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Pathophysiology of Pain Pathogenesis, Mechanism, Pathology Prognosis

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Annotation: Pain is the most common symptom that causes suffering to millions of people worldwide. The treatment and elimination of pain is one of the most important tasks, comparable in importance to life-saving measures. What is pain?

The International Association for the Study of Pain defines pain as: “Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

Pain is a specific psychophysiological state of a person, which occurs as a result of the action of extremely strong or destructive stimuli and causes functional or organic disorders in the body. The word "disease" itself is directly related to the concept of "pain". Pain should be considered as a stress factor, which activates functional and metabolic systems with the participation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal cortex system. These systems provide protection of the body from the effects of pathogenic factors. Pain includes such components as consciousness, emotion, motivation, feelings, as well as vegetative, somatic and behavioral reactions. The perception and perception of pain is based on nociceptive and antinociceptive mechanisms.

Keywords: Pain mechanism, pathogenesis, pathology, types, diagnosis, classification.

Introduction: The system of transmission and perception of pain signals belongs to the nociceptive system. Pain signals cause adaptive responses aimed at eliminating the stimulus or the pain itself. Under normal conditions, pain plays a role as the most important physiological mechanism. If the strength of the stimulus is great and its effect lasts for a long time, then the adaptation processes are disrupted and physiological pain turns from a protective mechanism into a pathological mechanism.

Under the influence of a damaging factor, a person can experience two types of pain. When acute injury (for example, when struck by a sharp object, when injected), local intense pain occurs. This is primary, epicritic pain. The structural basis of such pain is myelinated A d fibers and the spinothalamocortical tract. They provide a clear localization and intensity of pain. After 1-2 seconds, epicritic pain disappears. In its place, secondary, protopathic pain appears, which gradually increases in intensity and lasts for a long time. Its occurrence is associated with slowly conducting unmyelinated C-fibers and the spinocortical system.

Visceral pain is pain localized in the internal organs. It is diffuse in nature, often not clearly localized and is accompanied by depression, inhibition, and changes in the functions of the autonomic nervous system. Pain in diseases of internal organs occurs as a result of: 1) impaired blood flow (atherosclerotic changes in blood vessels, embolism, thrombosis); 2) spasm of the smooth muscles of internal organs (in peptic ulcer, cholecystitis); 3) stretching of the walls of hollow organs (gallbladder, renal pelvis, urinary tract); 4) inflammatory changes in organs and tissues.

Pain impulses from internal organs are transmitted to the central nervous system through thin fibers of the sympathetic and parasympathetic nervous systems. Visceral pain is often accompanied by the formation of referred pain. This type of pain occurs in organs and tissues that do not have morphological changes and is caused by the involvement of the nervous system in the pathological process. Such pain can occur with heart disease (angina pectoris). When the diaphragm is damaged, pain occurs in the back of the head or shoulder blade. Diseases of the stomach, liver and gallbladder are sometimes accompanied by toothache.

A special type of pain is phantom pain - pain localized by the patient in the limb lost. During surgery, nerve fibers cut off can become stuck in the scars and press on the healing tissue. In this case, impulses from the damaged nerve endings through the nerve nodes and dorsal roots enter the spinal cord, where the pain-sensing apparatus of the lost limb is preserved, and reach the visual thalamus and cerebral cortex. The main focus of excitation occurs in the central nervous system. In the development of this pain, fine nerve conductors play a major role.

Pain reaction can be caused by any stimulus (sound, light, pressure, temperature factor), if its strength exceeds the sensitivity threshold of the receptors. Chemical factors (acids, alkalis), biologically active substances (histamine, bradykinin, serotonin, acetylcholine), potassium and hydrogen ions play a major role in the development of pain reactions. Excitation of receptors also occurs during their prolonged irritation (for example, in chronic inflammatory processes), under the influence of tissue decomposition products (during tumor decay), and compression of the nerve by scar or bone tissue.

Skin damage, fatigue, insomnia, and cold increase the sensation of pain. The time of day affects the characteristics of pain. At night, pain in the stomach, gallbladder, renal pelvis, pain in the hands and fingers, and pain from damage to the vessels of the limbs have been noted. Hypoxic processes in nerve conduction and tissues contribute to the increase in pain.

Research methods and materials: Inhibitory processes in the central nervous system prevent the development of pain, while excitation of the central nervous system enhances the effect of pain. Fear, anxiety, and self-doubt increase pain. If the body expects to apply a painful stimulus, the sensation of pain decreases. In diabetes mellitus, an increase in pain sensation in the trigeminal nerve, which innervates the oral cavity (jaws, gums, teeth), has been noted. A similar effect is

observed with gonadal insufficiency.

The nature of pain changes with age. The pain sensation becomes chronic, the pain becomes dull, which is caused by atherosclerotic changes in blood vessels and impaired microcirculation in tissues and organs.

According to this theory, a mechanism for controlling the transmission of nociceptive impulses operates in the afferent input system to the spinal cord, in particular in the dorsal horns of the spinal cord. It has been established that somatic and visceral pain are associated with slow-conducting impulses of small-diameter fibers belonging to the A d (myelinated) and C (unmyelinated) groups. Thickly myelinated fibers (A □ and A □) serve as conductors of tactile and deep sensitivity. Control of the transmission of pain impulses is carried out by inhibitory neurons of the gelatinous substance of the spinal cord (SG). Thick and thin nerve fibers form synaptic connections with neurons of the dorsal horns of the spinal cord (T), as well as neurons of the gelatinous substance (SG). In this case, thick fibers increase, and thin fibers inhibit and reduce the activity of SG neurons. In turn, SG neurons act as gates that open or close pathways for impulses that excite spinal T neurons.

If impulses come through thick fibers, then the inhibitory neurons of the SG are activated, the “gates” are closed, and pain impulses along thin nerve fibers do not reach the dorsal horn of the spinal cord.

When thick myelin fibers are damaged, their inhibitory effect on SG neurons decreases and the “door” opens. In this case, pain impulses are transmitted through thin nerve fibers to the T-neurons of the spinal cord, creating a sensation of pain. From this perspective, the mechanisms of phantom pain can be explained. When a limb is amputated, thick nerve fibers suffer more, the inhibition processes of SG neurons are disrupted, the “doors” open, and pain impulses are transmitted through thin fibers to the T-neurons.

This is the theory of GN. Kryzhanovsky. According to this theory, the formation of pathologically enhanced excitation (GPE) generators in the nociceptive system plays an important role in the occurrence of pathological pain. They appear when the pain stimulus is long enough and is able to overcome the "gate" control.

Results: Such GPUV is a complex of hyperreactive neurons capable of increasing activity without additional stimulation from the periphery or other sources. GPUC can occur not only in the afferent input system to the spinal cord, but also in other parts of the nociceptive system. Under the influence of primary GPUK, other systems of pain sensitivity are involved in the pathological process, which together form a pathological system with increased sensitivity. This pathoalgic system forms the pathophysiological basis of the pain syndrome.

Both polymodal receptors and specific nociceptive receptors are capable of perceiving pain stimuli. Polymodal receptors are represented by a group of mechanoreceptors, chemoreceptors and thermoreceptors located both on the skin surface and in internal organs and in the vascular wall. The effect of a very strong stimulus on the receptors leads to the appearance of a painful impulse. Overexcitation of the auditory and visual analyzers plays a major role in the appearance of pain. Thus, very strong sound vibrations cause a pronounced sensation of pain, up to and including disruption of the central nervous system (airports, train stations, discos). A similar reaction occurs due to irritation of the visual analyzers (light effects at concerts, discos).

Primary, epicritic pain occurs as a result of the transmission of a pain signal along myelinated type A δ fibers. Secondary, protopathic pain occurs as a result of the transmission of excitation along thin, slowly conducting fibers of type C. Violation of nerve trophism leads to a blockade of tactile sensitivity along thick pulp nerves, but pain sensation remains. When local anesthetics are used, pain sensitivity disappears first, and then tactile sensitivity. This is due to the cessation of excitation conduction along thin unmyelinated type C fibers. Thickly myelinated fibers are more sensitive to oxygen deficiency than thin fibers. Damaged nerves are more sensitive to various

humoral influences (histamine, bradykinin, potassium ions), to which they do not react under normal conditions.

The central pathophysiological mechanisms of pathological pain are the formation and activity of generators of increased excitability in some part of the nociceptive system. For example, the cause of the appearance of such generators in the dorsal horns of the spinal cord may be prolonged stimulation of peripherally damaged nerves. With chronic compression of the infraorbital branch of the trigeminal nerve, pathologically increased electrical activity and the formation of a pathologically increased excitability generator occur in its caudal nucleus. Thus, pain of peripheral origin takes on the character of a central pain syndrome.

Discussion: The cause of the appearance of generators of high excitability may be partial deafferentation of neurons. During deafferentation, the excitability of nerve structures increases, inhibition and disinhibition of deafened neurons are disrupted, their trophism is disturbed. Increased sensitivity of tissues to pain impulses can also occur with denervation syndrome. In this case, there is an increase in the area of receptor zones capable of responding to catecholamines and other biologically active substances, and pain perception is enhanced.

The trigger for the development of pain is the primary generator of pathologically increased excitation. Under its influence, the functional state of other areas of pain sensitivity changes and the excitability of their neurons increases. Gradually, secondary generators are formed in different parts of the nociceptive system, with the participation of the higher parts of pain sensitivity in the pathological process - the thalamus, somatosensory and orbitofrontal cortex of the brain. These zones carry out the perception of pain and determine its nature.

The central mechanisms of pain sensitivity are represented by the following formations. The neuron that responds to a nociceptive stimulus is located in the dorsal root ganglion (D). As part of the dorsal roots, the conductors of this ganglion enter the spinal cord and end on the neurons of the dorsal horns of the spinal cord (T), forming synaptic connections with them. The processes of T-neurons along the spinothalamic tract (3) transmit excitation to the optic thalamus (4) and end on the neurons of the ventrobasal complex of the thalamus (5). Neurons in the thalamus transmit impulses to the cerebral cortex, which determines the process of pain perception in a particular area of the body. The greatest role in this process belongs to the somatosensory and orbitofrontal zones. With the participation of these zones, responses to nociceptive stimuli from the periphery are carried out.

In addition to the cerebral cortex, an important role in the formation of pain belongs to the thalamus, where nociceptive irritation receives unpleasant, painful sensations. If the cerebral cortex ceases to control the activity of the main areas, thalamic pain without a clear localization is formed.

The localization and type of pain also depend on the involvement of other nervous system formations in the process. An important structure that processes pain signals is the reticular formation. When it is destroyed, the transmission of pain impulses to the cerebral cortex is blocked, and the adrenergic response of the reticular formation to pain stimulation is suppressed.

The limbic system plays a major role in the development of pain. The involvement of the limbic system is determined by the formation of pain impulses coming from internal organs: this system is involved in the formation of visceral pain. Irritation of the cervical sympathetic ganglion leads to severe pain in the teeth, lower jaw, and ear. When the somatic innervation fibers are compressed, localized somatology occurs in the innervation zone of the peripheral nerves and their roots.

In some cases, with prolonged irritation of the damaged peripheral nerves (trigeminal, facial, sciatic), a pain syndrome may develop, which is characterized by severe burning pain and is accompanied by vascular and trophic disorders. This mechanism underlies causalgia.

Functional neurophysiological mechanisms of the pain sensitivity system are implemented through

neurochemical processes.

Peripheral pain receptors are activated by many endogenous biologically active substances: histamine, substance P, kinins, prostaglandins, leukotrienes, potassium and hydrogen ions. Stimulation of pain receptors has been shown to cause the release of neuropeptides such as substance P by unmyelinated C-type nerve fibers. This is a pain mediator. Under certain conditions, it can promote the release of biologically active substances: histamine, prostaglandins, leukotrienes. The latter increases the sensitivity of nociceptors to kinins.

Conclusion: Potassium and hydrogen ions play an important role in the development of pain. They facilitate the depolarization of receptors and contribute to the emergence of an afferent pain signal in them. With increasing nociceptive stimulation, a large amount of excitatory substances, in particular glutamate, appears in the dorsal horn of the spinal cord. These substances cause depolarization of neurons and are one of the mechanisms for the formation of pathologically increased excitation generators.

The formation of a pain impulse is closely related to the functional state of the antinociceptive system. The antinociceptive system exerts its effect through neurogenic and humoral mechanisms. Activation of neurogenic mechanisms leads to blockade of ascending pain impulses. When neurogenic mechanisms are impaired, even low-intensity painful stimuli cause severe pain. This can occur, for example, in cases of CNS damage or neuroinfection, when there is a deficiency of antinociceptive mechanisms responsible for the gate control system. Neurochemical mechanisms play a large role in the activity of the antinociceptive system. They are carried out by endogenous peptides and mediators.

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