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# EFFECT OF STRESS ON THE DEVELOPMENT OF ARTERIAL HYPERTENSION

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**Abstract:** The system of cardiovascular regulation is the most sensitive to the influence of negative social and psychological factors which play an important role in the beginning and development of AH in most patients. In the present article we describe the results of clinical studies on the assessment of the impact of emotional stress, informational overload, occupational stress, degree of social integration and insomnia on the risk of AH development. In the recent studies it was demonstrated that depression, anxiety level and psycho-emotional stress are independent risk factors for cardiovascular pathology, which should be considered together with other generally recognized cardiovascular risk factors. The clinicians are faced with the task to develop optimal ways of influence on psychosocial risk factors. So it is necessary to clearly identify the most important of them, the mechanisms of their negative effect on cardiovascular pathology, as well as the implementation of preventive measures aimed at the prophylaxis of AH and its negative consequences.

**Keywords:** arterial hypertension, stress, occupational stress, psychosocial stress, insomnia.

Arterial hypertension (AH) is one of the commonest diseases around the world, which, according to experts, affects nearly one-fourth of the world's adult population, and is a leading cause of deaths and disabilities in the world [40]. The tendency of the present day is a steady increase in the number of stressful and frustrating factors, negatively affecting man, his professional success and health [12]. Cardiovascular regulation system is the most sensitive in relation to the impact of negative social and psychological factors which play an important role in the onset and development of hypertension in most patients. Since the brain is one of the target organs in hypertension, the increase of blood pressure may affect human mental functions [29]. It was found that increase of blood pressure is a significant risk factor in the formation of mild and moderate cognitive impairments. And it is being known that the presence of high blood pressure affects the emergence of cognitive disfunction [4]. In addition, changes in brain activity may secondarily affect blood pressure values. It has been demonstrated that a number of psychosocial factors are

independent risk factors for the development of cardiovascular diseases and unfavorable outcomes and deaths from the cardiovascular diseases [16].

**Psychological risk factors of AH**

Several studies have proved the key role of emotional stress in the development and significant rejuvenation of cardiovascular diseases. Young age demands particular concern in this regard, what is the most critical and difficult in respect to the adaptation of the organism [3]. The most important component among different components of psycho-emotional stress is the **informational load** – psychogenic stress, which occurs during unfavorable combination of three factors: volume of information, the time necessary for the assimilation of new material and high motivation, which is marked as informational stress.

**Occupational stress**

The most widely studied model of occupational stress is a model of the operating stress "demand-control" [23], which is focused on two characteristics of the working environment: responsibility and control ("the scope of work" and "psychological requirements"). It was demonstrated that the model of work overload is associated with the increase of ambulatory AH at one's place of work, at home and during sleep, as well as with an increase of left ventricular mass as a result of persistent long-term AH increase [35]. Another model of work stress is a model of disbalance "effort-reward" [17]. The latter defines a chronic stressogenic situation at work in terms of the disbalance between the efforts spent and a low level of compensation obtained. It is significant that in the conditions of disbalance "effort-reward" an increase in heart rate and systolic AH as well as a decrease in the vagal tone in all control points [24] are found in the surveyed persons during working hours and after work.

In a multicenter study CARDIA (Coronary Artery Risk Development in Young Adults) [25], which included 3,200 employees at the age from 20 to 32 years old with normal AH at the initial conditions, an interconnection between hard work and development of hypertension was studied. The period of observation lasted 8 years. It was demonstrated that hard work was significantly associated with the incidence of AH ($p < 0.05$) for the entire cohort including women and men. During

the multifactorial analysis it was indicated that under conditions of disbalance "effort-reward" a greater incidence of AH in the entire cohort was discovered (odds ratio 2.06 at 95% of CI from 1.01 to 4.26).

In a prospective study [30], which included 8395 office workers, the effect of the hard work on blood pressure levels was studied. After 7.5 years 84% of participants have been re-examined for the cumulative impact of hard work. Compared with the men who had never been subjected to work overload, a significant increase of systolic AH by 1.8 mm Hg (95% CI from 0.1 to 3.5) was observed in the men, whose professional activity was associated with hard work. The effect was less in women. Moreover, a more pronounced effect appeared in men and women with low social support at work.

**Mental health.** Among the psychological risk factors of cardiovascular diseases, the personality traits, which include "coronary" behavioral type A [32] and the personality type D [18], are described. The individuals with type D (distress) simultaneously experience a high level of negative excitability (tendency to experience negative emotions) and social suppression (suppression of emotions and behavioral reactions in social interactions). [18] In patients with AH personality type D is diagnosed up to 53% [18], in IHD – in 25-38% of cases [36]. The presence of type D personality in cardiac patients adversely affects the quality of life and prognosis.

**The level of social integration.**

A high level of social integration, defined as the presence of 4 to 5 social relationships (marital status, contact with parents, children and neighbors, volunteering activity) was associated with a 41% reduction in the probability of development of increased AH among the participants of Health and Retirement Study [39]. This effect was more evident among the participants under the age of 65 years, males and persons with low income and educational level. [18]

Loneliness, lack of (or insufficient) social relations are the factors which increase the risk of AH development in persons aged 50 years and older. In the survey made by Hawkley L. et al. [22], which included 229 lonely people aged 50 to 68 years old, the effect of the absence (or insufficient number) of social relations on

the AH levels during 4-year follow-up period was studied. It was noted that in the persons who indicated almost complete solitude in the first survey, the average AH indexes were 14.4 mm Hg higher than of those who had social contacts (relatives, friends and colleagues with the same interests, etc.).

**Sleep disturbances**

Insomnia is the most common sleep disorder – from 3.9 to 22.1% [33]. Sleep disorders represent a significant problem, substantially affecting quality of life, especially in elderly persons. It was found that sleep disturbances cause worsening of a number of somatic diseases [21]. The sleep length affects life span, and there is a connection between insomnia and increased risk of mortality in the elderly [27]. The influence of sleep duration, insomnia and obstructive sleep apnea syndrome (OSA) on the increase of risk of AH development has been confirmed [19].

According to the concepts of H. Selye, the development of the general adaptation syndrome is characterized by three stages or phases: anxiety (activation), effort (resistance) and exhaustion [11]. It is proved that the state of acute stress response is accompanied by a transient AH increase. The essential role of emotional stress and the influence of stress factors as a cause of hypertension have been determined [14]. An example of acute emotional stress may be a white-coat hypertension, which is characterized by variability in blood pressure levels, measured in a doctor's surgery (high) and at home (normal values). It is assumed that chronic stress contributes to the appearance of the persistent hypertension [37]. The etiological role of psycho-emotional factors in the development of hypertension was considered by G.F. Lang, who proposed a neurogenic theory. According to this theory the main cause of hypertension is a prolonged mental trauma and emotional overload, leading to the formation of pathological dominant and impaired AH regulation by the cortex of cerebral hemispheres and hypothalamic centers. These studies were continued in the works by A.L. Myasnikov, who also considered hypertension a result of the dysfunction of the nervous regulation of the blood-vascular system.

The systematic review [37], including 10 cohort investigations and 4 case-control studies involving 52,049 people, was devoted to the study of a relationship

between psychosocial stress and hypertension. In 5 of 7 studies a significant positive connection between chronic stress and hypertension and risk factors in the range from 0.8 to 11.1 was found. In 3 of 5 researches a high and significant risk for affective response to stress in AH was mentioned, in 1 – a significant risk close to 1, and in 1 – a distinct lack of risk. The authors concluded that acute stress, apparently, is not a risk factor for AH, while chronic stress may more likely be the cause of sustained increase of AH.

In the pathogenesis of AH an important place is given to the activation of the sympathetic nervous system, especially in the early stages [9]. The subject of the Exploration Tecumceh Blood Pressure Study [26] is a study of the role of the sympathetic nervous system in the development of AH. An essential activation of the sympathetic nervous system not only in the early stages of AH formation, but also in the further development of the disease was confirmed. A correlation between the activation of the sympathetic nervous system in essential AH and a degree of AH increase was established [7]. Moreover, the renal sympathetic denervation is used for the treatment of the patients with resistant AH [34]. On the other hand, stress stimulates the activation of the sympathetic nervous system. At the same time, in the epidemiological studies no relationship between the state of chronic stress and AH was revealed [38].

Recent studies have revealed that in the structure of the stress system central and peripheral units are distinguished. Central units of this system are represented by the hypothalamus and brainstem structures, and peripheral ones – by the hypothalamic-pituitary-adrenal and sympathetic-adrenal systems. The main result of stress system activation is a release of stress hormones – glucocorticoids and catecholamines into the blood [10]. It was found that stress is manifested as a systemic response of the body, involving psycho-emotional, physiological, neuroendocrine and biochemical processes [13].

In accordance with the modern concepts stress is conventionally divided into physiological and psychological ones due to the fact that any stress is accompanied by physiological (reflex, endocrine, immune) disorders and reactions of the mind [2,15]. And combined stress influence is found more often. It has been demonstrated

that a combination of "stressors" influence more negatively than an isolated "stressor" according to the effect on cerebral blood flow [6]. Moreover, pre-existing insufficient blood supply of the brain, i.e., hypoxia of the brain, as a result of atherosclerosis, prolonged persisting AH or other causes, is itself a factor causing homeostatic malfunction [1].

Activation of the stress system is accompanied by the activation of the stress-limiting system, the effects of which are also implemented at various levels [7]. GABAergic and opioidergic systems are attributed to the central links of stress-limiting system. They combine neurons in the hypothalamus and secretory cells in the pituitary gland. These structures have an inhibitory effect on catecholamine link of the stress system as in the central nervous system as on the peripheral level. Peripheral units of the stress-limiting system are represented by prostaglandins, antioxidants, adenosine and a number of neuropeptides [8].

Coordinated and balanced activity of the stress and stress-limiting systems determines the significance of the stress response not only in pathogenesis, but also in sanogenesis for any pathology [1]. Optimal balance of the stress and stress-limiting systems provides high resistance of the body to the factors stimulating stress and to other stimuli, what increases the body's non-specific resistance to stress and is also called a phenomenon of cross stress adaptation [31]. However, the suppression of the stress-limiting system at different levels by the systemic unidirectional and intensive pathogenic regulatory effects is naturally accompanied by the development of pathological conditions. Thus, the character of the stress system activity may determine the compensatory potential of the body in conditions of chronic pathology. It has been noted that cardiovascular pathology has a disadaptive effect on the body, involving central, neurohormonal and vegetative phases of regulation, destabilizing the balance of stress and stress-limiting systems [5].

In the study Garcia-Vera MP et al. [20] the analysis of indices of the personal emotional state and psychosocial stress in patients with AH and normotonia revealed no significant differences on the emotion of anger. However, in the AH group a higher level of trait anxiety, personal depression and stress was registered in comparison with the persons with normal AH levels. According to the discriminant

analysis the most important psychological variable, allowing to distinguish AH and normotension, was depression. Thus, the results confirm the presence of correlation between emotional personality traits and stress and AH, the necessity of AH diagnostics on the ground of clinical and home / ambulatory BP measurements. After successful AH diagnostics it should be necessary to assess psychological factors, in particular, negative emotional states.

In the meta-analysis conducted by Pan Y. et al. [28] the data of the epidemiological studies which assessed the relationship between anxiety and AH was summarized. In 13 cross-sectional studies (n = 151389) in the calculation of the combined odds ratio, this association was statistically significant and made up 1.18 (95% CI from 1.02 to 1.37; PQ <0,001; $I^2$ = 84,9%). According to 8 prospective studies with a total sample size of 80146 and 2394 patients with AH the total adjusted hazard ratio: 1.55 (95% CI from 1.24 to 1,94; PQ <0,001; $I^2$ = 84, 6%). Thus, the existence of the correlation between anxiety and increased risk of AH development was confirmed, what proves the necessity for early diagnostics and treatment of anxiety in patients with AH.

## Conclusion

In the recent studies it was demonstrated that depression, anxiety level and psycho-emotional stress are independent risk factors for cardiovascular pathology, which should be considered together with other generally recognized cardiovascular risk factors. The clinicians are faced with the task to develop optimal ways of influence on psychosocial risk factors. So it is necessary to clearly identify the most important of them, the mechanisms of their negative effects on cardiovascular pathology, as well as implementation of the preventive measures aimed at the prophylaxis of AH and its negative consequences.

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## ВЛИЯНИЕ СТРЕССА НА РАЗВИТИЕ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ

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**Аннотация.** Система кардиоваскулярной регуляции является наиболее чувствительной в отношении воздействия неблагоприятных социально-психологических факторов, которые играют важную роль в возникновении и развитии АГ у большинства больных. В представленной статье рассмотрены результаты клинических исследований по оценке влияния эмоционального стресса, информационной нагрузки, профессионального стресса, степени социальной интеграции и инсомнии на риск развития АГ. В исследованиях последних лет продемонстрировано, что депрессия, уровень тревожности и психоэмоциональный стресс являются независимыми факторами риска сердечно-сосудистой патологии, которые следует рассматривать в совокупности с другими общепризнанными факторами кардиоваскулярного риска. Перед клиницистами стоит задача выработки оптимальных воздействий на психосоциальные факторы риска, для этого необходимо четко идентифицировать наиболее значимые из них, механизмы их неблагоприятного влияния на сердечно-сосудистую патологию, а также проведений превентивных мероприятий, направленных на профилактику артериальной гипертензии и ее негативных последствий.

**Ключевые слова**: артериальная гипертензия, стресс, профессиональный стресс, психосоциальный стресс, инсомния,

## ВПЛИВ СТРЕСУ НА РОЗВИТОК АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ

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**Анотація:** Система кардіоваскулярної регуляції є найбільш чутливою відносно дії несприятливих соціально-психологічних чинників, які відіграють важливу роль у виникненні і розвитку АГ у більшості хворих. У представленій статті розглянуті результати клінічних досліджень по оцінці впливу емоційного стресу, інформаційного навантаження, професійного стресу, міри соціальної інтеграції і інсомнії на ризик розвитку АГ. У дослідженнях останніх років продемонстровано, що депресія, рівень тривожності і психоемоційний стрес є незалежними чинниками ризику серцево-судинної патології, які слід розглядати в сукупності з іншими загальновизнаними чинниками кардіоваскулярного ризику. Перед клініцистами стоїть завдання вироблення оптимальних дій на психосоциальні

чинники ризику, для цього необхідно чітко ідентифікувати найбільш значимі з них, механізми їх несприятливого впливу на серцево-судинну патологію, а також проведень превентивних заходів, спрямованих на профілактику АГ і її негативних наслідків.

**Ключові слова:** артеріальна гіпертензія, стрес, професійний стрес, психосоціальний стрес, інсомнія.