme.** The nervous system as a main regulatory system of an organism in this or that measure participates in pathogenesis of each diseases. The earliest and obligatory form of participation of the nervous system in pathology is defensive and adaptive the response. The protective reflexes (cough, vomiting), protective inhibition, response hypothalamo-hypophysial-adrenal system belong to such responses. At the same time during development of diseases the nervous system becomes the object of a defeat itself. It is defensive and adaptive the response of the damaged nervous system are reduced, and it becomes a source of pathological, harmful to an organism reflexes. The disturbance of nervous activity is always reflected in the function of internal organs. The fundamental knowledges of the reasons and mechanisms of disorders motor, sensitive and trophic functions of the nervous system are necessary for understanding of pathogenesis nervous diseases, and also many symptoms of a damage of internal organs.

**Learning goals of the lesson:** to study pathogenetic mechanisms of development and manifestation of pathological pain, to form a comprehensive understanding of typical pathological processes taking place in central nervous system.

**Educational goals of the lesson:** formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

**Objectives of the lesson:**

1. To know central and peripheral mechanisms of pain.
2. Consider neurochemical aspects of pain and pain syndrome.
3. To consider a trace mechanisms in central nervous system, which determine a resistance to the therapy of neurological diseases.
4. To consider compensatory adaptive mechanisms of brain and spinal cord.

**To repeat the following questions from related disciplines to ensure absolute mastery of the material:**

1. Structure of neurons (histology, cytology, embryology disciplines).
2. Structure of central and peripheral nervous system (anatomy discipline).
3. Basic scheme of conditioned reflex, basic electrophysiological constants of nerve fibers (normal physiology discipline).

**Control questions of the lesson:**

1. General etiology of nervous system disorders.
2. General pathogenesis of nervous system disorders.
3. Typical pathological processes in nervous system.
4. Neurogenic sensitivity disorders. Pain, its types, mechanisms and biological value. Basics of anesthesia.
5. Neurogenic disorders of locomotor function: types, manifestations.
6. Violations of autonomic nervous system function, their types and basic manifestations.
7. Neurogenic disorders of trophism.
8. Violations of higher nervous activity. Principles of therapy of neurological disorders.

**Calculation of study time**

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes

## Additional materials

### Etiology of NS disfunction:

I.	<ul style="list-style-type: none"><li>• <i>Exogenous factors</i></li><li>• <i>Endogenous factors</i></li></ul>
II.	<ul style="list-style-type: none"><li>• <i>Specific (neurotropic)</i></li><li>• <i>Nonspecific</i></li></ul>
III.	<ul style="list-style-type: none"><li>• <i>Physical</i>,</li><li>• <i>Biological</i> (viruses: rhabdovirus, polomyelitis; microbes: syphilis, leprae; microbe toxin: botulinous, tetanic toxin; phytotoxins),</li><li>• <i>Chemical</i> (ethyl, methyl alcohol, phosphorganic substances, drugs),</li><li>• <i>Psychosocial (information)</i>.</li></ul>
IV.	<ul style="list-style-type: none"><li>• <i>Primary</i>: direct pathological effects on the components NS (typical pathological processes localized in the NS, genetic factors, the direct effects of exogenous factors on NS).</li><li>• <i>Secondary</i> (disorders of organs and systems with complication of CNS damage): liver failure, uremic come, diabetic neuropathy</li></ul>
V.	<ul style="list-style-type: none"><li>• <i>Hereditary</i></li><li>• <i>Acquired</i></li></ul>

### Etiology factors lead to changes in NS:

- changes in neuron
- impairment of secretion and reception of neuromediators
- acquired alteration of neuron genome
- change in transneuronal interaction
- changes in neuron trophic
- formation of Ab to NS
- impairments in antisystems action (antipainful, anticonvulsant...)

### Typical pathogenic changes are formation of:

- aggregates of hyperactive neurons, which are the generator of pathologically intensified excitation (GPIE),
- pathological determinants
- pathological systems
- pathological dominant.

The **plasticity** of NS— is the ability to consolidate the occurred changes. Plasticity establishes not only biologically useful, but also pathological changes. Due to the plasticity fixed structural-functional abnormalities of the nervous system (e.g., synaptic disorders, excitation generators, pathological systems, etc.).

**Afterimpression** — a reaction of the body or organs, systems based on structural-functional trail preserved from the former sanogenetic and pathological processes. The basis of afterimpressions are structural and functional changes that persist after every physiological process. Normally afterimpression underlie memory, sanogenetic protective and immune mechanisms; in the pathology — based on these features are reproduced former pathological processes.

### Protection mechanisms of the nervous system:

- tissue barrier, lining of the brain and nerves. Protection of the neuron provide surrounding glial, Schwann cells, membrane of the neuron.
- immunological barrier
- regulation "balancing" mechanism (according to Pavlov), aimed at the prevention and mitigation of emerging changes. Under pathological conditions, this principle is implemented in the activities of antisystems. For example, if there is excessive pain activates antinociceptive system regulating pain sensitivity. Activation of antinociceptive system suppresses the occurrence of pain.

Antiepileptic system monitors the level of excitement in various parts of the CNS. Tonic activity of anti-system is one of the mechanisms to support sustainable health.

### **Impairment of the function of neurons:**

#### ***Nonspecific mechanisms:***

- violations of energy supply (due to violation of entering to the cells of O<sub>2</sub> and / or Gl, reducing the activity of OXPHOS enzymes, processes of formation, transport and use of high-energy compound;
- disorders of protein biosynthesis in amino acids deficiency or defects endoplasmic reticulum;
- ions and fluid imbalance in energy deficit, damage cell membranes;
- rupture of the membranes, as a result of mechanical action,
- activation of lipid peroxidation, generation of ROS and FR, action of phospholipases, which leads to breakdown electrogenesis, disturbance of the excitation and transmission of it on effector cells;
- Apoptosis of neurons (f.e. during cerebral hypoxia);
- Autolysis of neurons or their components.

#### ***Specific mechanisms:***

1. disorders of neurotransmitter biosynthesis;
2. disorders of the mediator transport in axon;
3. disorders of the mediator deposit in nerve endings;
4. disorders of the mediator release into the synaptic cleft;
5. disorders of the mediator interaction with the receptor;
6. disorder of the mediator removal processes from synapse (f.e., inactivation of enzymes that destroy mediator);
7. disorders of generation and conduction of excitation.

Distinguish **primary and secondary** disorders of the nervous activity.

1. **Primary** associated with the direct effect of damaging factor on nerve cells,
2. **Secondary** disorders occur when there is insufficient or excessive production of neurotransmitters transsynaptic transmission, deafferentation of neurons, development of a "protective inhibition" and the blockade of postsynaptic receptors.

#### **There are three main forms of NS disorders:**

1. By the intensity of functioning:
  - pathological attenuation of nervous effect;
  - pathological intensification of nerve effect.
2. By the adequacy of nerve cells response:
  - inadequacy of the response to parameters of the stimulus;
  - inadequacy of the response to needs of the body — the phase states.

Phase states — disorders of adequate relationship between the intensity and / or character ("quality") response (conditionally or unconditioned reflex) and the parameters of the stimulus that causes this reaction.

3. By predominant type of the nervous activity disturbance:
  - a) sensory disturbances;
  - b) locomotor disorders (motor) function;
  - c) trophic disorders of the nervous system;
  - d) dysfunction of the autonomic nervous system;
  - e) dysfunction of the higher nervous activity - neuroses.

### **Synapses**

**Synapses** — is specialized contacts, through which the transmission of excitatory or inhibitory influences from neuron to neuron or another cell (eg muscle). In mammals, there is mainly chemical synapses transfer type, in which the activity of one cell to another is transmitted via mediators.

All synapses are divided into **excitatory** and **inhibitory**.

#### **1. Disorders of neurotransmitter biosynthesis:**

- decrease in activity enzymes involved in the formation of neurotransmitter

- decrease formation of mediators associated with energy (blockade of metabolic processes in the mitochondria and reduced maintenance high-energy compound in the neuron as a result of hypoxia, toxins, etc.)

## **2. Disorders of the mediator transport in axon:**

- The mediator can be synthesized in the body of the nerve cell and in the nerve ending. Mediator synthesized in the body transported by the axon to the presynaptic part (by cytoplasmic microtubules). Microtubules easily disintegrate under the influence of anesthetic agents, high temperature, proteolytic enzymes, substances such as colchicine, etc. that may reduce the amount of neurotransmitter in the presynaptic part.

## **3. Disorders of the mediator deposit in nerve endings:**

Neurotransmitters are stored in presynaptic vesicles (a mixture of mediator molecules, ATP and specific proteins). Some substances can disrupt the process of depositing a mediator. F.e. reserpine prevents the accumulation of norepinephrine and serotonin of vesicles in the presynaptic.

## **4. Disorders of the mediator release into the synaptic cleft:**

The process of neurotransmitter release into the synaptic cleft may be disrupted by the action of certain pharmacological agents and toxins. Tetanus toxin prevents the exit of inhibition neurotransmitter glycine. Botulinum toxin blocks the release of acetylcholine. Calcium and magnesium ions, prostaglandins affect neurotransmitter secretion by nerve ending.

## **5. Disorders of the mediator interaction with the receptor:**

There are a large number of substances that have a competitive type of action, ie, easily come into contact with receptors on the postsynaptic membrane. Tubocurarine blocks H-cholinergic, strychnine, blocking the receptors sensitive to glycine, etc. These compounds block the action of the mediator on the effector cell.

## **6. Disorder of the mediator removal processes from synapse:**

To properly function of the synapse, a neurotransmitter upon its interaction with the receptor should be removed from the synaptic cleft.

There are two mechanisms for removal:

1) destruction of mediators by enzymes localized in the postsynaptic membrane (Acetylcholine is destroyed by cholinesterase in the synaptic cleft. Organophosphorus inactivate cholinesterase. This acetylcholine for a long time bound with a lot of cholinergic receptors, providing a stimulating first, and then the inhibitory effect.)

2) reuptake of mediators by nerve ending. (Adrenergic neurotransmitter in the synapse back captured his sympathetic nerve ending. When exposed to toxic substances may be disturbed neurotransmitter transportation from the synaptic cleft into presynaptic vesicles.)

## **Generator of pathologically intensified excitation (GPIE)**

Generator of pathologically intensified excitation (GPIE) — is the unit of hyperactive interact neurons, producing an uncontrollable stream of pulses. The neurons of the generator activate each other, the generator is capable of self-sustaining its activity without the need for constant additional stimulation from the outside. Neurons generator constantly active, they can easily be excited even under the weak pulse and some not need extra stimulation.

The generator can be formed by:

- violation of inhibitory control mechanisms (which entails disinhibition and hyperactivation of neurons)
- direct causes an hyperactivation of neurons. The brakes mechanisms are stored, but they are functionally inefficient and unable to normalize the activity of neurons.

The main pathogenetic significance of the generator is that it hyperactivate that department of CNS in which it arose or to which it is directly connected, so that this department becomes important determinants of abnormal, forming pathological system

Under the influence of the generator all the pathological system is out of control of the central nervous system. The mechanism for the formation of pathological systems are pathological vicious circles.

Thus, the nervous system is formed neuropathological syndrome, the pathogenesis of which is composed of a series of consecutive events:

formation of GPIE → appearance of pathological determinants → appearance of pathological systems → formation of the neuropathological syndrome.

### **Lack of inhibition, disinhibition**

At rest, and the active state of neurons experience persistent inhibitory effects. In the excitation of neurons is a weakening of inhibitory processes. This disinhibition is dosed, it is controlled and the required level of neural activity, so it is a physiological nature. When disinhibition having pathological, a neuron becomes hyperactive and out of control. Pathological disinhibition occurs when a significant deficiency and uncontrolled braking. This condition occurs in direct damage to brake mechanisms for selective action upon them some toxins (e.g., tetanus toxin strychnine).

If disinhibited and hyperactivated inhibitory neurons, there is a pathologically enhanced braking effect, which can manifest as suppression and loss of function.

### **Denervation syndrome**

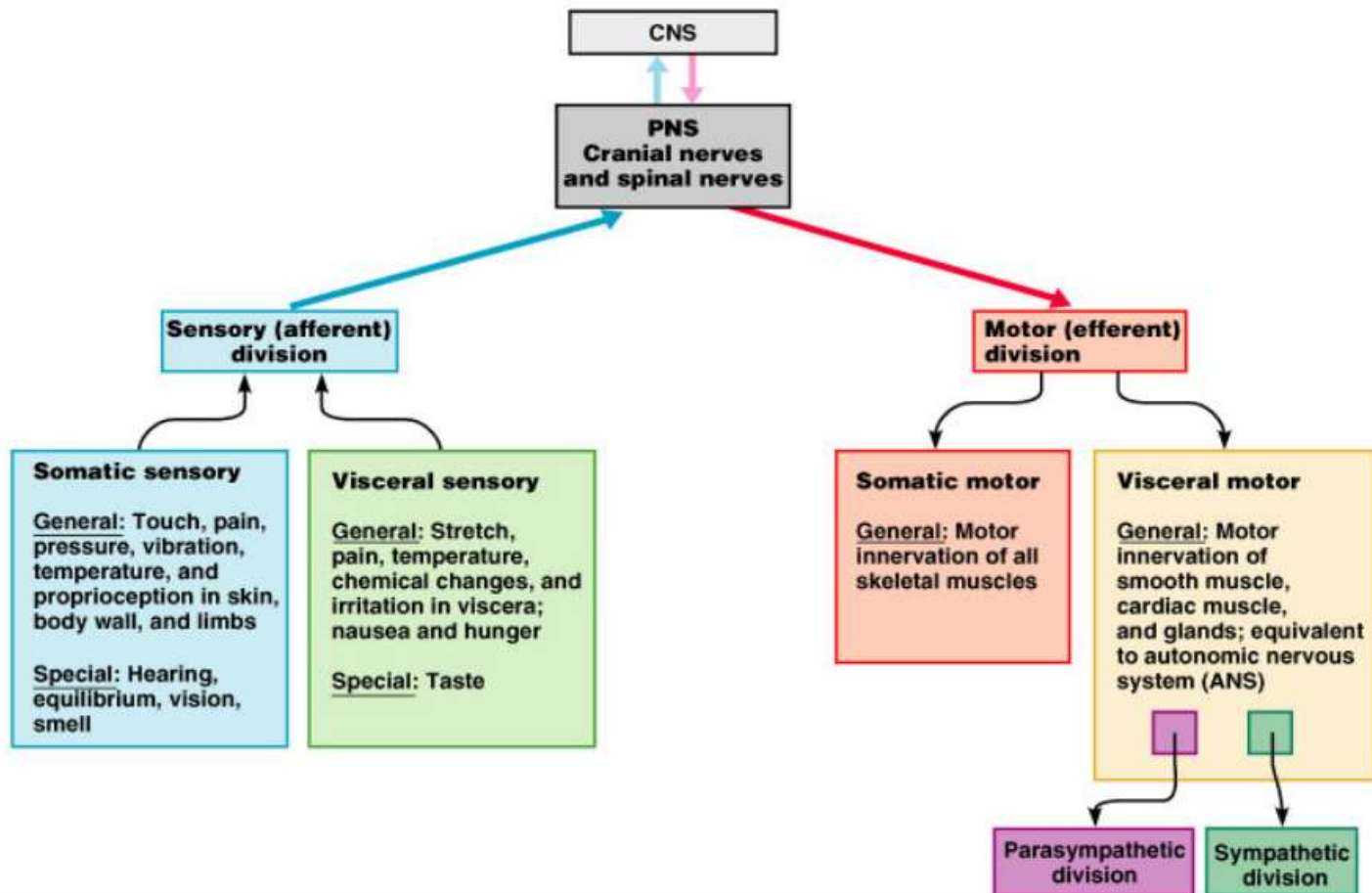
Denervation syndrome is a set of changes that occur in the post-synaptic neurons, organs and tissues after loss of nervous influence on these structures. Denervated structure (muscle, neuron) becomes more sensitive to physiologically active substances (Act Cannon-Rosenbluth). The main manifestation of the denervation syndrome in the muscle is the disappearance of the end plate areas of muscle fibers, which focuses its entire cholinergic apparatus. Instead there are new acetylcholine receptors throughout the muscle fibers and are therefore increasing overall sensitivity to acetylcholine of the fiber. This effect is mainly due to the fallout of the trophic effects of nerve. Another characteristic feature is fibrillary twitching denervated muscle. This effect reflects the reaction of the denervated muscle fibers coming to them from various outside sources of acetylcholine.

### **Deafferentation**

Impulses coming into the neuron, from whatever source it may come from, is afferent for the neuron. Disabling this afference is a deafferentation neuron. The latter can be caused either by fallout of the incoming impulses (at break of neural pathways, disorders of neurotransmitters release by presynaptic terminal), or blockade of sensing receptors on the postsynaptic neuron (the action of toxins, pharmacological agents, etc.). In partial deafferentation occurs increase in the excitability of the neuron or its single part and a violation of inhibitory mechanisms. Thus, deafferentation group of neurons may acquire properties of GPIE.

### **Spinal shock**

Spinal shock occurs after spinal cord break and represents a profound but reversible inhibition of motor and autonomic reflexes that take place below the break. Lost reflexes include those controlling posture, bladder and bowel function, blood pressure, and maintenance of body temperature. Inhibition of reflexes associated with loss of activating stimulation by brain. In humans, spinal shock lasts a few months. In humans complete areflexia after spinal cord break is the initial stage of complete paraplegia. In the future, there is a gradual recovery of motor and autonomic reflexes. Initially appear flexor reflexes of fingers having the character of pathological reflexes (Babinski et al.), after that are performed more significant and then generalized spinal reflexes and movements such as spinal automatism.

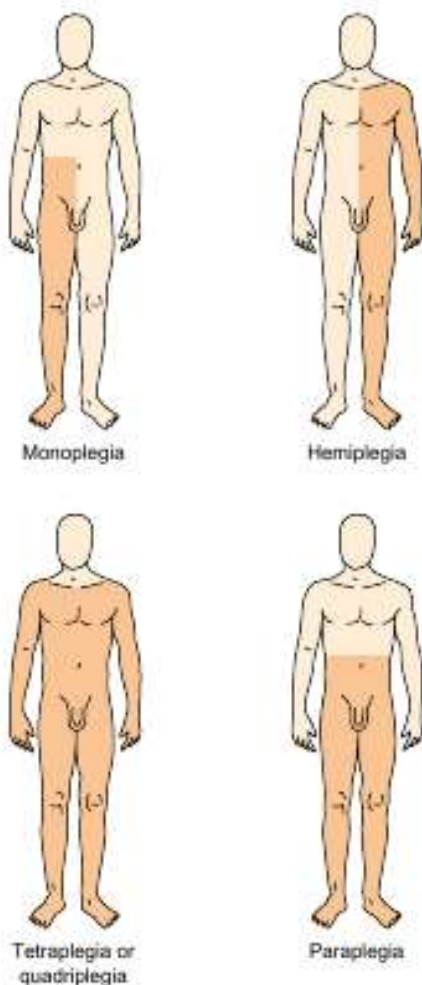


### Types of locomotor dysfunction:

- muscle weakness;
- movement disorders;
- ataxia, imbalance, other disturbances in the initiation or coordination of movement.

### Typical manifestations of the pyramidal upper motor neuron lesions:

- central weakness (spasticity);
- hyperreflexia;
- clonus;
- pathologic segmental reflexes;
- synkinesis.



**Weakness** (or palsy) is a reduction in normal power of one or more muscles. Weakness is commonly described by severity and distribution. Paralysis and the suffix «-plegia» indicate weakness that is so severe that it is complete or nearly complete. «Paresis» refers to weakness that is mild. The prefix «hemi-» refers to one half of the body. For example, hemiplegia means paralysis of one side of a body. Prefix «para-» refers to both legs or both hands, and «quadric-» to all four limbs. Tone is the resistance of a muscle to passive stretch.

**Spasticity** is an increased tone that is velocity dependent, has a sudden release after reaching a maximum (the «clasp-knife» phenomenon), and predominantly affects

antigravity muscles (i.e., upper limb flexors more than extensors and lower limb extensors more than

flexors).

*Clonus* is spasmodic alteration of muscular contractions between antagonistic muscle groups caused by a hyperactive stretch reflex.

*Pathologic segmentary reflexes* are those observed in children in early postnatal period, such as Babinski's reflex. Babinski's reflex is a dorsiflexion of the great toe when the sole of the foot is stimulated.

*Synkinesis* is an involuntary movement produced in association with a voluntary one.

**Typical manifestations of the lower motor neuron lesions:**

- muscle weakness of the flaccid type;
- areflexia;
- muscles atrophy;
- fasciculations (isolated small twitches);
- changes in excitability of the muscle fibers.

The disturbances of motor function are manifested by pareses, paralyses, spasms and convulsions.

Central paresis	Peripheral paresis
<ul style="list-style-type: none"> <li>• brisk tendon reflexes, muscle cloni</li> <li>• uni- or bilateral increased stretch reflexes and enlarged reflex zones</li> <li>• pathological reflexes (Babinski sign, Gordon and Oppenheimer reflexes), uni- and/or bilateral</li> <li>• increased muscle tone</li> <li>• para- or hemi-like distribution of motor deficit</li> <li>• spinal lesions from C1 to L1 (conus medullaris)</li> </ul>	<ul style="list-style-type: none"> <li>• diminished or absent tendon reflexes</li> <li>• reduced or absent polysynaptic reflexes</li> <li>• no evidence of pathological reflexes</li> <li>• flaccid muscle tone</li> <li>• distribution related to peripheral nerve innervation</li> <li>• lesions below L2</li> </ul>

Typical disorders observed during damage to the extrapyramidal system:

- muscle dystonia;
- movement disorders:
  - hypokinetic type;
  - hyperkinetic type.

*Muscle dystonia* is a prolonged muscle tonic contraction that may cause twisting and progress to abnormal posture.

**Movement disorders**

*Movement disorders* are neurologic syndromes in which abnormal movements (or dyskinesias) occur due to a disturbance of fluency and speed of voluntary movement or the presence of unintended extra movements.

***Hypokinetic movement disorders.***

These syndromes are manifested as bradykinesia, with a masked expressionless facial appearance, loss of associated limb movements during walking, and rigid turning.

***Hyperkinetic movement disorders.***

Abnormal involuntary movements are divided into those that are rhythmical and those that are irregular. Those that are rhythmical are termed tremors.

**Table 1. Types of hyperkinetic movement disorders**

Rhythmical	Irregular
Tremors: <ul style="list-style-type: none"> <li>- rest tremor</li> <li>- postural tremor</li> <li>- intention tremor</li> </ul>	Athetosis
	Chorea
	Tics
	Myoclonus

**Table Involuntary movements disorders associated with extrapyramidal disorders**

Movement Disorder	Characteristics
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<b>Tremor</b>	Rhythmic oscillating contractions or movements of whole muscles or major portions of a muscle. They can occur as resting tremors, which are prominent at rest and decrease or disappear with movement; intention tremors, which increase with activity and become worse when the target is reached; and postural tremors, which appear when the affected part is maintained in a stabilized position. Tremor can be caused by hyperthyroidism and by Parkinsonism, but it is also a typical side effect of alcohol, narcotics and drug abuse.
<b>Tics</b>	Irregularly occurring brief, repetitive, stereotyped, coordinated movements such as winking, grimacing, or shoulder shrugging. The tics may begin in childhood for unknown reasons. Tics are extremely resistant to any therapy.
<b>Chorea</b>	Brief, rapid, jerky, and irregular movements that are coordinated and graceful. The face, head, and distal limbs are most commonly involved. They often interfere with normal movement patterns.
<b>Athetosis</b>	Continuous, slow, wormlike, twisting and turning motions of a limb or body that most commonly involve the face and distal extremities and are often associated with spasticity. Athetosis is seen following neonatal insults (cerebral palsy)
<b>Myoclonus</b>	Sudden, brief jerks or spasms, usually involving the limbs.
<b>Ballismus</b>	Involve violent sweeping, flinging-type limb movements, especially on one side of the body (hemiballismus)
<b>Dystonia</b>	Abnormal maintenance of posture results from a twisting, turning motion of the limbs, neck, or trunk. Motions are similar to athetosis but involve larger portions of the body. They can result in grotesque and twisted postures.
<b>Dyskinesias</b>	Rhythmic, repetitive, bizarre movements that chiefly involve the face, mouth, jaw, or tongue, causing grimacing, pursing of the lips, protrusion of the tongue, opening and closing of the mouth, and deviations of the jaw. The limbs are affected less often.

### Phase states

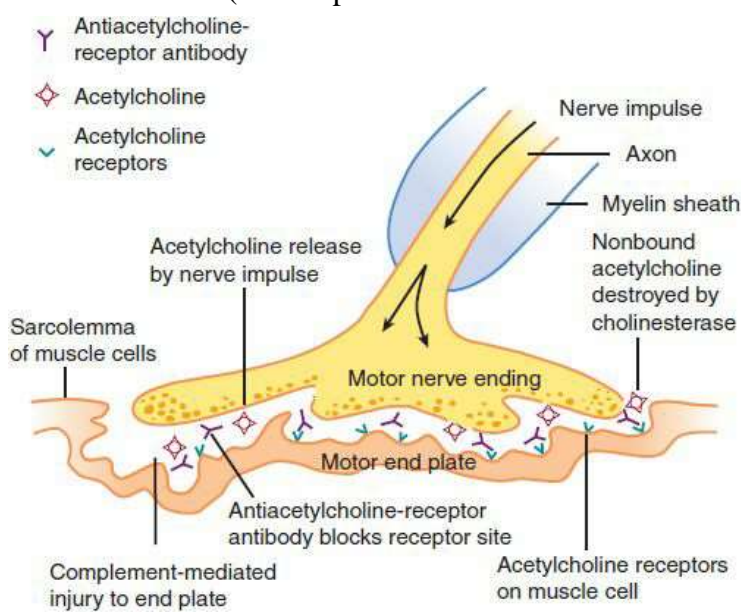
Phase states — disorders of adequate relationship between the intensity and / or character ("quality") response (conditionally or unconditioned reflex) and the parameters of the stimulus that causes this reaction.

#### Consequences of phase states :

- Loss of normal interneuron relations, functional sets of neurons or systems (functional disintegration of NS)
- Formation of pathological functional connections between neurons (pathological integration), new sets of neurons and functional systems (pathological system)

#### Types of phase states:

- equalizing (similar responses of neural structures on the impact of different intensities)
- middle stimuli (only responses to stimuli of medium intensity)
- paradoxical (weak or no reaction to a strong stimulus, maintain or enhance the reaction to weak stimuli)
- narcotic (loss response on weak reactions and then to strong stimuli)



- braking (lack of response to any stimulus)
- ultraparadoxical (qualitative change between nature of stimulus and reactions they provoke: negative reactions occur in response to positive stimuli and vice versa)

### Myasthenia Gravis

Myasthenia gravis is a disorder of transmission at the neuromuscular junction that affects communication between the motoneuron and the innervated muscle cell. The disease may occur at any age, but the peak incidence occurs between 20 and 30 years of age and affects women more often than men. A smaller second peak occurs in later life and affects men more often than women. Now recognized as an autoimmune disease, the disorder is caused by antibody-mediated loss of acetylcholine receptors in the neuromuscular junction. In persons with myasthenia gravis who have fewer acetylcholine receptors in the postsynaptic membrane, each release of acetylcholine from the presynaptic membrane results in a lower-amplitude end-plate potential. This results in both muscle weakness and fatigability with sustained effort. Most commonly affected are the eye and preorbital muscles. Either ptosis caused by eyelid weakness or diplopia caused by weakness of the extraocular muscles is an initial symptom in approximately 50% of persons with the disease. The disease may progress from ocular muscle weakness to generalized weakness, including respiratory muscle weakness. Chewing and swallowing may be difficult, and persons with the disease often choose to eat soft foods and cereals, rather than meats and hard fruit. Weakness in limb movement usually is more pronounced in proximal than in distal parts of the extremity, so climbing stairs and lifting objects are difficult. As the disease progresses, the muscles of the lower face are affected, causing speech impairment. When this happens, the person often supports the chin with one hand to assist in speaking. In most persons, symptoms are least evident when arising in the morning, but they grow worse with effort and as the day proceeds.

### Parkinson's Disease

Parkinson's disease is a degenerative disorder of basal ganglia function that results in variable combinations of tremor, rigidity, and bradykinesia. The disorder is characterized by progressive destruction of the nigrostriatal pathway, with subsequent reduction in striatal concentrations of dopamine. The clinical syndrome arising from the degenerative changes in basal ganglia function often is referred to as parkinsonism. Parkinson's disease, the most common form of parkinsonism

**Figure – The clinical features of Parkinson's disease.**



### Guillain-Barre Syndrome (GBS)

Group of five autoimmune peripheral neuropathies.

- acute inflammatory demyelinating polyneuropathy (90% of cases)
- acute motor axonal neuropathy (young people)
- acute motor sensory axonal neuropathy (uncommon)
- Miller-Fisher syndrome (rare)
- acute pandysautonomia (rarest)

1-3 cases/100,000/year. All age groups. No gender preference. Incidence unrelated to current influenza vaccines.

### Pathophysiology

Common pathogens are campylobacteriosis (most common), cytomegalovirus, Epstein-Barr virus, varicella zoster virus, mycoplasma pneumonia.

- Antecedent infection - one to three weeks before GBS onset
- Interaction of pathogen and nerve tissue activates autoimmune response - immunity to self
- Antecedent infection - one to three weeks before GBS onset
- Autoimmune response produces antibodies that cause demyelination of nerve cells
- Demyelination impairs neural conduction

### Manifestations:

- Severity is variable - weakness to total paralysis with autonomic dysfunction
- Evolves over hours to days
- Ascending paralysis - starts as 'rubbery legs'

- Tingling in extremities
- Does not affect consciousness -patients are alert and frightened
- May involve cranial nerves – bulbar weakness
- Loss of deep tendon reflexes
- Pain in affected muscles; sometimes back pain
- Ventilatory failure in 30% of patients

### **Huntington's chorea**

Huntington's chorea is clinically characterized by extrapyramidal involuntary or choreiform movements. Biochemically, there is marked decrease in endogenous gamma-amino-butyric acid and in glutamic acid decarboxylase. There is also a decrease in choline-acetyltransferase and in the muscarinic cholinergic receptors. It leads to a deterioration of the filtering ability of the striatum, allowing uncontrolled stimulation of the lower centers by the globus pallidus, resulting in abnormal involuntary movements and chorea. Motor deficit (bradykinesia, akinesia) joins an abnormal activation of the motor system, resulting in rigidity.

### **Typical forms of sensation disorders**

Abnormal perception of stimulus intensity (dysesthesia) abnormal perception of stimulus pattern, number, and localization

- hyperesthesia
- hypoesthesia
- anesthesia
- hypalgesia
- paresthesia
- hyperpathia
- polyesthesia
- synesthesia
- allodynia

#### **Types of hypoesthesia**

- Receptor –damage to nerve ending (t<sup>o</sup>, tactile)
- Conductive – damage to nerve, spinal cord (proprio, tactile)
- Central– damage to neurons of CNS
- Total–lose of all types of sensitivity
- Partial – lose of single types of sensitivity (tactile)

*Hyperesthesia* — exaggerated perception of sensations in response to mild stimuli (e.g. hyperalgesia).

#### **Types of hyperesthesia**

- Receptor
- Central
- Total
- Partial

*Allodynia* — an ordinarily nonpainful stimulus, once perceived, is experienced as painful.

*Hyperpathia* — a broad term, encompasses all the phenomena described by hyperesthesia, allodynia, and hyperalgesia.

*Polyesthesia* — an abnormal sensation of touch in which a single stimulus is felt at two or more places.

*Synesthesia*: a sensation in one area from a stimulus applied to another part; a subjective sensation of a sense other than the one being stimulated (hearing sound may also produce the sensation of smell).

#### **Types of dysesthesia**

- Thermalgia – cold and hot feeling as pain
- Polyesthesia – feeling of many irritants in real one
- Allodynia – feeling unpainful factors as painful
- Hyperpathy –intensive pain in effect of different irritants with combination of losing of location of it's action
- Paresthesia – tactile unpainful unusual sense
- Synesthesia –several sense in irritation of one sense organ (colored smelling)

Depending character of lost sensitivity:

- tactile anesthesia
- pain (analgesia)
- thermal (thermanesthesia)
- loss of deep or proprioceptive sensitivity

Systems of sensitivity

- main afferent pathways conducting conscious overall sensitivity are: the path of pain, temperature and tactile sensitivity; the path of conscious proprioceptive sensitivity.
- main afferent pathways unconscious overall sensitivity are: anterior and posterior spinal cerebellar path.
- pathways special sensitivity include auditory, visual, vestibular, olfactory and gustatory path

### **Three levels of sensation disorders:**

1 disorders of reception:

- changes in threshold parameters, surface density and number of receptors.

2 damage of the sensory pathways:

- polyneuropathy during metabolic disorders (diabetes), intoxication or inflammatory reactions.

3) disorders of the central analyzers of sensation (postcentral gyrus of the parietal cortex):

- complex sensational deficits, such as stereognosis.

*Stereognosis* — the ability to identify common objects by palpation, recognizing their shape, texture, and size

## **Pain**

*Pain* that is classified on the basis of its presumed underlying pathophysiology is broadlycategorized as nociceptive or neuropathic pain.

*Nociceptive pain* is caused by the ongoing activation of A- and C-nociceptors in response to a noxious stimulus (e.g., injury, disease, inflammation). Pain arising from visceral organs is called visceral pain, whereas that arising from tissues such as skin, muscle, joint capsules, and bone is called somatic pain. Somatic pain may be further categorized as superficial (cutaneous) or deep somatic pain .

In contrast to neuropathic pain, the nervous system associated with nociceptive pain is functioning properly. Generally, there is a close correspondence between pain perception and stimulus intensity, and the pain is indicative of real or potential tissue damage. Differences in how stimuli are processed across tissue types contribute to the pain's varying characteristics

**Table1. Examples and characteristics of Nociceptive pain**

	Superficial Somatic Pain	Deep Somatic Pain	Visceral Pain
Nociceptor location	Skin, subcutaneous tissue and mucous membrane	Deep somatic pain. Muscles, tendons, joints, fascial, bones	Visceral organs
Potential stimuli	External mechanical, chemical or thermal events. Dermatologic disorders	Overuse strain, mechanical injury, cramping, ischemoia, inflammation	organ distension,muscle spasm, tration, ischemia, inflammation
Localization	Well localized	Localized or diffuse and radiating	Well or poorly localized
Quality	Sharp, pricking or burning sensation	Usually dull or aching, cramping	Deep aching or sharp stabbing pain, which is often referred to cutaneous sites

Associated symptoms and signs	Cutaneous tenderness, hyperalgesia, hyperesthesia, allodynia	Tenderness, reflex muscle spasm, and sympathetic hyperactivity	Malaise, nausea, vomiting, sweating, tenderness, reflex muscle spasm
Clinical examples	Sunburn, chemical or thermal burns, cuts and contusions of the skin	Arthritis, pain, tendonitis, myofascial pain	Colic, appendicitis, pancreatitis, peptic ulcer disease, bladder, distension

Although pain classes are not diagnoses, categorizing pain helps guide treatment. Multiple systems for classifying pain exist. These include multidimensional classification systems, such as the IASP Classification of Chronic Pain, and a variety of systems based on a single dimension of the pain experience. Of the latter systems, those based on pain duration (i.e., acute vs. chronic pain) and underlying pathophysiology (i.e., nociceptive vs. neuropathic pain) are used most often.

We explore the distinction between acute and chronic pain. It also reviews elements of a mixed pain classification system in which pain is categorized as acute pain, cancer pain, or chronic noncancer pain (CNCPP).

#### **Types of pain**

- Physiological
- Pathological
- Epicritic (sharp)
- Protopathic (non severe prolonged nonintensive)

Protopathic	Epicritic
Is conducted through S-fibers into thalamus and hypothalamus	Is conducted through S- fibers of thalamus and cortex nuclei
Slowly realized Poorly localized	Is quickly realized Easily localized and determined
Adaptation does not appear Is preserved for a long period of time	Adaptation appears fast
More ancient and less dangerous signal of danger	Continues no longer than stimulus action

Neuropathic pain is caused by aberrant signal processing in the peripheral or central nervous system. In other words, neuropathic pain reflects nervous system injury or impairment. Common causes of neuropathic pain include trauma, inflammation, metabolic diseases (e.g., diabetes), infections (e.g., herpes zoster), tumors, toxins, and primary neurological diseases. Neuropathic pain can be broadly categorized as peripheral or central in origin. Painful peripheral mononeuropathy and polyneuropathy, deafferentation pain, sympathetically maintained pain, and central pain are subdivisions of these categories. Neuropathic pain is sometimes called «pathologic» pain because it serves no purpose. A chronic pain state may occur when pathophysiologic changes become independent of the inciting event.

#### **Pain types and features**

*Acute pain.* Pain usually concordant with degree of tissue damage, which remits with resolution of the injury. Reflects activation of nociceptors and/or sensitized central neurons. Often associated with ANS and other protective reflex responses (e.g., muscle spasm, «splinting»).

*Chronic pain.* Low levels of identified underlying pathology that do not explain the presence and/or extent of the pain

Perpetuated by factors remote from the cause. Continuous or intermittent with or without acute exacerbations.

Symptoms of ANS hyperactivity less common. Irritability, social withdrawal, depressed mood and vegetative symptoms (e.g., changes in sleep, appetite, libido), disruption of work, and social relationships.

*Cancer pain.* Strong relationship between tissue pathology and levels of pain. Limited time frame that permits aggressive pain management. Rarely involves medical-legal or disability issues.

CNCP. Weak relationship between tissue pathology and pain levels. Prolonged, potentially life-long, pain. May involve medical, legal, disability issues/conflicts, work or relationship problems, physical deconditioning, psychological symptoms.

May progress to CPS Weak relationship between tissue pathology and pain levels. Prolonged, potentially life-long, pain

May involve medical, legal, disability issues/conflicts, work or relationship problems, physical deconditioning, psychological symptoms. May progress to CPS.

CPS .Preoccupation with somatic functioning. Lifestyle centered on seeking immediate Pain relief, with excessive, nonproductive, and often harmful use of health care services. Repeated attempts to obtain pain-related financial compensation (e.g., Social Security, Veterans' benefits). Numerous symptoms and signs of psychosocial dysfunction that the patient attributes to the pain (e.g., anger, depression, anxiety, substance abuse, disrupted work or personal relationships).

### **Pathological pain**

- **Central pain** is a sensation of pain in absence of peripheral nociceptive stimuli (processed in cortical pain areas)
- **Phantom pain** (patient suffers from severe pains, and sensation is projected to the amputated limb, due to pressing of surrounded tissues on formatted neurinome)
- **Causalgia** is strong poignant pain connected to strong deformation of nerve for want of wound by high-speed shell (by bullet, splinter). Causalgia is characterized by unabating intensive pain, which amplifies for want of operation even weak irritable, which in healthy person of pain do not cause (touch, unexpected noise, sharp light, emotional effect).
- **Neuralgia** is characterized by a strong pain also connected to damage of peripheral nerve. On the manifestations it is similar to causalgia. The reasons it is a virus infection (herpes zoster), degeneration of nerves for want of diabetes mellitus, ischemia extremities, beri-beri, poisoning arsenic or lead.
- **Thalamic pain** episode of depletive pain with movement, phsyhoemotional disorders and disturbances of autonomic NS. Mechanisms is a damage of thalamic nuclei and formation of GPIE focus
- **Eccentric pain** is a pain in the certain sites of a skin for want of internal organs defeat. Afferent impulsation from internal organs and from appropriate dermatom acts in same neuron of dorsal horns of spinal cord, which give beginning to spinothalamic path. If the internal organ is injured, from it is going extremely powerful streams of painful impulses. They increase sensitivity skin receptors appropriate dermatom. In the total the pain going from an internal organ, is perceived simultaneously and as pain in the certain site of skin.

### ***Systems of excitability and recipient of pain signal.***

The main processes of physiologic nociception:

1. transduction – injury transformation into the nerve end electric activity
2. transmission – transmission of impulse in CNS
3. modulation – change of nociceptive information by antinociceptive influences
4. perception – subjective emotional feeling forming under the action of CNS genetically determined features and muscular irritations from periphery

***Pathologic algic system.*** It is a new pathologic integration forming from primary and secondary achanged formations of pain system under the influence of pathologically increased excitability generator.

It has peripheral, spinal, central levels of organisation. It is a pathological base of pain syndrome.

### ***Endogenous anti-nociceptive system***

It controls the pain signal transmission and analyze pain signal (modulation). It is characterized by the constant activity level. That forms sensation threshold (adaptive role).

***Mechanisms of anti-nociceptive system:***

- neurogenic
- humoral

### **Abnormalities in autonomic nervous system: types, mechanisms.**

Impaired function of the autonomic nervous system is manifested in the appearance of the complex or the individual signs of increased activity of a part of autonomous nervous system, which depend on the functional state.

Autonomic centers positioned in the medulla oblongata, thalamus and hypothalamus. These centers are considered as common autonomic centers with forward and backward linkages with the cerebral cortex. In one and the same body depending on the environmental conditions in different time can dominate the activity of various autonomic centers.

Increased activity of parasympathetic autonomic nervous system (vagotonic) is characterized by:

- a) The narrowing of the pupils;
- b) hypersalivation;
- c) sweating;
- d) bradycardia;
- e) asthmatic breathing, etc.

Long vagotonia may lead to the development of pathological conditions such as hypotension, spastic constipation, peptic ulcer, etc.

Increased activity of sympathetic nervous system (sympathicotony) is characterized by:

- a) dilated pupils;
- b) sialoschesis;
- c) tachycardia;
- d) increased irritability etc.

Persistent sympathicotony predisposes to the development of hypertension and atonic constipation.

### **Neurodystrophic process: etiology, pathogenesis. Role of pathotrophogenes. Manifestations of neurodystrophia.**

**Trophic of cells** - a set of processes that ensure its vitality and maintenance of genetically inherent properties

Dystrophy – the disorder of the trophic

Dystrophic process is developing degenerative changes

**Loss of nervous influence is consisting:**

- 1) in arrest of stimulation of the innervated structures in connection with violation of release neurotransmitter or its action
- 2) in the violation of secretion or action comediators — substances released together with neurotransmitters (act as neuromodulators, provide receptor regulation, membrane and metabolic processes
- 3) in the violation of releasing and action trophogenic

**Trophogenes** - various substances, mainly of protein nature, that made trophic effects on life support and genetically inherent properties of the cell

**Sources trophogenes:**

- 1) Neurons from which trophogenes with orthograde axoplasmatic current come in the recipient cells (other neurons or tissue at the periphery)
- 2) Cells of the peripheral tissues, from which trophogenes by nerves comes with retrograde axoplasmatic current to neurons
- 3) Schwann cells and glia, which interchange their trophic substances with the neurons and their branches
  - Substances which act as trophogenic, formed from the serum and immune proteins
  - Some hormones have trophic effect

In the regulation of trophic processes involved peptides, gangliosides, some neurotransmitters

**Normotrophogenes** - proteins that promote growth, differentiation and survival of neurons and somatic cells, preserve their structural homeostasis (e.g., nerve growth factor)

**Pathotrophogenes**

- trophic substances causing pathological changes resistant recipient cells
- can be distributed on the NS, as in trophic net, it is one of the mechanisms of generalization of the pathological process

- For example, such substances are synthesized in epileptic neurons - acting with the axoplasmatic current in the other neurons can induced in the recipient neurons epileptic properties
- Pathotrophogenes formed in other tissues

**Neurodegenerative process** — trophic developmental disorder, which is caused by change or fallout of nervous influence.

Pathogenetic basis:

- ✓ Violation of the trophic function of the NS
- ✓ Influence of pathotrophogenes inducing sustained changes in the cells
- ✓ Vascular changes in the tissues
- ✓ Violation of transport nutrients and plastic materials into the cell

Symptoms: structural and functional changes in organs and tissues (atrophy, ulceration, malignancy).

Typical variant - denervation syndrome.

### **The manifestations of the Denervation syndrome**

When damaged, the NS may experience **generalized forms of neurodegenerative process**

**Manifestations:**

- gum disease (ulcers, aphthous stomatitis)
- tooth loss
- bleeding in the lungs
- mucosal erosions and bleeding in the stomach (often in the pylorus), intestine (especially in the region. Buaginievoy flap), rectum

### **Neuroses**

**Neuroses** is typical form of NS pathology as a result of functional effect over it, which exceeds HNA's resources

**Reason:** Lingering psycho-emotional stress.

**Pathogenetic basis:** Functional, microstructural and neurochemical changes in the central nervous system, which lead to a disruption of balance between excitation and inhibition or their collision.

**Conditions of neurosis.**

#### **1. Biological**

- Genetic predisposition: a weak type of HNA.
- Sex: more common in women.
- Age at puberty and often menopause.
- Constitutional features: prone asthenics.
- Asthenization of NS

#### **2. Social.**

- Information overload.
- The poor marital status.
- Poor living conditions, etc.

#### **3. Psychogenic.**

- Personal characteristics (a way of thinking, perception, behavior and response).
- traumatic situation, a long process of analysis "ideational processing»

### **Methods of experimental neuroses**

I. Stress and disruption of cortical excitation:

Developing a neurosis with a predominance of inhibition.

Characterized by the development of passive defense reactions, depression, drowsiness.

II. Stress and disruption of the inhibitory process:

Developing a neurosis with a predominance of excitation.

Characterized by inadequate agitation, aggressiveness and malice.

III. Stress and disruption of the optimal change of excitation and inhibition:

Neurosis develops with abnormal mobility of nervous processes:

- neurosis with pathological inertia and the frequent development of phobias.
- neurosis with pathological lability, manifested "fussiness" pending actions, increased physical activity.

The classification of the neuroses of the ICD-10 (group F4).

### **I. Obsessive-compulsive disorder.**

F40. Anxiety and phobic disorders

F41. Other anxiety disorders

F42. Obsessive-Compulsive Disorder

Reason: the pathological focus in the cortex brain

The most common types of disorders:

- Simple phobias: claustrophobia, agoraphobia, cancerophobia.
- Social phobias.
- Obsessive-compulsive disorder: the obsessive thoughts.

### **II. Hysterical neurosis.**

F44. Dissociative (conversive) disorders

F45. Somatoform disorders

Reason: The stress and exhaustion of the cortical processes with development of phase states.

Manifestation:

- ✓ Inappropriate behavior with somatoform disorders (excessive attention to health, "the desire of the disease", "suicide blackmail").
- ✓ autonomic dysfunction
- ✓ Movement disorders (seizures without loss of consciousness and bruises, transient paresis / paralysis, transient aphonia).
- ✓ Sensory disturbances (transient blindness, deafness, paresthesia, loss of smell sense).
- ✓ Sexual deviance

### **III. Neurasthenia.**

F48.0 Neurasthenia (or fatigue syndrome).

Reason: The stress and disrupt the process of cortical arousal.

Manifestation:

- ✓ Autonomic dysfunction.
- ✓ Increased irritability, fatigue, exhaustion of the NS.
- ✓ Excessive irritability, incontinence, impatience.
- ✓ disorders of attention.
- ✓ Reduced workability.
- ✓ The instability of mood.
- ✓ Sleep disorders.
- ✓ Sexual violation.

### **Manifestations of experimental neuroses**

- Disturbances of HNA (prolapse of conditional reflexes and impossibility of production of new ones)
- Development of phase conditions
- Vegetative disorders (the earliest and firm disorders)
  - ✓ Headaches
  - ✓ Cardio-vascular disorders: (heart pains, feeling of pulsation, tachycardia, arrhythmia, dyspnea)
  - ✓ Trophic disturbances (derma-dystrophic: aczema, papilloma, neoplasma)
  - ✓ Sensitivity disorders
  - ✓ Disorders of motion function (hyper- and hypokinesia)

### **Informational neurosis**

- Increase of volume of information, subject to processing in order to take important decision
- Time deficiency for such brainwork
- High level of motivation, defining the importance of information and necessity of its processing

### **Neuroses as causes**

- Hypertension
- Coronary insufficiency
- Myocardial infarction
- Peptic ulcer

- endocrinology

### **Brain Death**

Brain death is irreversible loss of cerebral hemisphere, brainstem, and cerebellum function. Consciousness is lost, as is maintenance of respiration, cardiovascular, and temperature control function. There is no sleep-wake cycle, no pain response, and no reflexes. The electroencephalogram (EEG) is flat in an individual with brain death.

Establishing brain death has several legal implications. A patient cannot be legally discontinued from life support without prior living will instructions unless brain death is established. Organ donation is allowed only when brain death is established. Unfortunately, a donated organ is more likely to be healthy when taken from an individual before brain death occurs.

#### **Questions for self-control of knowledge:**

1. Results of nervous system trophic function impairments.
2. Types of higher nervous system activity specified by academic I.P. Pavlov. Features of excitation and processes of each type.
3. What are main causes of neurosis?
4. Conditioned reflex activity in neuroses.
5. What are vegetative-somatic manifestations of neuroses?
6. What is difference between pathologic and physiologic conditioned reflexes?
7. Pain definition. What is biological role of pain?
8. What is difference between pain and nociception?
9. What are factors that cause pain?
10. What substances are mediators of pain?
11. Specify a properties characteristic of pathological and physiological pain?
12. What neurotransmitters is antinociceptive system?
13. What are possible pharmacological treatments for pain?
14. What are possible ways of surgical treatment of severe chronic pain?

#### **Tasks for self-managed student work:**

1. Myasthenia gravis, convulsive state; their types and mechanisms.
2. Modern principles of pain correction.
3. Multiple sclerosis, Parkinson's disease.
4. Neurophysiological theories of neuroses.

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