PATHOFYSIOLOGY OF STRESS

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CONTENT

1. INTRODUCTION

Stress, or a general adaptation syndrome, as a less well-known name, is an often used term, and it is a condition that belongs to life. And as the author of this term, Hans Selye said, "stress is life and life is stress". Although we now know that stress is a phylogenetically developed life-rescuing reaction of higher organisms to promptly prepare them for an attack or flight. We also know that it can be a significant pathogenetic factor if it is excessive or long-term). Stress can not be avoided because the strenuous effort to do so at all costs would be stressful in itself. Therefore, it is necessary to accept the fact that some degree of stress does not hurt, but on the contrary, if this reaction does not exceed a certain limit in terms of intensity and frequency, there is no doubt that stress is useful. It is a useful mechanism necessary for the survival of an individual in stressful situations, and if the burden is not excessive and long-term, the organism can even strengthen and increase its resistance. It is also known that when stress is not at all, people even seek after it (adrenaline sports, bloody matches of people or animals, etc.). At the same time, the threshold when the stress is already harmful is entirely individual. From the apparent capability of some individuals to cope with it, up to an ever-increasing range of diseases whose pathogenesis is, in spite of all doubt, in connection with stress. At the same time, it is obvious that the role played by both external influences and internal factors, ie innate, genetically conditioned, are related to the psychic state of man, his lifestyle and behavior. It is these factors that play a role today in most of the diseases which we call civilization ones. These include a wide range of vascular diseases (hypertension, atherosclerosis and its consequences, eg cerebrovascular accident or heart attack), but also tumor growth, stomach ulcerative disease, bronchial asthma, where present the aforementioned factors are also known as risky (eg smoking, improper nutrition, alcoholism, drugs, lack of movement and other stress factors called stress). These, together with disturbed psychics, prepare the ground for the emergence of diseases, which are also called psychosomatic (formerly cortico-visceral The essence of these diseases studies so-called psychosomatic medicine, which examines in particular the relationship between emotions or emotional processes and some diseases (ulcer disease, asthma) or newly so-called behavioral medicine, which combines the knowledge of biomedical sciences with psychological experience (especially the mechanisms of individual behavior) in a broader context with the aim of complex approach to the patient and causally influencing the treatment , but also to prevent these diseases. What, most surprisingly, is the fact that stress

factors influence the hereditary information as epigenetic changes that are transmitted to offspring with an impact on their health. In the case of stress, this is a complex issue, from the already mentioned relations to psychosomatic and behavioral medicine, but also to immunology, endocrinology, / epi / genetics and to neuroscience.

In this context, it is worth mentioning 3 names that are close to the history of stress research and also in relation to Czech science. The first is the already mentioned author of the stress theory or GAS (General Adaptation Syndrome) Hans Selye, further then Josef Charvát and finally Vratislav Schreiber. All these men, later professors successfully studie and then graduated at the Faculty of Medicine, Charles University in Prague.

Hans Hugo Bruno Selye (1907-1982) was born in Vienna, lived in Komárno, studied medicine at the German Charles University in Prague, and was a Czechoslovak citizen (of Jewish origin) until his emigration to Canada in 1933. As stated earlier, 1936 used the word stress in relation to the body's response to stress. However, he has started his research in endocrinology as a student at the Institute of Experimental Pathology of the Charles University in Prague. His knowledge subsequently profoundly influenced the concept of the burden and pathogenesis of diseases both in theoretical and clinical terms, including psychological sciences that study the influence of psychobiological stress on the body. Hans Selye pronounced his theory of the so-called general adaptation syndrome in Montreal, where he worked at the institute of experimental physiology of the two universities, basically until the end of his life.

Josef Charvát (1897-1984), a prominent internist - endocrinologist who further developed the theory of stress in application to clinical research. He has held an internal clinic and department for many years and has been appointed a member of the United Nations Scientific Advisory Committee and a member of the WHO Task Force for the role of behavioral and psychosocial factors in health and illness. His most famous work, in collaboration with foreign colleagues, in 1964, entitled "Mental Factors in Cardiovascular Diseases", brought him great international recognition and recognition. He was the first to point out the importance of psychic stress in the onset of myocardial infarction (MI) and other circulatory disorders.

Vratislav Schreiber (1924-2015) was basically a pupil and younger co-worker of J. Charvát, our foremost physiologically and pathophysiologically oriented endocrinologist. As one of the first, he discovered hypothalmic "releasing" factors and, among other things, with his co-workers published a "Stress" monograph.

2. THE PRINCIPLE OF STRESS, FORMS, STRESSORS

2.1. Definition of stress, eustres, distres

Stress is a set of reactions of the organism to internal or external changes that interfere with the normal "resting" function of the organism or even threaten its existence. These reactions

are stereotypical, typical for each individual, and their course therefore does not depend on the nature of the influences they have caused. Influencing effects are referred to as stressors or simply as stress. In fact, it is about starting up mechanisms to resume the disturbed homeostasis. For the purpose of specifying stress level in particular, to the definition above is added the fact that stress is all the effects that increase the secretion of ACTH in normal individuals. According to this concept, there is an advantage of a clear diagnosis of stress according to the level of ACTH and consequently cortisol (the so-called stress hormone) in the blood. The problem is that then also pleasant events are stress and (eg winnings in lottery, adrenaline sports). For this reason, a suggestion was made to mark this stress as eustres (from the Greek eu - joyful, good) and negative dangerous influences like distress. Reasonable levels of eustres (eg, mild, optimal stress) can significantly increase performance, excessive eustres (eg, extreme joyful excitement) however may be stressful. At the same time, the impact of distress (in human very often as a psycho-social phenomenon, also called psychobiological stress) can have a pernicious effect on his performance.

2.2. Stressors

Already H. Selye assumed that the action of the stressors induces a common neurohumoral response, represented by increased secretion of ACTH and subsequent corticoid secretion. Research over the last decades has shown that it is not just ACTH but a complex response of many pituitary hormones and peptides along with the CNS response. In this case, the stressor, whether physical or psychological, is in close connection with the person of the recipient, the personality structure and the organism's response is then uniformly conducted according to his own formula. Psychic and physical manifestations are reciprocal in stress. Often, the psychic stressor is accompanied by a physical response, and on the contrary, the action of physical stressors causes a psychic response. It depends on the general state of the organism at the time of stressors. Role play here: age, illness, circadian rhythm, sleep and wakefulness, pain threshold etc.

2.2.1. Types of stressors:

1. Biological influences.

2. Environmental influences.

3. Life situation.

4. Behavior - lifestyle.

5. Rational, cognitive and thought activities.

Ad 1: Biological influences (Affecting the state of the organism), examples of which are diseases and physical exhaustion, excessive physical burden of different origins, hunger, thirst etc.

Ad 2: Environmental influences act from the environment where the person is located and they are eg noise; overcrowded rooms or vehicles; in other words "jam" of a different kind. But it also includes material misery and natural disasters, in milder form also weather factors.

Ad 3: Life situations - applied when the effect on psyche is primarily greater than somatic one. An example is the death of a life partner or other close person (on the scale of the stress seriousness - 1st place). But it also includes loss of employment or even forced stay in hostile environments.

Ad 4: Behavior, resp. a lifestyle that includes smoking, but also inappropriate diet or lack of sleep.

Ad 5: Rational, cognitive and thought activities - in short, the events associated with the state of psyche can be the cause of stress. These include, for example, various tests and examinations (eg at school), but also sports games and important events in psychologically challenging, especially individual sports (tennis, figure skating, etc.), where not only the time factor but also the success or failure with different consequences play role.

3. PHASES OF THE STRESS REACTION

3.1. Alarm reaction

– prompt reaction to stress when the hypothalamus gets signals from oher parts of the brain:

a) HPA (hypotalamus - pituitary - adrenal) axis is activated by CRF (corticooleberin) and triggered secretion of ACTH and glucocorticoids.

b) At the same time from the reticular formation of the hypothalamus, the SAS (sympathoadrenal system) is activated with the release of catecholamines from the adrenal medulla.

3.2. Stage of resistance

– a time of when adaptation to stress is maximal; increased activity of the ACTH system in cooperation with the adrenal cortex is fully developed but still has reserves.

This phase arises from prolonged or repeated stress, if its intensity is not too high and no transition into phase 3 occurs. However, during this phase, resistance to other influences (eg infection) may be impaired.

3.3. Stage of exhaustion

– occurs when stress resistance is inadequate or is lost. This can be caused by excessive stress intensity (this phase follows the alarm reaction directly), too much stress and depletion of the body's reserves, impaired adaptation reactions (eg changes in secretion in the pituitary system - adrenal cortex) or abnormal adaptation reactions. Then the diseases of adaptation are talked about. The exhaustion phase can sometimes lead faster (rarely and completely acutely) - sometimes slower (often under long-term stress - chronic stress), to death (myocardial infarction).

However, according to a number of authors, the negative effects of stress (stress diseases) also arise from normal stress reactions in the resistance phase. This concerns in particular the activation of SAS and HPA and their metabolic consequences. These are necessary for coping a stressful situation (threat), but they are damaging when they are long-term.

In the literature, a unique case of death was described and explained as a undoubtedly result of enormous acute stress (probably due to massive leakage of catecholamines and lethal arrhythmia). It happened with one prisoner in the US sentenced to death. It was announced on the day of execution that he would be killed in the interest of science by slowly removing blood from the vein injected. His eyes were made closed, his arms and legs strapped so he could not move on the chair. Then a vein was injected on one upper limb and the blood began to drip into a container on the ground. In reality, however, a minimal amount of only a few milliliters of blood was dropped. Shortly thereafter, the needle was closed, and beside another, a dripping of water was arranged to simulate the original sound of dripping blood. The prisoner died after a few minutes (most likely by imagination of near death and therefore of excessive psychological stress).

4. RELATIONSHIP BETWEEN STRESS AND SHOCK

Stress and shock is difficult to compare, because of not complete uniform and exhaustive definitions of these states. Nevertheless, it is necessary to point out the context of these two states and to define each other.

A) Provoking factors - are similar or identical. The same gentle stimulus will cause stress, and by a higher intensity, it leads to shock. In humans, stressful can also be onlya thought, imagination, a stress reaction can also occur in sleep. Anesthesia (local or general) will significantly affect stress, not shock.

B) Metabolic response - similar (ie systemic, organ, tissue and cellular). It varies with the intensity of the answer. We can say that in the case of stress, the changes are in the regulative band, ie most of the purposeful reactions, in shock they sharply deviate from the band of regulatory changes and/or they are therefore useless.

C) Shock is always a life-threatening condition where the regulatory mechanisms of the body fail and requires specialist health care (anti-shock measures and treatment). It depends on what kind of shock it is. On the contrary, stress is a purposeful reaction of the organism, in difficult situations saving life, without the need for professional assistance.

D) Stress may exist in isolation. Shock is always accompanied by stress. (Clinically, however, there are sometimes signs of shock so prompt and dominant that stress is extinguished (eg severe anaphylactic shock).

E) The intactness of the pituitary-adrenal axis is a condition of the successful stress response. In shock, this functional readyness is not a prerequisite; on the contrary, in the case of shock, the adrenal gland is often anatomically destroyed. Therefore, in such situations (disruption of the functioning of the pituitary-adrenal axis), stress stimuli often become shock.

F) Acute stress - it usually does not lead to death (with the above exceptions). Chronic stress usually leads to exhaustion, rarely to death. On the other hand, in shock, the fatal course (without medical help) is regular.

5. SCHEME OF THE STRESS REACTION

In the development of the stress response are very important:

Neural mechanisms and humoral or hormonal mechanisms.

5.1. Neural mechanisms of stress

- can then be further divided into neuroendocrine and neurogenic

5.1.1. Neuroendocrine mechanisms

- mainly concern the hypothalamus, where:

(a) Classical neurons whose secretory and electrical activity is modified by various neurotransmitters (noradrenaline, acetylcholine, dopamine, serotonin, GABA, histamine) that act on the belonging cellular receptors and this way they affect their function. Although this mode of regulation is more or less local, there is no doubt that these mechanisms are also linked to the below mentioned neurogenic ones.

b) neurosecretory cells - somewhat different from classical neurons (contain, for example, larger vesicles) and are capable of neurosecretion (neurocrinia). In this case, some of their hormone products (more precisely neurohormones) travel to the blood and through it they act on relevant receptors in various peripheral organs and tissues.

At the same time, these neurohormones also act on nerve cell receptors, where they also act as modulators of their sensitivity. The situation is even more complicated in that the various neuropeptides and neurotransmitters are found, except the CNS, also in addition in various peripheral organs (digestive tract, endocrine system, immune system). These, therefore, can via feed-back also act on the relevant receptors in the CNS.

5.1.2. Neurogenic mechanisms

- are realized by the role of the reticular formation (SAS, centers of the autonomic nerves) and the limbic system, which represent the phylogenetically old structures of the CNS, with the aforementioned hypothalamus. Their task is primarily to preserve the individual and the genus, and all hormonal and neural reactions serve for this purpose. In addition, the cerebral cortex is involved in these processes, especially in humans, where interferes with the stress response through its receptor regions, but integrative activity, higher nervous functions, speech and social influences are also here involved. Moreover emotions and other psychological influences as well play role here.

5.2. Humoral (hormonal) mechanisms of stress

The main humoral mechanisms represent activation of two axes:

I. hypotalamus - SAS - adrenal medulla resulting in secretion of catecholamines

II. hypotalamus - CRH - adenohypophysis - ACTH - adrenal cortex with secretion of glucocorticoids and mineralocorticoids.

This is followed by a number of additional reactions, the most effective of which is the activation of vasopressin, prolactin and somatotropin secretion, variable TSH alterations, and mostly decrease of gonadotropines secretion. Recently recognized and very significant factors for the humoral response to stress are the secretion of other fragments of proopiomelanocortin, which, in addition to ACTH, still represent: α, β MSH (melanocyte stimulating hormone) and β endorphin. The formation of enkephalins, which are formed from proenkephalin, is also increasing. Further there is also possible mention hypophyseal ß LTH

(lipotropic hormone), then glucagon (pancreas) and then under STH control the formation of IGF-1 in the liver (previously somatomedin), together with increased gastrin production, decreased T3 and increased reverse T3 (triiodothyronine) production.

Catecholamines (adrenaline and noradrenaline) are the first hormones producedin the time course.They are released by the activation of SAS from the adrenal medulla and their effect is immediate.They have a significant metabolic effect, in particular hyperglycemic (due to glycogenolytic action, stimulation of glucose resorption from the intestine and insulin inhibition) and then also lipolytic. Catecholamine secretion provoke situations that require immediate maximal physical and mental preparedness , including the mobilization of energy resources for extraordinary, though short-term stress such as escape from the enemy or struggle to live or prey. The basic emotions that cause catecholamine secretion are fear or anger. In such a situation, the cardiovascular system and also other functions are brought to a standby within a few seconds.

5.2.1. Body reaction induced by hypersecretion of catecholamines in the first phase of stress

1) Increase of arterial blood pressure.
2) Increased blood flow through working muscles including the heart and brain and, on the other hand, limiting blood flow to organs whose activity is not necessary for prompt motor activity (gastrointestinal tract, kidney).
3) Increased cellular metabolism of the body in general.
4) Increase of glucose and free fatty acids levels in the blood as a sources of energy for myocardium.
5) Increased degree of glycolysis in the liver and muscles, independently on insulin.
6) Increased muscle strength and performance (including heart).
7) Increased mental activity - thanks to a preferential supply of glucose to the brain.
8) Changes in blood clotting; rather in the sense of an increase, in induced by prostaglandin. Fibrinolysis is then a matter of catecholamines.

The aim of the above is primarily the success of the alarm response (escape, attack), as has been said. But the fact is that emotion (anger, fear) will also cause catecholamines release, even if they are not followed by the physical activity for which everything was prepared. Unfortunately, this is so the case with today's man called by Prof. Schreiber "Homo sedentarius" (a sedentary person) what is rather the rule than opposite. In such a case, a very

well-developed reaction, often in a difficult conditions, life-saving, becomes harmful and, if repeated, causes at least hypertension but also other so called stress diseases (insulin-resistant diabetes etc.).

It should be noted here that the effects of catecholamines are closely related to ACTH and glucocorticoids because they stimulate ACTH and on the other hand, cortisol (glucocorticoid) stimulates (alongside other factors) secretion of catecholamines.

In the second sequence of the release of hormones of the first phase of stress it is then the secretion of glucocorticoids and mineralocorticoids induced not only by activation of the HPA axis but also by catecholamines, which further promote secretion of other stress factors.

In this situation, so-called positive feedback acts, when elevated level of glucocorticoids does not inhibit ACTH secretion, so their blood amount may be further increased.

5.2.2. The effects of glucocorticoids:

1) Stimulation of gluconeogenesis, hyperlipidemia and hypercholesterolemia - as sources of additional energy.

2) Increasing blood pressure and CNS excitability.

3) They generally have a catabolic effect on proteins, which increases the concentration of free amino acids in the blood. The importance of this is to provide sufficient amount of protein to synthesize proteins after the end of stress. However, to maintain mobility and strength, initially, this gluconeogenesis does not affect the muscles and therefore does not reduce the physical performance. In the muscles, proteosynthesis is ensured via IGF-1 which is produced due to STH!

4) Reduction of the amount of eosinophils and also lymphocytes in the blood.

5) The number of leukocytes and platelets, but also the erythrocytes, is rising.

6) Lymphatic tissue breaks down and globulins are released.

7) Proliferation of fibroblasts is inhibited, protein synthesis and antibody formation are reduced.

8) They have anti-inflammatory and anti-immune effects.

In the second phase of stress, the influence of STH and mineralocorticoids, which are already subjected to their own regulation and are important for maintaining the circulation, prevails.

The concentration of glucocorticoids decreases and these processes (characteristic of longer, milder stress) so help to develop anabolic processes and normalize the state of the organism.

5.2.3. Effects of other factors

STH, IGF-1 and prolactin (PRL) inactivate insulin receptors and thus block its effect during stress. Catecholamines then, independently on insulin, provide for the transport of glucose through the plasma membrane, mainly in the muscles, thus ensuring there the preferred use.

Catecholamines also further stimulate secretion of gastrin, which stimulates the production of gastric juices. This is followed by increased appetite caused by secretion of ß endorphin (which increases in parallel with ACTH). The reason is to ensure energy intake even in case of injury, because ß endorphine acts analgesically. On the contrary, its secretion, in a situation where the food source is not available, allows for better psychological toleration of starvation and physical exertion.

Maintained elevated blood glucose provides an increased supply of glucose into the brain, which is unconditionally dependent on its supply and does not respond to the blockage of insulin receptors, such as in inactive muscles. If the organism is not in a too deep energy crisis, glucocorticoids provide glycogen synthesis as a source of instantaneous energy in parallel in the liver. In case of a new acute need (attack or escape), the inhibited usage of glucose in the muscles will be cancelled by the new releasele of catecholamines. The normal storage of glycogen in humans represents only about 24hour reserve in case of fasting without exercise, in more demanding situations then significantly less. Cortisol stimulates gluconeogenesis from proteins in itself, lipolysis is realized by its effect on the already mentioned pituitary lipolytic hormones (ACTH, STH, ß LTH, α ß MSH, vasopressin, PRL) (see Figure 1).

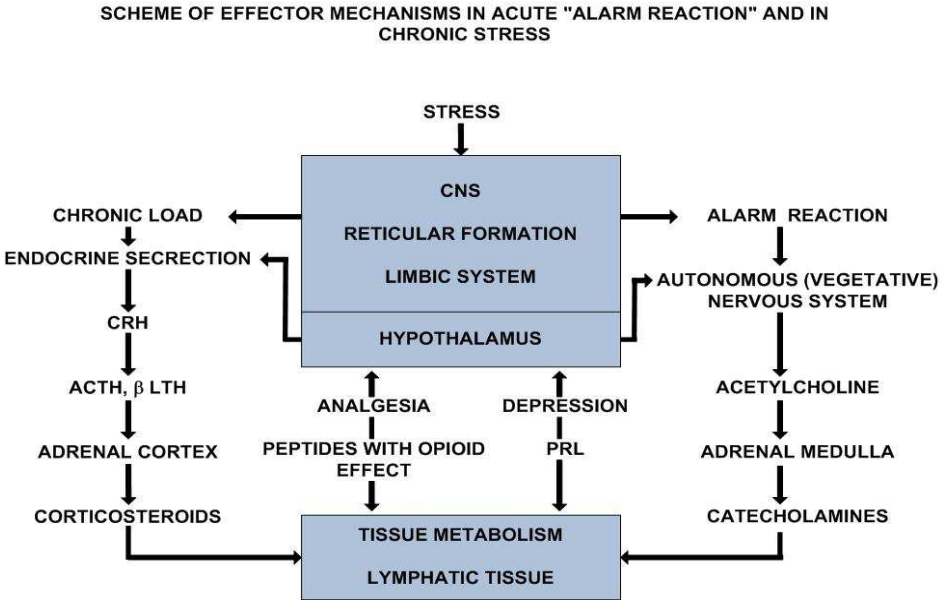

Fig. 1: Mechanisms of acute and chronic stress reaction.

The cortisol level begins to rise in plasma in 5-10 minutes; reduced energy requirements (in inactive tissues) are further ensured by a decrease in T3 production (triiodothyronine) and a rise in reverse T3 which binds T3 receptors.

It follows from this that the whole complex stress response has the only task from the metabolic point of view - to provide adequate resources for the energy deficit that is caused by the intense physical exertion or hunger in the wild nature, but also by psychological tension, which is quite a common cause of obesity in humans as a result of psychobiological stress.

6. STRES AND PATHOGENY OF DISEASES

6.1. Stress diseases

As has been noted, stress is an important pathogenetic factor in so-called stress diseases. In this context, it is important to mention the importance of the so-called psychological or psychobiological or psychosocial stress typical of man. This type of stress is associated with psychosomatic disorders and diseases already mentioned. Mental stress can be acute or chronic, and it is not easy to define it.

6.1.1. Acute stress

- is a social risk factor, especially for those who already have cardiovascular problems, as well as for those "adepts" of cardiovascular diseases with the so-called A type of behavior (competitive, ambitious). Here, as a risk factor is considered permanent adrenergic hyperactivation, resulting in "faster body wear". In recent years, this concept has been abandoned by some authors and is being replaced by a personality of the type D. It is also characterized by the tendency to achieve the highest possible performance but also has other so-called psychosocial characteristics. The first is the predominance of negative affectivity (poor mood), irritability, anxiety, self-estimation, and non-manifestation of emotions, but with constant alertness to possible dangers. In addition, there may be persistent psychological strain, avoidance and uncertain behavior. Individuals with these personality traits found higher levels of TNF (tumor necrosis factor - inflammatory cytokine), cortisol, and other parameters of the distress reaction. It is proved that even holders of this type of personality are candidates mainly for cardiovascular diseases but also other health problems.

Concretely, catecholamines and their acute release may induce cardiac ischemia, in particular by inducing vascular spasm, sometimes not very atherosclerotic vessels. In addition, serious to lethal cardiac arrhythmias can occur in the same way, but also thrombosis in the vascular system due to the influence catecholamines on platelet aggregation. This can explain the death caused by acute stress. As it has been already mentioned the stress is an important pathogenic factor of so called stress diseases.

6.1.2. Chronic stress

- For people with A, respectively. D type of behavior it creates preconditions of myocardial infarction but also sudden strokes due to atherosclerotic obstruction of coronary arteries and cerebral arteries. Although this process is essentially multifactorial, stress is an important supportive factor here. Additionally, evidence of the effect of cellular and humoral immune mechanisms as activated T lymphocytes and antigen-acting cells in atheromatous plaques is provided. Repeated stresses together with excessive nutrition and reduced mobility soon lead to hypertension from the excess of catecholamines and glucocorticoids, and the effect of mineralocorticoids also occurs. To the overall picture of premature atherosclerosis, particularly coronary artery (IM, angina pectoris), also contributes besides hypertension also hyperlipoproteinemia due to alcohol-mediated lipomobilizing hormones, overeating and metabolic hypothyroidism caused by a decrease of T3. Also, insulin-resistant diabetes, induced by inhibition of insulin secretion and function, by both STH, glucocorticoids and non-esterified fatty acids - and endogenous glucose hyperproduction due to by glucocorticoids, catecholamines and glucagon, is also an image of the impact of chronic stress. These factors also increase blood clotting and thrombosis. Excess of glucocorticoids support muscular atrophy and premature osteoporosis, atrophy of lymphatic tissue and thereby weakening immune protection against infections and tumors.

This syndrome also includes hyperuricemia due to accelerated nucleic acid synthesis and degradation. Excessive secretion of adrenalin stimulates secretion of gastrin, hyperacidity and ulcerative disease (here also thanks to spasm of blood vessels on the psychosomatic basis). Conversely, increased secretion of endorphins enhances appetite and thus contributes to obesity, which itself is accompanied by mild hypercorticalism, insulin-resistant gluco-regulative disorders, hypertension, thrombosis, hyperuricemia, etc. Permanent hypersecretion of catecholamines and cortisol may also contribute to psychological imbalance in chronically stressed persons. In contrast, reproductive disorders, hypogonadism, and sexual dysfunction are caused by decreased gonadotrophic hormone secretion. However, infertility due to

hyperprolactinaemia may also be related to stress because of the overproduction of this stress hormone in stress associated with depression and anxiety.

Last but not least, the negative effect of chronic stress on the CNS which should be mentioned is the loss of neurons which die much earlier and faster than normaly, (on the contrary, adequate physical exercises, which may act as eustres, supports neurogenesis ie. creation of new nerve cells). Therefore, it is not surprising that long-term or often repeated psychobiological stress has a devastating effect on human psyche. This may be in direct connection to this stress, even a few months away from a psychologically demanding, strained and terrible experience, as it is in posttraumatic stress disorder. Scary experiences can be of a different nature: from the threat of harm to health (assault, kidnapping, rape, torture, child abuse, traffic accidents) to natural disasters such as floods or earthquakes. With this disorder, which is actually a psychiatric unit with an international abbreviation PTSD (Posttraumatic Stress Disorder), may suffer both persons who have been directly affected, but also their relatives or acquaintances who had avoided of disaster but only witnessed the event in question. Diagnosis of PTSD is determined by a psychiatrist and is based on a history and the presence of typical symptoms (feelings of re-experiencing trauma often associated with heart pounding and sweating, dreadful dreams and thoughts, emotional dysfunction, guilt, depression, fear, loss of interest in previous hobbies, tension and sleep disorders, variable moods and rage blasts). The primary method of treatment of PTSD is psychotherapy in the order of weeks to months, with a significant role played by support from the family and friends of the affected. An additional medication is often needed. The basic group of drugs for the treatment of PTSD are antidepressants from the SSRI group (selective serotonin reuptake inhibitors), which areoften used to avoid arise and development of PTSD. Alternative choices, when intensity of the disorder process is very dominant, are thymoprophylaxis or use of tricyclic antidepressants, possibly with the addition of low doses of antipsychotics. Even with pharmacotherapy, however, psychotherapy is always in place because the patient needs a traumatic event and its consequences rationally to elaborate. Why PTSD someone suffers from and not someone else, is not yet clear. Currently, scientists are also focusing on studying genetic information in people suffering from this disorder in order to possibly influence it. Some findings suggest that in relation to stress resistance are clearly more vulnerablehomozygotes with a short gene allele for serotonin transport compared to heterozygotes; the most durable then are homozygotes with the long allele of this gene.

6.2. Is it possible to avoid stress?

Complete avoiding stress is not possible, even as already mentioned stress is sometimes deliberately sought out: either by spectators, for example, in sports matches or directly by some people (sports, sauna, but also cold showers, etc.). Stress avoidance would be unwise, as the whole regulatory system would atrophy, and in the first inevitable impact we would perish (as is the case with untreated Addison's disease). However, in order to avoid the adverse effects of stress in a civilized environment, we must return to a way of life that corresponds, from the point of view both nutrition and body movement, to the encoded regulation of metabolism. Here, there is hope for the proper functioning of body functions, including sleep and waking, and the possibility of proper regulation of organs and systems involved in the stress response. Stress is the cause of poor sleep, which results in a lack of regeneration of the body; and this is in itself a stressful affair and such as becomes a vicious circle. The problem is that today's, mostly low-movable person ("homo sedentarius") has essentially created from a useful stress response a suicide weapon by an inadequate life-style. And that it happened despite this useful and protective regulatory process that allowed animals to survive even stronger enemies or radical changes in the environment during development. Therefore, changing and adjusting the lifestyle, and not avoiding stress, as well as not to be exposed to permanent stress, is the foundation of health. Instead, it is either to avoid psychological stress or even better to overcome it by physical activity, making use of the mechanisms that can not be harmed.

7. CONTROL OF STRESS

People therefore need a certain level of stress to strengthen their adaptation mechanisms to their advantage. Nevertheless, too much of everything is harmful and in stress it is true twice. Therefore, not only people, but also so called behavioral medicine is looking for ways to cope better with stress in life. It is well known that for the body's ability to cope with stress (even with its psychic component) is important the presence of vitamins and minerals. It is cited most often vitamin C, the complex of vitamins B and first of all Mg^{2+} ions. These are even called anti-stress ions, important for the proper functioning of the brain but also for other tissues and organs, especially during stress. One of the richest natural sources of Mg is bananas, which are sometimes called a "magnesium bomb".

Also, good physical fitness and therefore regular physical activity have a favorable psychological impact on coping with stress. Well, good physical training, but enough sleep

already mentioned, is an important prerequisite for that. Permanent lack of sleep is one of the most common forms of chronic stress of today's people. Besides, various relaxation and meditation techniques are also a good means of managing stress. Along with this, stress can also be reduced by a rational reflection about the factors that cause it and the change in attitude towards them. Last but not least, the important role of life-style should be mentioned. It means having good eating habits and relevant nutrition.

7.1. Stress and drugs

There is no doubt about the relationship between drug addiction and stress. Many people suffering from stress become addicted because they can not cope with their stressful reactions. The most widespread is smoking, coffee and, of course, the most widespread drug - alcohol. Especially smoking is inappropriate in this situation because it causes further secretion of catecholamines. Coffee, otherwise substantially innocuous, under stress, prolongs the lipolytic effect of cAMP because caffeine inhibits phosphodiesterase. Similarly, it is an alcohol that significantly stimulates the synthesis of cortisol, promotes liver lipogenesis and increases serum triglycerides levels. The essence of drug use is the conscious or unconscious confession of hedonism. Hedonism (derived from the Greek hedoné - pleasure) is based on the belief that pleasure and the feeling of blessing are the highest good, the main objective of man, and his behavior is also based on it. There is a nonspecific system of reward in the brain, and the need to strengthen it, unwarranted leads to drug addiction. The continuity of addiction and stress has long been evident from the fact that some endurance athletes feel blessed from running when they activate this opioid reward system. During this physical exercise, endorphins, endogenous opioid peptides are released to an increased degree, and the athlets deserve them a sense of satisfaction. This beneficial so-called "endogenous morphinism" is also the essence of reasoned recommendations to perform regular active body movement, preferably sports, to increase stress resistance. This leads to good physical fitness with a feeling of physical well-being and goes hand in hand with a balanced psychic state. Somewhat problematic is the induction of stress reactions in some people with tendency to look at the misfortunes of others (eg, flood tourists, crowd viewing executions), but also stunt stunts or sex, which are known phenomena from the repertoire of modern human activities. If it is not enough for the well-being, one will begin to strengthen his hedonic brain system with drugs and it get into a spiral of misfortune. The mesolimbic dopaminergic system, where dopamine plays the role of mediator in activating not only useful life-saving systems (food intake) but also feelings of

well-being (sex but also drugs - including smoking), plays a major role here. Interestingly, in smoking, where dopamine release with a consequent senses of satisfaction occurs after a few inhalations of cigarette smoke, there is no more intense nice feelings despite further inhalation of hundreds of harmful substances because then it is only the consequence of some additional habits on this act, but without the continued involvement of mediators of "Good moods".