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Учреждение образования
«Гомельский государственный медицинский университет»

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

Тема: **Экстремальные состояния**

Theme: **Extreme conditions**

Время 3 ак. часа

Actuality of the theme. Extreme conditions are characterized by maximum stress of protective reactions and significant disturbances in vital activity of organism. The organism ceases to be a monolithic structural and functional complex: internal integrative connections are broken, chain reactions are rampant, which inevitably leads to severe damage to the body. Treatment and prevention of extreme conditions are based on a deep knowledge of pathophysiological mechanisms of organism's interaction with pathogenic factors.

Learning goals of the lesson: on an example of various extreme conditions to disassemble the implementation of typical pathological processes that threaten human life

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 compensatory-adaptive mechanisms at all levels in extreme conditions.
2. To characterize shock as a general pathological process, to explain nature of changes in shock, possibility of their correction.
3. To know types, causes, main links of pathogenesis, manifestations, consequences of collapse.
4. To know causes, mechanisms of development, features of pathogenesis of coma.
5. Form an idea of stress; be able to explain causes and mechanisms of occurrence adaptation diseases.

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

1. Structure and function of the vegetative nervous system. General structure of the neuroendocrine system (histology, cytology, embryology disciplines).
2. Principle of nervous system function (normal physiology discipline).

Control questions of the lesson:

1. General characteristics of extreme conditions, their difference from terminal conditions. Conditions that contribute to emergence of extreme conditions.
2. Shock: definition, types, pathogenesis, similarity and differences of individual types of shock.
3. Stages of shock, functional and structural disorders at different stages of shock. Pathophysiological basis for prevention and therapy of shock.
4. Crush-syndrome: etiology and main pathogenetic mechanisms of development.
5. Collapse: types, causes, main links of pathogenesis, manifestations and consequences. Principles of therapy. Syncope, etiology and pathogenesis.
6. Coma: species, etiology, pathogenesis, stages, violation of bodily functions. Principles of therapy.
7. Stress: stages, mechanisms of development, role of neuro-hormonal factors, main manifestations.
8. Value of stress. "Diseases of adaptation ".

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:

Extreme conditions are the conditions occurred under the influence of extreme pathogenic factors and characterized by the limiting effort of organism protective reactions.

Classification of extreme conditions:

According to clinical course:

- acute
- subacute
- chronic

According to the occurrence rate:

- flash-like (the first 10 min)
- immediate (the first day)
- delayed (weeks, months, years)

Features of extreme conditions:

1. extreme conditions are characterized by the occurrence of pathological reactions aggravating the frustrations in organism («vicious circles»)
2. extreme conditions have a set of similar metabolism and physiological function changes
3. extreme conditions can be autonomous reversible
4. extreme conditions demand urgent and effective medical actions

Similarities to terminal conditions:

- extreme conditions and terminal conditions are the boundary conditions between life and death
- there is a real threat of organism destruction in extreme and terminal conditions
- extreme conditions in case of the adverse development pass into terminal conditions

Differences between extreme and terminal conditions:

- extreme conditions are less severe, than terminal conditions
- extreme conditions usually precede the development of terminal conditions
- some forms of extreme conditions can be autonomous reversible
- terminal conditions without the emergency help of a doctor result in organism destruction (death)
- the effective methods of extreme condition treatment is the pathogenic factor elimination and blockage of the basic pathogenic mechanisms

SHOCK

Shock refers to “widespread hypoperfusion of cells and tissues to reduction in blood volume or cardiac output, or redistribution of blood resulting in a decrease of effective circulating volume”

Classification of shock:

1) CARDIOGENIC SHOCK.

Causes: rupture of heart, arrhythmias, myocardial infarction(>40%), pulmonary embolism, cardiac tamponade

Mechanism: failure of myocardial pump (due to intrinsic myocardial damage or extrinsic pressure or obstruction to outflow) → decreased cardiac output → hypotension → Impaired tissue perfusion → cellular hypoxia → **Shock**

Leading pathogenic link: pain, impairments of contractile function and rhythm of heart

2) HYPOVOLEMIC SHOCK

Causes: fluid loss (vomiting, diarrhea, dehydration).

Mechanism: fluid loss → inadequate blood or plasma volume → decreased cardiac output → hypotension → impaired tissue perfusion → cellular hypoxia → **Shock**

Leading pathogenic link: hypovolemia

3) SEPTIC SHOCK (endotoxic shock)

Causes: overwhelming bacterial infections: gram-negative septicemia (escherichia coli, klebsiella pneumonia, proteus species, pseudomonas aeruginosa, bacteroids, serratia); gram - positive septicemia (streptococci, pneumococci)

Mechanism: endotoxins → complement activation → release of c3a and c5a → mast cell degranulation and histamine release → peripheral vasodilation → peripheral pooling of blood → relative hypovolemia → impaired tissue perfusion → cellular hypoxia → **Shock**

Leading pathogenic link: ↑demand of organism in O₂ transport to tissue; ↓ blood oxygenation in lung and inefficient extraction of O₂ by tissue; activation proteolytic enzymes by endotoxine (kallikrein-kinin, complement, fibrinolytic)

4) TRAUMATIC SHOCK

Causes: crush syndrome, massive hardness trauma, broken of femur bone.

Mechanism: hemorrhage → hypovolemia → inadequate blood or plasma volume → decreased cardiac output → hypotension → impaired tissue perfusion → cellular hypoxia → **Shock**

pain → protective inhibition → disorganization between central nervous system and endocrine, cardio-vascular system → hypotension → impaired tissue perfusion → cellular hypoxia → **Shock**

There are two stage:

1. Erectile stage (voice, locomotor activation, pail skin, tachycardia, short term increasing BP);
2. Torpid stage.

Leading pathogenic link: pain, hypovolemia

5) HEMORRHAGIC SHOCK

Causes: massive hemorrhage

Mechanism: hemorrhage → inadequate blood or plasma volume → decreased cardiac output → hypotension → impaired tissue perfusion → cellular hypoxia → **Shock**

Leading pathogenic link: hypovolemia, hypoxia, may be pain

6) BURN SHOCK

Causes: extensive and deep burns > 15% (less surface for child and aged)

Mechanism: evaporation of fluid from damage skin → decreasing of total circulation blood → hypovolemia → impaired tissue perfusion → cellular hypoxia → **Shock**

Leading pathogenic link: hypovolemia, pain, ↑ permeability of vessels.

7) ANAPHYLACTIC SHOCK

Causes: allergens

Mechanism: allergen → allergic reaction type 1, 3 → mast cell degranulation and histamine release → peripheral vasodilation and increasing permeability of blood vessels → peripheral pooling of blood → relative hypovolemia → impaired tissue perfusion
bronchoconstriction and edema in upper airway → ↓ blood oxygenation in lung → cellular hypoxia → **Shock**

Leading pathogenic link: hypovolemia

8) NEUROGENIC SHOCK

Cause: anesthesia, brain stem injury, spinal cord injury.

Mechanism: injury of vasomotor center (due to over anesthesia; brainstem injury or spinal cord injury) → decreased sympathetic discharge → peripheral vasodilatation → peripheral pooling of blood → relative hypovolemia → impaired tissue perfusion → cellular hypoxia → **Shock**.

Criteria for diagnosis a shock and its hardness:

- Blood pressure
- Shock indexes
- CVP
- Heart output
- Total peripheral resistance of vessels

Three main components of shock it's a disorders of regulation, metabolism and blood supply.

Main leading pathogenic link:

- Hypovolemia (absolute, relative);
- Pain
- Infection process in stage of sepsis.

Their correlation and frank different in each type of shock.

Stages of Shock

I. NONPROGRESSIVE STATE OF SHOCK

This phase is characterized by activation of neurohumoral compensatory mechanism to preserve the perfusion of vital organs.

Neurohumoral Compensatory Mechanisms

- a) Catecholamine release by adrenal medulla → tachycardia + peripheral' vasoconstriction (cerebral & coronary vessels remain unaffected)
- b) Reninangiotensin axis activation → peripheral' vasoconstriction (cerebral & coronary vessels remain unaffected) + fluid retention by kidneys.
- c) Antidiuretic hormone release → fluid retention by kidneys.
- d) Baroreceptor reflex → peripheral' vasoconstriction (cerebral & coronary vessels remain unaffected)
- e) Generalized sympathetic stimulation → peripheral' vasoconstriction (cerebral & coronary vessels remain unaffected) + tachycardia

All these effects maintain cardiac output and blood pressure, so that perfusion of vital organs (e.g., brain, heart) is preserved

Clinical manifestation

- a) Rapid pulse (due to tachycardia)
- b) Skin pallor (due to peripheral vasoconstriction)
- c) Oligouria (due to fluid retention by kidneys).

II. PROGRESSIVE STAGE OF SHOCK

Uncorrected shock passes to progressive stage characterized by hypoxia of vital organs.

Mechanism

Persistent tissue hypoxia → Impairment of intracellular aerobic respiration → Anaerobic glycolysis → Lactate production → Metabolic lactic acidosis → decreased pH in tissues causes:

1. decreased vasomotor response → arterioles dilate → blood pools up in microcirculation → decreased cardiac output
2. anoxic injury to endothelial cells (due to peripheral pooling of blood) → DIC.
3. release of TXA₂ → platelet aggregation → occlusion of microvasculature.

Clinical manifestations:

Patient is confused

Urinary output begins to fall

III. IRREVERSIBLE STAGE OF SHOCK

This stage is characterized by severe cellular and tissue injury, so that even if therapeutic measures correct the hemodynamic effects, survival is not possible.

Mechanism

1. Decreased cellular pH → rupture of lysosomes → release of lysosomal enzymes → widespread cell injury → aggravate shock state.
2. ischemic pancreas liberate myocardial depressant factor (MDF) → worsen already poor cardiac functions.
3. endotoxic shock, may be superimposed on hypovolemic or cardiogenic shock if ischemic intestinal mucosa allows intestinal flora to enter circulation.

Clinical manifestations:

1. Complete renal shutdown (anuria) (due to acute tubular necrosis)
2. Death

MORPHOLOGY OF ORGANS INJURED BY SHOCK

Late stages of shock are characterized by “failure of multiple organ systems”.

BRAIN → ischemic encephalopathy

HEART → myocardial infarction; subendocardial hemorrhages and necrosis; zonal lesions (i.e. apparent hyper constriction of a myocyte)

LUNGS → lungs are resistant to hypoxia → no effect in hypovolemic shock; bacterial sepsis causes alveolar damage and ARDS → “Shock lungs”

KIDNEYS → acute tubular necrosis → oliguria, anuria and electrolyte imbalance

COLLAPSE

Collapse is an **acute vascular insufficiency** which is characterized by fall of a vascular tone, and also acute reduction of circulating blood volume. **A basis of collapse development is discrepancy between volume of circulating blood and capacity of a vascular system lays.**

At the collapse there is reduction of venous blood inflow to heart → decrease of heart output → fall of arterial and venous pressure → infringement of tissues perfusion and metabolism → comes hypoxia of brain → the vital functions of an organism are oppressed.

It is shown in clinics by short-term loss of consciousness, general weakness, features of acute vascular insufficiency with infringements hemodynamics practically in all organs and tissues.

The reasons may be sudden reduction of blood volume (blood loss, dehydration), and sudden dilatation of vessels. Collapse develops as complication at heart diseases and pathological conditions.

Type of collapse by I.R. Petrov:

- **Infectious-toxic collapse** develops as complication of acute infectious diseases: meningoencephalitis, and typhoid fever typhus fever, acute dysentery, pneumonia, botulism, the Siberian ulcer, virus hepatitis, toxic influenza. The reason of such complication is the intoxication by endo- and exotoxins of microorganisms, mainly that influence on central nervous system, or receptors of pre- and postcapillaries.
- **Hypoxic collapse** may appear in conditions of reduced partial pressure of oxygen in air. The direct reason of circulation infringements thus is insufficiency of adaptive reactions of an organism to hypoxia. To development of collapse in these conditions may promote also hypocapnia owing to hyperventilation which leads to expansion of capillaries and vessels, and from here to deposition and decrease of circulating blood volume.
- **Orthostatic collapse** appears at fast transition from horizontal position in vertical, and also at long time of standing. Thus there is a redistribution of blood with increase of total amount of a venous system and decrease of inflow to heart. In a basis of this condition insufficiency of a venous tone lays. Orthostatic collapse may be observed at recovers after heart diseases of endocrine and nervous system, in the postoperative period, at fast removal of ascitic liquids or as a result of spinal and peridural anesthetics. Iatrogenic orthostatic collapse sometimes appears during wrong use of neuroleptics, ganglioblockers, adrenoblockers, sympatolytics. Among pilots and cosmonauts orthostatic collapse may be caused by redistribution of blood at action of acceleration when blood from vessels of the upper half of body and a head moves into vessels of organs of abdominal cavity and inferior extremities, causing hypoxia of brain. Also it may be observed at practically healthy children and teenagers.
- **Hemorrhagic collapse** develops at massive blood loss as a result of fast reduction of circulating blood.
- **Pancreatic** in case of acute pancreatitis, when pancreatic enzymes released to the blood.
- **Hyperthermic.**
- **Enterogenic** – dumping syndrome,
- **reflexive, radiation, histamine or peptone** (only in experiment) and other types

Collapse also may be observed at acute diseases of internal organs (peritonitis, acute pancreatitis, duodenitis, erosive gastritis), at diseases of heart which are accompanied by acute and fast reduction of stroke volume (heart infarction, infringements of heart rhythm, acute myocarditis or pericarditis with accumulation of exudation in cavity of pericardium).

It is possible to mark **two basic mechanisms in pathogenesis:**

1. **fall of veins and arteriols tone** as a result of action of infectious, toxic, physical, allergic and other factors directly on a vascular wall, vasomotoric centre and on vascular receptors (sinocarotid zones, arches of an aorta);
2. **fast reduction of circulating blood volume** (blood loss, plasma loss).

Reduction of circulating blood volume results in decrease of return of blood to heart by veins of the big circle of blood circulation and heart output. Thus the system of microcirculation is damaged, blood accumulates in capillaries, the blood pressure falls, develops circulatory hypoxia, metabolic acidosis, permeability of vessels increases. It promotes transition of water and electrolytes from blood in intercellular space, are damaged rheologic properties of blood, there is a hypercoagulation of blood and pathological aggregation of erythrocytes and thrombocytes, that creates conditions for formation of microblood clots. At a long lasting collapse as a result of hypoxia and disturbances of metabolism are

released vasoactive substances (histamine, kinins, prostaglandins) and formed tissue metabolites - lactic acid, adenosine and its derivatives which cause hypotonia.

Progressing changes lead to infringement of functions of a brain, deepening of regulatory and hemodynamic disorders. The death at a collapse comes owing to an exhaustion of power resources of brain, intoxication and disturbances of metabolism.

Table 1. Differences between shock and collapse

Parameters	Shock	Collapse
The name and essence of the process	Nosologic unit	Syndrome, which is not a nosologic unit
Etiology	Shock — «collapse resulting from trauma». It results from exteroceptor irritation	Collapse — «shock without trauma». It results from inter-receptor irritation because of intoxication
Presence and prevalence of the basic pathogenic link	Changes in CNS are primary	Changes in NS are secondary
Peculiarities of clinical course	Phase, rapid development	It is not phase, slow development
The severity depends on arterial blood pressure	No	The severity depends on the arterial blood pressure
Consciousness	It is present	It is lost or confused
Change in circulating blood volume	a decrease in circulating blood volume, blood is deposited	Normal or decreased
Narcosis and analgesia	At the beginning it has preventive or treatment role	Its role is negative
Protective adaptive reactions	Primary in CNS, than the whole organism	dyspnea, an increase in cardiac rate, stimulation of hemopoietic organs, mobilization of blood from the depot

Faint

Faint — «syncope» (in greek *synkop* — reduction, chopping).

It is the mildest form of vascular insufficiency.

Faint — sudden, short loss of consciousness owing to the passing ischemia of brain. It occurs reflexly. The leading factor — a decrease in arterial blood pressure down to the level, on which it is not provide sufficient brain perfusion.

The basic parts of faint pathogenesis

1. A decrease in arterial blood pressure owing to a decrease of peripheral vascular resistance in vasodilating system (the psychogenic faints caused by hyperactivity of n. vagus).
2. Impairments of cardiac rhythm.
3. Hypoxemia.

Coma

Coma (in greek «coma» — a deep dream). However according to etiology and pathogenesis coma essentially differs from dream. Consciousness does not reverse even in intensive nociceptive irritation.

Coma is an extreme condition characterized by the deep CNS neuron oppression, loss of consciousness, loss of various reflexes, absence of reactions on external irritants, deep respiration impairments, impairments of blood circulation and metabolism.

Etiology of comatose states

Exogenous:

- ✓ **Traumatic factors** (usually brain) such as an electrical current, mechanical trauma
- ✓ **Thermal** (overheating, sunstroke, hypothermia)
- ✓ Hypo- and hyperbaric
- ✓ **Neurotropic toxins** (alcohol or its surrogates, toxic doses of drugs, sedatives, barbiturates)
- ✓ **Infectious agents** (neurotropic viruses, botulinum and tetanus toxins, pathogens of malaria, typhoid, cholera)

- ✓ Exogenous hypoxia and anoxia
- ✓ Large radiation doses

Endogenous:

- ✓ Pathological processes in the brain (ischemic, stroke, tumor)
- ✓ Violation of blood circulation and respiration
- ✓ Pathology of blood (massive hemolysis, severe anemia)
- ✓ Endocrinopathy (DM, hyperinsulinism, adrenal insufficiency)
- ✓ Violation of digestive system (malabsorption syndrome, intestinal autointoxication)
- ✓ Renal and hepatic failure

Classification of coma according to origin

I. Exogenous — action of environmental pathogenic agents or deficiency of necessary factors for normal existence of organism: traumatic; hypothermic (overcooling); hyperthermal (heatstroke); exotoxic (alcoholic poisoning, medicinal substances, mushrooms); alimentary (severe starvation); hypoxic; radiating.

II. Endogenous — impairments of various organs or physiological system activity: apoplectic; anemic; endocrine coma (hypoglycemic, diabetic); uraemic; hepatic; asthmatic; asphyxial; cholera.

Classification of coma:

- **Neurological** due to primary CNS lesion, in stroke, head injury, inflammation and swelling of the brain and its meninges
- **Endocrinological** arising as a failure at some endocrine glands (diabetic, hypo corticoid, hypo pituitary, hypothyroid coma), and at their hyperfunction (thyrotoxic, hypoglycemic);
- **Toxic** arising from endogenous (uremia, hepatic failure, toxicoinfection, pancreatitis) and exogenous (alcohol poisoning, barbiturates, and other organophosphorus compounds) intoxication;
- **Hypoxic** caused by impaired gas exchange in different types of oxygen starvation.

Pathogenesis of coma

Diseases ^{adverse development} damage of central nervous system → CNS damage becomes leading in their pathogenesis → impaired function of the reticular formation with the fallout of the activating influence on the cerebral cortex and inhibition of the function of the subcortical structures and centers and the autonomic nervous system

Leading pathogenetic link:

brain hypoxia, acidosis, electrolyte imbalance, formation and release of neurotransmitters in the synapses of CNS, cerebral circulatory disorder, liquorodynamic violation

Morphologically, these disorders are manifested in the form of swelling and edema of the brain and meninges, small hemorrhages and foci of softening.

Severity of coma depends on:

1. Degrees of brain function impairments.
2. Degrees of the vital parameter deviations.

Coma is characterized by:

- complete loss of consciousness;
- absence of reaction to various influences;
- loss of reflexes;
- pathological forms of respiration;
- a decrease in cardiac activity;
- hypotonia;
- a decrease in the body temperature

Stages of coma

1. initial — mental anxiety
2. pre-coma — confusion of consciousness
3. superficial coma
4. deep coma — full loss of consciousness, areflexia, vegetative impairments

STRESS

Hans Selye (1985) defined stress as "nonspecific" in that the stress response can result from a variety of different kinds of stressors and he thus focused on the internal aspects of stress. Selye noted that a person who is subjected to prolonged stress goes through **three phases**:

- Alarm Reaction,
- Stage of Resistance,
- Exhaustion.

He termed this set of responses as the General Adaptation Syndrome (GAS). This general reaction to stress is viewed as a set of reactions that mobilize the organism's resources to deal with an impending threat. The Alarm Reaction is equivalent to the fight-or-flight response and includes the various neurological and physiological responses when confronted with a stressor. When a threat is perceived the hypothalamus signals both the sympathetic nervous system and the pituitary. The sympathetic nervous system stimulates the adrenal glands. The adrenal glands release corticosteroids to increase metabolism which provides immediate energy. The pituitary gland releases adrenocorticotrophic hormone (ACTH) which also affects the adrenal glands. The adrenal glands then release epinephrine and norepinephrine which prolongs the fight-or-flight response. The Stage of Resistance is a continued state of arousal. If the stressful situation is prolonged, the high level of hormones during the resistance phase may upset homeostasis and harm internal organs leaving the organism vulnerable to disease. There is evidence from animal research that the adrenal glands actually increase in size during the resistance stage which may reflect the prolonged activity. The Exhaustion stage occurs after prolonged resistance. During this stage, the body's energy reserves are finally exhausted and breakdown occurs. Selye has noted that, in humans, many of the diseases precipitated or caused by stress occur in the resistance stage and he refers to these as "diseases of adaptation." These diseases of adaptation include headaches, insomnia, high blood pressure, and cardiovascular and kidney diseases. In general, the central nervous system and hormonal responses aid adaptation. However, it can sometimes lead to disease especially when the state of stress is prolonged or intense.

Through many experiments, Selye exposed animals to noxious agents and found that they all responded with the same syndrome of changes, or "stress triad"

Stress Selye triad:

1. enlarged adrenals
2. shrunken lymphatic organs
3. bleeding gastrointestinal ulcers

Stress-related Diseases.

- Cardiovascular: coronary artery disease, hypertension, stroke, arrhythmia.
- Muscles: tension headaches, backache
- Connective tissues: rheumatoid arthritis
- Pulmonary: asthma
- Immune: immunosuppression, deficiency, autoimmunity
- Gastrointestinal: ulcer, irritable bowel syndrome, diarrhea, nausea and vomiting, ulcerative colitis
- Integumentary: eczema, neurodermatitis, acne
- Endocrine: diabetes mellitus, amenorrhea
- Central nervous: fatigue and lethargy, overeating, depression, insomnia.

GENERAL ADAPTATION SYNDROME

Definition

General adaptation syndrome, or GAS, is a term used to describe the body's short-term and long-term reactions to stress.

Stressors in humans include such physical stressors as starvation, being hit by a car, or suffering through severe weather. Additionally, humans can suffer such emotional or mental stressors as the loss of a loved one, the inability to solve a problem, or even having a difficult day at work.

Description

Originally described by Hans Selye (1907–1982), an Austrian-born physician who emigrated to Canada in 1939, the general adaptation syndrome represents a three-stage reaction to stress. Selye explained his choice of terminology as follows: "I call this syndrome *general* because it is produced only

by agents which have a general effect upon large portions of the body. I call it *adaptive* because it stimulates defense.... I call it a *syndrome* because its individual manifestations are coordinated and even partly dependent upon each other."

Selye thought that the general adaptation syndrome involved two major systems of the body, the nervous system and the endocrine (or hormonal) system. He then went on to outline what he considered as three distinctive stages in the syndrome's evolution. He called these stages the alarm reaction, the stage of resistance, and the stage of exhaustion.

Stage 1: alarm reaction

The first stage of the general adaptation stage, the alarm reaction, is the immediate reaction to a stressor. In the initial phase of stress, humans exhibit a "fight or flight" response, which prepares the body for physical activity. However, this initial response can also decrease the effectiveness of the immune system, making persons more susceptible to illness during this phase.

Stage 2: stage of resistance

Stage 2 might also be named the stage of adaptation, instead of the stage of resistance. During this phase, if the stress continues, the body adapts to the stressors it is exposed to. Changes at many levels take place in order to reduce the effect of the stressor. For example, if the stressor is starvation (possibly due to anorexia), the person might experience a reduced desire for physical activity to conserve energy, and the absorption of nutrients from food might be maximized.

Stage 3: stage of exhaustion

At this stage, the stress has continued for some time. The body's resistance to the stress may gradually be reduced, or may collapse quickly. Generally, this means the immune system, and the body's ability to resist disease, may be almost totally eliminated. Patients who experience long-term stress may succumb to heart attacks or severe infection due to their reduced immunity. For example, a person with a stressful job may experience long-term stress that might lead to high blood pressure and an eventual heart attack.

Stress, a useful reaction?

The reader should note that Dr. Selye did not regard stress as a purely negative phenomenon; in fact, he frequently pointed out that stress is not only an inevitable part of life but results from intense joy or pleasure as well as fear or anxiety. "Stress is not even necessarily bad for you; it is also the spice of life, for any emotion, any activity, causes stress." Some later researchers have coined the term "eustress" or pleasant stress, to reflect the fact that such positive experiences as a job promotion, completing a degree or training program, marriage, travel, and many others are also stressful.

Selye also pointed out that human perception of and response to stress is highly individualized; a job or sport that one person finds anxiety-provoking or exhausting might be quite appealing and enjoyable to someone else. Looking at one's responses to specific stressors can contribute to better understanding of one's particular physical, emotional, and mental resources and limits.

Causes and symptoms

Stress is one cause of general adaptation syndrome. The results of unrelieved stress can manifest as fatigue, irritability, difficulty concentrating, and difficulty sleeping. Persons may also experience other symptoms that are signs of stress. Persons experiencing unusual symptoms, such as hair loss, without another medical explanation might consider stress as the cause.

The general adaptation syndrome is also influenced by such universal human variables as overall health and nutritional status, sex, age, ethnic or racial background, level of education, socioeconomic status (SES), genetic makeup, etc. Some of these variables are biologically based and difficult or impossible to change. For example, recent research indicates that men and women respond somewhat differently to stress, with women being more likely to use what is called the "tend and befriend" response rather than the classical "fight or flight" pattern. These researchers note that most of the early studies of the effects of stress on the body were conducted with only male subjects.

Selye's observation that people vary in their perceptions of stressors was reflected in his belief that the stressors themselves are less dangerous to health than people's maladaptive responses to them. He categorized certain diseases, ranging from cardiovascular disorders to inflammatory diseases and mental disorders as "diseases of adaptation," regarding them as "largely due to errors in our adaptive response to stress" rather than the direct result of such outside factors as germs, toxic substances, etc.

Diagnosis

GAS by itself is not an official diagnostic category but rather a descriptive term. A person who consults a doctor for a stress-related physical illness may be scheduled for blood or urine tests to measure the level of cortisol or other stress-related hormones in their body, or imaging studies to evaluate possible abnormalities in their endocrine glands if the doctor thinks that these tests may help to establish or confirm a diagnosis.

The American Psychiatric Association (APA) recognizes stress as a factor in anxiety disorders, particularly post-traumatic stress disorder (PTSD) and acute stress disorder (ASD). These two disorders are defined as symptomatic reactions to extreme traumatic stressors (war, natural or transportation disasters, criminal assault, abuse, hostage situations, etc.) and differ chiefly in the time frame in which the symptoms develop. The APA also has a diagnostic category of adjustment disorders, which are characterized either by excessive reactions to stressors within the normal range of experience (e.g. academic examinations, relationship breakups, being fired from a job) or by significant impairment in the person's occupational or social functioning.

Treatment

Treatment of stress-related illnesses typically involves one or more stress reduction strategies. Stress reduction strategies generally fall into one of three categories: avoiding stressors; changing one's reaction to the stressor(s); or relieving stress after the reaction to the stressor(s). Many mainstream as well as complementary or alternative (CAM) strategies for stress reduction, such as exercising, listening to music, aromatherapy, and massage relieve stress after it occurs.

Many psychotherapeutic approaches attempt to modify the patient's reactions to stressors. These approaches often include an analysis of the patient's individual patterns of response to stress; for example, one commonly used set of categories describes people as "speed freaks," "worry warts," "cliff walkers," "loners," "basket cases," and "drifters." Each pattern has a recommended set of skills that the patient is encouraged to work on; for example, worry warts are advised to reframe their anxieties and then identify their core values and goals in order to take concrete action about their worries. In general, persons wishing to improve their management of stress should begin by consulting a medical professional with whom they feel comfortable to discuss which option, or combination of options, they can use.

Selye himself recommended an approach to stress that he described as "living wisely in accordance with natural laws." In his now-classic book *The Stress of Life* (1956), he discussed the following as important dimensions of living wisely:

- Adopting an attitude of gratitude toward life rather than seeking revenge for injuries or slights.
- Acting toward others from altruistic rather than self-centered motives.
- Retaining a capacity for wonder and delight in the genuinely good and beautiful things in life.
- Finding a purpose for one's life and expressing one's individuality in fulfilling that purpose.
- Keeping a healthy sense of modesty about one's goals or achievements.

STRESS-LIMITING SYSTEM

1. **GABA-ergic** (γ -aminobutyric acid) system - the brain GABA neurons and GABA receptors, GABA neurotransmitter postsynaptic and presynaptic inhibition:
 - 1) inhibits the function of "command" neurons to the action of the stressor;
 - 2) inhibits the production of corticotropin-releasing hormone;
 - 3) limits the mobilization pituitary-adrenal level in the stress response;
 - 4) decreases the release of norepinephrine in peripheral synapses.
2. **Benzodiazepine system** - all potentiates the effects of GABA-limiting stress reaction.
3. **Opioidergic** system - a opioidergic brain neurons that produce opioid peptides and receptors of these peptides:
 - 1) increases the synthesis and release of opioids (enkephalins and endorphins);
 - 2) limits the production of neurotransmitters in the adrenergic system.
4. **Serotonergic system** - serotonergic neurons of the brain that produce serotonin, and serotonin receptors – are closely linked to opioidergic:
 - 1) The analgesic effect;
 - 2) inhibit interneuronal transmission of excitation and the activity of adrenergic structures.
5. **Prostaglandin system** - stress-limiting system of peripheral actions:

1) prostaglandins (group E, and prostacyclin) inhibit the output of noradrenaline from sympathetic nerve terminals;

2) inhibit adenylate cyclase by blocking the formation of secondary mediator - and cAMP prevent the damaging effect on cells of catecholamines.

6. Antioxidant system - a set of biologically active substances of the body, eliminating the cytotoxic effect of POL:

1) antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase) and proteins, transporting metals (ceruloplasmin, etc.), perform the role of "interceptors" free radicals;

2) a-tocopherol reacts with the primary products of lipid peroxidation;

3) ascorbic acid potentiates membranoaktivnye phenolic antioxidants;

4) uric acid, ubiquinone, uracil, thiourea, histidine, carotenoids, albumin, alanine, serine, valine, glycine, dimethyl sulfoxide, easily oxidized peptides, which have in their composition of SH-containing amino acids (methionine, cystine, and cysteine) inhibit the activated oxygen metabolites

Questions for self-control of knowledge:

1. Difference between extreme and terminal conditions.
2. What are the shock starting factors?
3. What is the pathogenic role of post-capillary, vasoconstriction in shock development?
4. What is a morphological basis of "shock lung"?
5. What is a morphological basis of "shock kidney"?
6. What does underlie changes of shock phases?
7. The main principles of pathogenic therapy in shock
8. Define the leading typical pathological process stereotypic for all types of coma.
9. About what does change of periodic respiration testify in coma?
10. Stages of GAS. The biological role of stress.
11. Give the examples of adaptation diseases. Peculiarity of pathogenesis.

Tasks for self-managed student work:

1. Mechanisms of emergency adaptation in shock.
2. Role of hypoxia in pathogenesis of traumatic shock.
3. Microcirculatory disorders in traumatic shock.
4. Disturbance of body functions in coma

Literature

Basis literature:

1. Литвицкий, П. Ф. Патофизиология = Pathophysiology: лекции, тесты, задачи : учеб. Пособие / П. Ф. Литвицкий, С. В. Пирожков, Е. Б. Тезиков. – М. : ГЭОТАР-Медиа, 2016.– 432 с.

Additional literature:

2. Kumar, V. Robbins and Cotran Pathologic basis of disease, 7th Edition / V.Kumar, A.K. Abbas, N. Fausto. — Philadelphia: Elsevier Inc., 2005. — 1629 p. Режим доступа: <http://www.rkmyat.in/up1/34/1629.pdf>. – Дата доступа: 30.08.2016.

3. Кидун, К. А. Общая нозология = General nosology : учеб.-метод. пособие для студ. 3 курса фак. по подг. спец. для зарубеж. стран, обуч. на англ. яз. по спец. «Лечеб. дело», мед. вузов / К. А. Кидун.– Гомель : ГомГМУ, 2015. – 74 с.

4. Кидун, К.А. Test tasks on pathological physiology: Workbook for students of the faculty for training specialists for foreign countries, studying in english on specialty «General medicine», for higher medical education institution In three parts Part 1. General pathophysiology. / К.А. Кидун; под ред. Т.С. Угольник — Гомель: ГомГМУ, 2016. — 108 с.

5. Научная электронная библиотека eLIBRARY.RU [Электронный ресурс] / Научная электронная библиотека. – М., 2005. – Режим доступа: <http://www.elibrary.ru>. – Дата доступа: 26.08.2017.

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