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Immunological Features of Juvenile Offenders.

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ABSTRACT

We assume that complex mental changes caused by penal stress are often accompanied by a decline in the immune response. Evaluation immunophysiological shifts in people adolescence that are conditions of detention are the target of this study. A total of 57 adolescents, 47 of them - students of educational colonies of Russia's largest cities, and 10 - students of secondary and higher educational institutions of the city are surveyed. They examined the immune status by standardized methods. Phagocytic index and phagocytic number of polymorphonuclear leucocytes of the adolescents containing in educational colony, had considerably below norm. At the analysis of absolute quantity T-helpers and T-suppressors is revealed CD4, or isolated activation of CD8. It is drawn a conclusion, that adaptable reaction to conditions of a punishment cell is accompanied by phase changes of the immune status which expressiveness has specific features. In conditions of holding in custody strengthening immunosuppressor and cytotoxic effect that is shown by activation T-effectors and NK-cells becomes leader and a parallel decrease in the proportion of T-helper cells. It is formed Th2-helper type of immune response, characterized by the suppression of cellular responses and prerequisites for the prevalence of humoral response.

Keywords: cellular immunity, humoral immunity, immunologic factors, suppressor T-lymphocytes.

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INTRODUCTION

As it is known, the conditions of detention of prisoners in the penal system are characterized by strict regulation of behavior, coupled with the continuous influence of criminal society, restriction of freedom - social deprivation, isolation from family and convict the usual social environment of existence. Influenced by significant strength and duration of internal and external stimuli, or more precisely, under chronic stress are consistently condemned in all its development stage adaptation syndrome [1, 2]. And if in the life around us influence of external stimuli on the body are often short and ends, mostly, his functional rehabilitation on some new level when adaptive resources of the organism again as balanced, the conditions of prolonged stress reaction reserve of protective forces gradually depleted with followed by disruption of compensatory possibilities and alteration of target organs. If short-term stress response is a protective adaptive, or eustress, mobilizing the body to overcome the obstacles to achieving the vital biosocial goals, in a brief but heavy or, on the contrary, a long and continuing influence, called distress, it is transformed into its opposite - pathogen factor leading to the breakdown of the compensation and the formation of psychosomatic diseases [3].

The human body as a dynamically balanced on the basis of neurohormonal mechanisms of self-functional system [4, 5, 6], becomes labile phase of short-term exposure to external stress factors, achieving homeostasis through change adaptation strategies of interaction of the subject with the external environment. In this primary response to an external stimulus Biosystems first nonspecific ultimately always specific and is a multistage reaction system for complex external environmental influences, the nonspecific and specific adaptation units are a single functional mechanism of defining typology response in accordance with external exposure [7]. Long and continuous stress, first transiently then stably affects the mechanisms of self-regulation of the autonomic nervous system, leading to a breach of her jet lag, disintegration nejrogumoralnoj, hormonal system, somatic dysfunction in the central nervous, cardiovascular, respiratory, and other life-support systems, breaking mechanism permeability various tissue barriers disorganization of connective tissue, secondary immunodeficiency. According to K.V. Sudakov [8], against the background of distress observed summation of pathological changes, it becomes a prerequisite for the formation of irreversible consequences, and somatic disorders. These are generally the basic pathophysiological mechanisms that accompany the psychological stress penitentiary in prison.

In recent years, prospective studies give good evidence that psychosocial factors are independent risk factors for hypertension, ischemic heart disease and the most serious cardiovascular events - myocardial infarction and cerebral stroke [9, 10]. In addition, the incidence of and mortality from hypertension and coronary heart disease, according to different authors, are largely dependent on psychosocial environment [11]. Thus, in the course of a prospective study of phobic anxiety and risk of coronary heart disease, which was attended by 34 thousand men who had no symptoms at baseline cardiovascular disease, found an increased risk of sudden death in patients with high levels of anxiety [12].

The penitentiary science topic of social deprivation and stress penitentiary devoted quite a lot of research, mainly psychological profile. It should be noted that the number of these materials is growing from year to year and reveals new aspects of the problem. [13]

It is possible that one of the first systems undergoing radical changes at stress, the immune system is. Such penal stress displays at adolescents as undue fatigability, the general weakness, chronic weariness, an indisposition, decrease in intellectual and physical working capacity in many respects are than other, as a consequence of immunodepression in the conditions of synchronisation of negative psychological influence at penal stress. To the told it is necessary to add that the complex of changes, characteristic for penal stress at physiological level, in many respects "duplicates" displays of a syndrome of the chronic weariness characterised first of all by displays of an immunodeficiency. However, detailed studies of the immune system in the available literature, we have not met.

PATIENTS AND METHODS

The case-control study was carried out on 57 adolescents (all of them are men) in 2014. Forty seven of them are in conditions of imprisonment in the Izhevsk educational colony. Middle age of the adolescents who are in conditions of social isolation, participating in our research, has made – $18,35 \pm 0,18$ years. Age ranging from 16 to 20 years. There are 29 (61,7 %) – townsmen and 18 (38,3 %) – countrymen from total number of

convicted persons. To determine the size of the study group used the formula with 95% confidence level [14]. 36 adolescents have the first conviction and never have been in prison previously, 11 adolescents are remained in places of restriction of freedom not for the first time. The greatest number of pupils served time for armed assault, on the second place on decrease degree – containing for a robbery, on the third – for property theft and the fourth place belongs to the subjects who are serving time for murder and rape. Having analysed structure of disease among the surveyed condemned adolescents, have found out that the chronic infection were present at 41 condemned (87,2 %). All diseases were in a remission stage. In case of manifestation of chronic diseases, the subjects were excluded from the group. Patients with viral hepatitis and HIV were excluded from study. As comparison group the given inspections of 10 healthy adolescents of 16-20 years (middle age – $17,02 \pm 1,16$ years) the pupils of higher and average educational institutions of a city of Izhevsk are used.

To all adolescents, along with ordinary researches, spent an estimation of the immune status which included definition in blood of indicators phagocyte activity of neutrophil, cellular (CD3+ - CD4+ - CD8+ - lymphocytes) and humor (IgA, IgG, IgM) immunity. All tests were standardized. Blood sampling was carried out on an empty stomach in the morning. Definition of the general leucogram (total number leucocytes listed in $10^9/l$ and relative quantity of separate leukocytes' pools – in %), subpopulations T- and the B-cellular link of lymphocytes (in %) carried out by method of polyclonal phenotyping with the subsequent fluorescent microscopy and flowing cytofluorometry. Sets of reagents of "Klonospektr" of NPC "Medbiospectrum" (Moscow), microscope MC 50 «MICROS» (Austria) were used. Also definition of concentration of Ig A, M, G (in g/l) in blood was carried out by method Manchini (1965). The activity of neutrophils' and monocytes' phagocytosis was defined. There was estimated an phagocytic index, phagocytic number, the base and stimulated NST-test and definition of a base and stimulated index of neutrophils' activation was carried out. Phagocytic activity of the test cells was studied on the model of the absorption of latex particles in the monolayer by method Freidlin I.S. (1976). In assessing the results determined by the phagocytic index (in %) as a percentage of macrophages, containing latex particles, and phagocytic number (all – in units), i.e. number latex particles in 100 cells counted, based on the cage 1. We used the reduction reaction of nitro tetrazolium (NBT-test) by the procedure Viksman A.M., Mayansky A.N. (1983), determined by the spontaneous and stimulated NBT test. It is based on the recovery in the cytoplasm of neutrophils nitro blue tetrazolium to diphormazane under the influence of the superoxide anion formed during cell activation. Diphormazane looks dark blue or black granules, the amount of which varies depending on the severity of oxygen explosion. To use a set of productions NBT test SPC "Medical immunology", activation of neutrophils was performed with latex. In addition in the basic group tests for cytomegalovirus, herpes simplex and virus Epstein-Barr presence at adolescents have been checked up by method PCR-diagnostics, and also – concentration of a thyreotrop hormone, thyroxine and cortizol is defined in serum (in mU/l, pmol/l, nmol/l respectively).

All subjects received individual informed consent to the test. There is a positive conclusion of the Ethics Committee to conduct the survey. The protocol does not conflict with ethical standards and rules Bioethics Committee SU SRI of Medical Sciences adopted in accordance with the Helsinki Declaration of 1975 and its 2000 revision.

SPSS software version 17.0 (SPSS Inc., Chicago, USA) was used for statistical analysis. The descriptive data were shown by the frequency and $Mean \pm SED$ (standart error of deviation). The data were analyzed by Chi square test, U-test. $P < 0,05$ was considered statistically significant.

RESULTS

Descriptive

In assessing the results of blood count, including leukocyte count, we noted a significant (below normal) reduction in the number of monocytes and a lymphocytes' statistically significant increase. The level of monocytes was $1,94 \pm 0,32\%$ in the group of convicts, while the comparison group $7,94 \pm 1,69\%$, which corresponds to standard values at this age ($P=0,006$). The level of lymphocytes in front exceeds the index of the comparison group, and also went beyond the standard values ($41,91 \pm 1,42\%$ vs. $31,375 \pm 3,59\%$ respectively) ($P=0,02$). Other indicators, such as the total number of white blood cells, relative quantity neutrophil, do not differ from the control group and in line with normative values for age (tab. 1).

The immune status of the surveyed adolescents first of all was characterised by functional insufficiency of factors of nonspecific protection, namely the expressed oppression phagocytic activity of leukocytes and monocytes. From the table 2 it is visible that a number of indicators, in particular - phagocytic index and phagocytic number polymorphonuclear leucocytes of the imprisoned adolescents, had considerably below norm, accordingly 17 % and 1,75. Thus lowered phagocytic neutrophil's activity can indicate the chronisation of inflammatory process both virus and the bacterial nature.

The spontaneous NST-TEST has made 3,02 % and also testified to decrease in bactericidal immunity with the tendency to chronisation. Besides, the stimulated NST-test has appeared almost areactive (13,74 %) that specifies in an exhaustion of a functional reserve the oxygen-relative mechanism of bacterial action of phagocytes. Also in 3 times there was more low an activation neutrophil's index, as spontaneous, and stimulated. The level of activation of neutrophils in the basic index terms was $0,03 \pm 0,003$ units, which significantly was more than 60% lower than the similar index of the comparison group ($0,096 \pm 0,0086$ u.) ($P < 0,001$). As for the index of activated neutrophils stimulated, in the study group, the figure was $0,149 \pm 0,015$ units, which is 67% lower than in the control group ($P < 0,001$).

Decrease in pool T-lymphocytes concerning standard values is shown (tab. 3). Interest has caused the analysis of components of cellular immunity. We have not noted changes of the relative maintenance of fractions T-lymphocytes. At the same time parity CD4 +/CD8 + (immunoregulatory index) has been sharply lowered – $0,95 \pm 0,05$ u. at norm 1,5-2,5 u. And the index did not exceed 1 at 68 % (32 adolescents). At the analysis of absolute quantity T-helpers and T-suppressors has attracted attention on isolated deficiency CD4 + ($CD4 + = 0,82 \pm 0,07 * 10^9/l$ in the general group; $0,23 \pm 0,05 * 10^9/l$ at 3 adolescents), or isolated activation CD8 + ($CD8 + = 0,91 \pm 0,07 * 10^9/l$). Redistribution of lymphocytes' pools towards prevalence immunosuppressive and cytotoxic effects and decrease of T-helper factors are most likely connected with constant circulation of steroid hormones in blood plasma. So, morning level of cortizol at adolescents-offenders has made $871,61 \pm 68,69$ nmol/l that practically twice exceeds an average level of standard values (150-660 nmol/l).

Specific features depending on features of influence long stressor the factor are thus possible. So, at condemned repeatedly absolute maintenance T-effectors (CD8 +) more low, than at appeared in similar conditions for the first time. Accordingly the immunoregulatory index is higher at the first category ($r = -0,56$, $p < 0,01$). At the same time, the more time left condemned within the precincts of correctional facility, in serum was observed lower levels of antibody A, that is, the local immunity has been weakened ($r = -0,36$, $p < 0,05$).

The maintenance T-effectors expressed in percentage (CD8), has the greatest correlation communication in due course stay of the adolescent in a colony, time of the remained term and "experience" of a prison life (quantity of previous convictions) accordingly $r = -0,22$, $p < 0,05$; $r = -0,54$, $p < 0,05$ and $r = -0,56$, $p < 0,05$. In the latter case, considering discrete the characteristic of number of episodes of stay of the adolescent in penal colony, the auxiliary Spearman's correlation factor was used.

By results of PCR-diagnostics it is established that at 49 % persistence virus Epstein-Barr (23 persons), a cytomegalovirus – at 4 adolescents, a virus herpes simplex 1 and 2 types – at 3. Thus it is not revealed any case of association of viruses Epstein-Barr and virus herpes simplex 2 types whereas the cytomegalovirus in all cases is found out together with the specified viruses.

DISCUSSION

If the acute stress, according to several authors [15], in addition to activation of sympathetic nervous system makes modulating impact on neutrophils' concentration and their activity, simultaneously stimulating humor immunity link but continuous influence of the stress factor (stress chronization) causes oppression of neutrophils' activity. As authors consider, such immunosuppressive influence on the nonspecific cellular answer has immunoprotective effect, protecting an organism from destructive influence anti-inflammatory cytokines and products of macrophage origins.

On this background, it is possible compulsory, B-cellular activation of immune system and increase in quantity NK + took place. So, it is known that CD20 + in blood raise, as a rule, in second half of developing inflammatory process or at its long current. According to leading Russian immunologists humoral in-cellular

proliferation is a harbinger of the subsequent beginning of active synthesis of high specified antibodies [16]. At the same time activation B-lymphocytes can be a sign of the got immunodeficiency, autoimmune diseases. Concerning NK-cages it is known that the mechanism of their cytotoxic action is similar to cytotoxic activity CD8 + suppressor T-lymphocytes [17]. Their distinctive functional feature is spontaneous ability to lyse tumoral and some normal cells without preliminary stimulation. Also it is assigned by a part in development autoimmune damages [18]. A number of researchers believes that cytotoxic activity of natural killers CD16 + directly correlates with level of cytotoxic activity of a macroorganism and on the contrary [19; 20].

Early clinical studies priderdivalis model of the relationship of stress and the immune system, in which chronic forms of stress accompanied by a decrease in natural killer cell cytotoxicity, suppressed the proliferative responses of lymphocytes and blunted antibody response to immunization [21, 22, 23]. Reduced immune responses such character was supposed to be responsible for the increased incidence of infectious and neoplastic diseases found among chronically stressed individuals [24, 25].

Several authors Dhabhar and McEwan (1997, 2001), an immune system response to stress exposure was considered as a two-phase model in which acute stress and chronic stress increases suppresses the immune response. Acute stressors fight or flight should lead to the redistribution and immune cells in the compartments in which they can act more quickly and effectively against the invaders. In contrast, during chronic stress, T-cells is shunted away from the skin and the immune response to a skin test challenge was reduced [26].

A modification of this model is that the short-term changes in all components of the immune system (natural and specific) are unlikely because they spend too much energy to be flexible, life-threatening circumstances. Instead, the emphasis should shift the balance of immune response to the activation of natural processes and the reduction of specific processes. The premise underlying this model is that natural immune responses, better suited to manage potential complications, life-threatening situations, what specific immune responses, because they can be deployed more quickly to be less brake limitations and require less energy to be distracted by other body systems supporting the fight or, for example, flying [27, 28].

The most famous of these models suggest that chronic stress causes a simultaneous increase and suppression of the immune response changes in patterns of cytokine secretion [29]. Th1 cytokines that activate cell-mediated immunity, to protect against many kinds of infections and certain types of neoplastic diseases are suppressed. This inhibition has the effect of permitting the production Th2 cytokines, which activate the humoral immune system and exacerbate allergy and many types of autoimmune diseases. This shift can occur via the effects of stress hormones such as cortisol [30]. Th1-Th2-shift change to the balance of the immune response without having to change the overall level of activation or function in the system. Because decreased Th1-mediated cellular immune response can increase vulnerability to infectious and neoplastic diseases, and enhance Th-2 mediated humoral immune response can increase vulnerability to autoimmune and allergic diseases [29]. This is consistent with our results: we note increasing the pool of T-suppressors and reducing the pool of T-helper cells and generally decrease immunoregulatory index that it is formed T2-helper type of immune response, characterized by the suppression of cellular responses. However, in our study we did not observe such a substantial increase in the activity of humoral immunity as research scientists from Belarus. Their studies convicted revealed a significant decrease in CD4 cells at a much smaller number of CD8 cells and increased synthesis of antibodies observed in the group of convicts, which indicate the suppression of cellular immune responses and the stimulation of the humoral immune system [31]. Such changes in the immunological profile characteristic of an immune system response to a stressful situation [32]. At the same time, we reiterate that the response of B-cell immunity been activated under the influence of prison stress.

Also, we studied the literature emphasizes the direct link between cortisol levels and changes in the immune system: chronic stress may elicit prolonged secretion of cortisol, to which white blood cells mount a counterregulatory response by downregulating their cortisol receptors. This downregulation, in turn, reduces the cells' capacity to respond to anti-inflammatory signals and allows cytokine-mediated inflammatory processes to flourish [33]. In connection with immunosuppressive effect the chronic stress inevitably leads to formation of the secondary immunodeficiency which is dangerous concerning formation autoimmune, oncological, infectious diseases or an aggravation of a chronic pathology, probably selective decrease in immunity to separate viruses: to virus Epstein-Barr, a virus of a simple herpes [34, 35, 36], that can be safely

extrapolated to a group of convicted juveniles who have been identified by us wide persistence of virus upper respiratory tract.

CONCLUSION

Results of the research can be formulated as follows:

- In the context of the prison environment in a significant number of persons with a state of the prison, which lead to the formation of adverse levels of somatic adaptation. Adaptable reaction to conditions of imprisonment accompanied by phase changes of the immune status which expressiveness has specific features.
- The prison stress is characterised by considerable decrease in factors of nonspecific protection: it is manifested by a significant decrease in the number (to $1,75 \pm 0,09$ u.) and phagocytic index ($17,19 \pm 1,27\%$) and low below 50% of normal neutrophils' test data both basal and stimulated in values.
- In conditions of holding in custody strengthening immunosuppressor and cytotoxic effect that is shown by activation T-effectors (increased to $31,00 \pm 1,01\%$) and NK-cells becomes leader ($28,55 \pm 1,50\%$) and a parallel decrease in the proportion of T-helper cells to $28,74 \pm 1,52\%$. It is formed Th2-helper type of immune response, characterized by the suppression of cellular responses and prerequisites for the prevalence of humoral response (pool of CD20 is on the level of $24,38 \pm 1,50\%$).
- The Chronic stress inevitably leads to formation of the secondary immunodeficiency which is dangerous concerning formation autoimmune, oncological, infectious diseases or an aggravation of a chronic pathology, and also selective decrease in immunity to separate viruses: to the Epstein-Barr virus, a virus herpes simplex, etc.

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