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EDITORIAL

Dear Colleagues, dear Readers!

We are delighted to present you the second edition of the outgoing year 2017. This volume comprises articles as well as short reports of conference proceedings. As the convener of the conference Euromedica-Hannover we could select a number of interesting studies on major medical fields. The issue represents a wide range of medical disciplines in its turn representing numerous medical universities and research institutes. We hope that it has made the journal more interesting and multifaceted.

The Journal has the history of 6 years and during this short period we can see, how fast medical science has developed and at the same time how hard the struggle with the deadliest diseases goes on. However, certain trends in medicine are becoming reality, such as globalization of medical knowledge, automatization and personalization of the attitude to a patient. This ensures better chances for prevention and treatment of many diseases.

Our Journal unites well-known scientists and specialists from different countries, therefore it is important for us not only to publish articles of our authors but also meet them in the frame of our annual events. The next meeting of the editorial board and the authors is scheduled on 24th May, 2018 in Munich. During a roundtable we are going to discuss the future of medicine and health care and the future of the Journal.

We hope that the Journal and professional meetings provide a discussion format, which enable to improve scientific communication, exchange of ideas and research results and also promotes introduction of new developments into theory and practice. We would like to thank our authors and members of the editorial board for their work on preparing and releasing this edition. We especially thank the team of authors from Astrakhan Medical State University, its President Prof. Khalil Galimzyanov and, above all, its Vice-President Prof. Alexey Zhidovinov, who contributes greatly to scientific development of the Journal and its supports.

We wish all our friends and colleagues health, happiness and prosperity in New Year 2018!

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ASSESSMENT OF HEALTH INDICATORS FOR STUDENTS OF DIFFERENT TYPES OF EDUCATION

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Dynamic assessment of health status for students at the present stage is one of the most important problems confronting medicine. Over the past three decades, the health of the younger generation is deteriorating, as evidenced by official statistics, the results of preventive examinations and scientific research [1, 2, 6]. Assessment of the health status and physical development of the younger generation in dynamics allows to determine the effectiveness of the ongoing reforms, both the educational process and medical measures to preserve the health of children.

At present, the medical community is interested in the problems of the health status of children of school age, in connection with the increasing loads and deepening of the school curriculum. The content of school programs varies mainly in the direction of the intensification of education and increasing the volume of training loads [3].

In addition, in the conditions of active introduction of new type schools, it is necessary to evaluate their educational and educational process, since subjects that are not included in traditional educational programs are introduced into the daily schedule and timetable [9]. Important risk factors for the health of children in educational institutions of a new type is the formation of a state of chronic stress [4, 5], which contributes to the development of neurotic states, functional deviations and chronic diseases.

The purpose of our study was a comparative assessment of the health and physical development of schoolchildren of 11–12 years of general education schools and pupils of the Ataman Biryukov Cossack Cadet Corps.

MATERIALS AND METHODS OF RESEARCH

Children of 6–7 classes of comprehensive schools and the Cossack Cadet Corps of the Astrakhan Region were examined. We assessed the level of physical development, the group of health, based on clinical examination and the conclusion of specialists. In total, 100 pupils of secondary schools (48 boys, 52 girls) and 83 students of the Cossack cadet corps aged 10.9–12.5 years were examined. The determination of the level of physical development, harmony, and somatotype was assessed according to the generally accepted method. Assessment of the main physical parameters (growth, weight, circumference of the chest) was carried out using a nonparametric (centile) method.

Differences in growth rate were characterized by the following somatotypes: microsomatic somatotype

— slowed-down rate of age development; macrosomatic — accelerated pace; mesosomatic — the average, was divided depending on the prevalence of one or another tempo on the meso-, micro- and mesomacrosomatotype.

Clinical evaluation of the state of health was carried out by traditional methods with the definition of nosology: copying of data from medical records (the history of the child's development, the child's medical card) with the verification of their results with the data of their own examination; Functional samples of cardiorespiratory system — mass-growth index of Quetelet, double product — Robinson index, Skibinsky index, Shapovalova index of power, Ruthier index.

RESULTS OF THE STUDY

When assessing the physical development of schoolchildren who attend 6–7 classes of comprehensive schools in Astrakhan, it was found that the average indicators (25–75 centile) of physical development (height, weight, circumference of the chest) were 67%, below average — 13%, above average — 20%. The physical development of the cadets of the Cossack corps was estimated as average in 84% of children, below average — 2.5%, above average — 13.5%.

When assessing the growth rates of students in general education schools, it was found that boys with a microsomatotype were 14.3%, a mesomicrocosmatotype — 51.4%, a mesomacrosatomotype — 14.3%, and a macrosomatotype — 20%. Girls have higher growth rates: 12.5% with a microsomatotype, 53.1% with a mesomicrocosmatotype, 18.8% with a mesomacrosatomatotype and 15.6% with a macrosomatotype.

Among the pupils of the Cossack corps, children with a mesomacrosatotype — 50.1%; with mesomicrocatomatotype — 34.3%. The share of macro- and microsomatotype accounts for 13.5 and 2.5% of children, respectively.

Analysis of the results of a comprehensive health assessment showed that the first group of health was established in 31%, the second group — 51%, the third group — 18% of schoolchildren. Among the girls of the first group of health met 3 times more often than among boys (36.5% vs. 12%). The second group of health among children of both sexes is established with a slight difference in frequency (girls — 52%, boys — 50%). The third group of health was more often determined in boys than in girls (25% vs. 11.5%).

Among the cadets of the Cossack corps the following distribution among health groups is observed: the first — 25%, the second — 69%, the third — 39%.

According to the results of the analysis of the medical examinations, it is established that the chronic pathology of students in general education schools is represented by diseases of the musculoskeletal system, respiratory and digestive organs.

The analysis of morbidity allowed to establish that the first two places in the structure of diseases are occupied by pathology of the musculoskeletal system and respiratory organs.

The structure of morbidity among pupils of the Cossack corps differs by prevalence of respiratory diseases, second place is occupied by trauma, diseases of the musculoskeletal system occupy the last place.

To clarify the level of physical health, a complex consisting of five morphological and functional indicators was used: the mass-growth index of Quetelet, the double product — the Robinson index, the Skibinsky index, the Shapovalova index of power, the Ruthier index. The results are shown in Table 1.

Table 1.

Indicators	The number of pupils in secondary schools corresponding to the average indicators (%)		The number of cadets of the Cossack corps, corresponding to normal indicators (%)
	boys	girls	
The Quetelet index	58,3	65,3	72,8
The Robinson index	52,0	55,8	60,2
The Skibinsky index	45,8	59,6	62,8
Shapovalova Index	43,7	71,1	82,0
The Ruthier Index	54,1	63,4	69,8

Average indicators of the vital index were found in 47%, below the average 15% and high indicators - 38% of students in general education schools.

The indicators of the Cossack corps pupils are shifted to higher values: 49% of the cadets have average values of the vital index, 11% are below the average, and 40% — are high.

CONCLUSIONS

Based on the results of the study, a conclusion was made about the positive impact on the physical development of children of the education system of the Cossack Cadet Corps, which includes elements of athletic and combat training. The tendency of displacement of the pathology of the musculoskeletal system to the last place in the structure of the overall morbidity is evaluated positively. Preservation of

posture is the key to the harmonious development of the child's organism and the proper formation of the functioning of all organs and systems. Students with disorders of posture differ from healthy peers in the level and harmony of physical development [7, 8].

However, in the structure of morbidity there is an increase in the percentage of diseases of the nervous system, which may be due to the state of chronic stress among children whose learning conditions are associated with a change in their place of residence, separation from the family and an increased level of responsibility.

The obtained data testify to the need for further dynamic study of health indicators and physical development of children and teenagers studying in different education systems in order to select the optimal conditions for maintaining and strengthening the health of the younger generation.

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ONCOPATHOLOGY IN THE OIL AND GAS INDUSTRY IN RUSSIA IN THE FAR NORTH AND OTHER REGIONS OF WORLD

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INTRODUCTION

According to Lin CK, Hung HY, Christiani DC, Forastiere F, Lin RT. (2017) the pooled risk of lung cancer mortality for residents living nearby PICs was 1.03-fold higher than people living in non-PIC areas (95% CI = 0.98–1.09), with a low heterogeneity among studies (I^2 = 25.3%). Such effect was stronger by a factor of 12.6% for the year of follow-up started 1 year earlier (p-value = 0.034) [6]. Their and other researches meta-analysis gathering current evidence suggests only a slightly higher risk of lung cancer mortality among residents living nearby PICs, albeit such association didn't receive statistically significance [9, 14. Reasons for higher risks of early residential exposure to PICs might be attributable to the lack of or less stringent air pollution regulations. But the objective research Osakwe KA, Cooper K, Stewart D, Wainwright CL, Klein S. (2017) is to collate, synthesize and present the available evidence on the policies and guidance statements for remote healthcare practitioners on managing medical emergencies in the offshore oil and gas industry [12].

Results of Whitworth KW, Marshall AK, Symanski E. (2017) are suggestive of an association between maternal residential proximity to UGD-activity and preterm birth and fetal death. Quantifying chemical and non-chemical stressors among residents near UGD should be prioritized [16].

In the opinion of Cox RS, Irwin P, Scannell L, Ungar M, Bennett TD. (2017) although relatively few studies have specifically focused on children and youth in this context, the majority of this research uncovers a range of negative health impacts that are directly and indirectly related to the development and ongoing operations of natural resource production, particularly oil and gas, coal, and nuclear energy [1]. Psychosocial and cultural effects, however, remain largely unexamined and provide a rich avenue for further research [10].

Purpose of our the study was identify data on the incidence of diseases associated with environmental factors in the oil and gas industry.

METHODS

To obtain the data, we used the analysis of scientific data from different regions of the world.

RESULTS

Oil and gas development emits known hematological carcinogens, such as benzene, and increasingly occurs in residential areas [3, 7]. At present, there is growing interest in research examining the relationship between occupational stress and mental health. Mason KL, Retzer KD, Hill R, Lincoln JM. (2017) observed during 2003-2013, fatality rates for oil and gas extraction workers decreased for all causes of death except those associated with fall events, which increased 2% annually during 2003-2013 [8, 13]. Sixty-three fatal falls were identified, accounting for 15% of all fatal events.

It was showed in the oil and gas industry and demonstrates that diagnoses of a digestive and traumatic nature are the most frequent [4, 5]. A holistic approach to health (as opposed to a predominant focus on fitness to work) bears more attention to female.

CONCLUSION

Due to development of oil and gas industry a larger population has the potential for exposure to known hematologic carcinogens, further study is clearly needed to substantiate both our positive and negative findings. Future studies should incorporate information on oil and gas development activities and production levels, as well as levels of specific pollutants of interest (e.g. benzene) near homes, schools, and day care centers; provide age-specific residential histories; compare cases to controls without cancer; and address other potential confounders, and environmental stressors [2, 11]. The use of rigorous methodologies to assess environmental, social and health impacts of specific interventions is crucial to disentangle the various components of environmental questions and to inform public opinion [15]. It was exercise highlights the knowledge gaps that need filling and taking into due consideration before future transnational and cross-border monitoring and management plans and activities can be addressed in in the oil and gas industry.

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MEDICO-SOCIAL ACTIVITY OF WORKERS OF SHIPBUILDING AND SHIP REPAIR INDUSTRIES

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INTRODUCTION

A leading role in maintaining the human population is lifestyle as a factor that determines the main trends in health. Under the influence of negative anthropogenic factors on population health in the preservation of the vital capacity contributes to health and social activity [1–4].

The aim of this work was to determine the level of medico-social activity of workers of shipbuilding and ship-repair enterprises within the paradigm of the healthy lifestyle of the population.

The objectives were the assessment of medico-social activity of the population connected with health and health care, disease prevention, healthy lifestyle, hygienic and medical recommendations, compliance, satisfaction with quality of medical care of workers of the shipyards of Astrakhan.

Methods

In this study we used the methods of sociological survey and non-parametric statistics.

THE RESULTS OF THE STUDY

In the structure of workers of shipbuilding and ship-repair enterprises 95% represent industrial personnel, only 5% of employees is accounted for non-industrial personnel.

For industrial personnel a number of adverse production factors associated with the industrial activity were singled out, which are of combinatory character.

The first rank position among the groups of unfavorable factors of production were given to the cold climate, accounting for 10.61%, the second place — working with electrical installations (8,1%), the third factors included noise, workload, insufficient lighting (7,8%), the fourth — noise, microclimate, uncomfortable posture (6,7%) and noise, vibration, physical stress, intensity of work (6,7%), the fifth elevated temperature, overall vibration, industrial noise, physical stress, work at height (5.03%) and contact with synthetic detergents (5,03%), the sixth elevated temperature, the local vibration (4,75%), seventh — noise, welding aerosols, meteorological factors, awkward posture (4,19%).

For the non-production personnel a number of adverse factors, mostly monofactors, were detected.

The first place among the unfavorable factors for the non-production personnel was attributed to electromagnetic field wideband frequency spectrum and a combination of electromagnetic, electrostatic and alternating magnetic fields (27%), alkali and formalin – the second place(6%) and other factors (5% each) – the third place.

The estimated risk of disease occurrence among workers of the shipbuilding and ship-repair enterprises amounted to 0.8, which was accounted by the highest proportion of the workers being in direct contact with industrial hazards of a combined character.

Negative work environment and high risk of disease has necessitated a thorough analysis of the medical activity of employees of shipbuilding and ship-repair enterprises. In this regard, all the employees of these enterprises were divided into 2 groups: dealing with professional hazards and working without occupational exposures. The first group of workers was the lowest and accounted for 43%, the second — dominated, accounting for 57%.

Whereas among men those working with occupational hazards were more than without occupational hazards: 51% and 49% respectively

Among workers, women in contact with industrial hazards 30%, the remaining 70% were not subjected to production hazards.

Sociological survey for the evaluation of medical activity of employees of shipbuilding and ship-repair enterprises was carried out. Among 400 respondents 57.3% were women, 42.7% — men. The level of social-medical activity was high and came to 82.1%. Doctor attendance for prevention reached 75,8% among workers. 92.6% of the respondents complied voluntarily with the prescription. Less than half of the respondents was actively involved in sport or physical activity (42.6 per cent), while 57.4 per cent were not motivated for physical activity.

Among the respondents, 46.2% were treated in hospital one time per year, 31.2% two or more times a year, and 22.6% — less than once a year. More than half of the respondents (51,1%) chose the same hospital for treatment, and 48.9% were treated in other hospitals of the city. All respondents who were hospitalized, were satisfied with inpatient medical care. Suggestions of respondents to improve the quality of medical care in the hospital was as follows: 41.1% offered to raise the comfort level of the patient's stay in hospital, 24.7% of the considered it necessary to improve the nutrition of patients in hospital, 7.4% are believed necessary to improve the provision of medicines in the hospital, the 24.2% of respondents had no suggestions for improving the quality of hospital care, an important component of medical activity of the studied contingent workers in the shipbuilding and ship-repair enterprises was their participation in the periodic medical examinations, the main goal of periodic medical examinations at work — detection of early signs of occupational diseases or poisoning, and diseases, etiologically not related to the profession, but in which continued contact with the data of occupational hazard is a danger. As a result of the periodic medical examinations the first group of health were assigned the 61.8% of the patients, the second group is 2.8%, the third group and 31.9% for the fourth group and 3.5% of patients.

In the structure of pathological defeats of the workers of the shipbuilding and ship-repair enterprises took the first place diseases of the circulatory system (25,4%), the second — illnesses of digestive organs and symptoms and signs of deviation from the norm (for 16.9%, respectively), the third — diseases of the musculoskeletal system and connective tissue (11%), fourth – diseases of the eye and adnexa and diseases of the endocrine system (10% respectively), the fifth — diseases of the genitourinary system (9.8%). In the past periodic medical examinations exacerbation of disease was 45% of workers, had 55%. Recommended treatment in a centre of occupational medicine, 44% of workers, outpatient treatment, 32% of workers rehabilitation – 15% of the employees, the Spa treatment – 5% employees, in-patient care – 4% of the employees. About high medical activity can be judged by a significant proportion of workers shipyards treated: 47% center for prevention,30% of outpatient care, 15% rehabilitation, 4% stationary and sanatorium-resort treatment. Of group recommended to outpatient treatment actually received outpatient treatment 89% of workers. Among workers in the shipyards who received the medical examination to inpatient treatment 100% received inpatient treatment. From the group of workers of shipbuilding and ship-repair enterprises that have received a recommendation to undergo rehabilitation, 97% have been rehabilitated. From the group of workers of shipbuilding and ship-repair enterprises that have received a recommendation as a result of periodic medical examination to obtain a Spa treatment 70% passed Spa treatment, and 30% did not pass it.

From the group of workers of shipbuilding and ship-repair enterprises that have received a recommendation as a result of periodic medical examination to prophylactic treatment in the prevention centre, 100% received this treatment. The result of the passage of periodic medical examinations and recommendations according to the conclusions of the examination were evaluated the outcomes of therapeutic and preventive measures among workers of the shipbuilding and ship-repair enterprises. Thus, among the treated, 58% of workers had no change in health status, 39% reported improvement, 2% — recovery and 1% — deterioration. According to the results of periodic medical examinations, 61% of workers were in the first health group; 31.8% — in the third; 3.5% in the fourth and 2.8% the second.

Thus, the results of the study indicated a high level of medical-social activity of workers of the shipyard and identified reserves for its further growth.

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SEVERITY OF DEPRESSIVE DISORDERS AND THEIR RELATIONSHIP WITH CEREBRAL, VEGETATIVE DISORDERS AND QUALITY OF LIFE IN PATIENTS WITH ARTERIAL HYPERTENSION

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ABSTRACT — 150 patients with arterial hypertension, who were registered at the dispensary of a general practitioner, were assessed for the severity of depressive disorders, the severity of cerebral, vegetative disorders, and the quality of life. It turned out that in patients with hypertension, depressive disorders are combined with cerebral and autonomic disorders and a decrease in the quality of life. All these factors must be taken into account by the primary care physician in the course of dispensary observation and the conduct of therapeutic and prophylactic measures.

KEYWORDS — Arterial hypertension, cerebral disorders, psychoemotional disorders, quality of life.

S.O. Medvedeva

S.V. Kolbasnikov

INTRODUCTION

Epidemiological studies of recent decades indicate a widespread prevalence of emotional disorders among patients with cardiovascular disease [1].

Depressive disorders are considered as an independent risk factor for coronary heart disease and arterial hypertension [2]. However, the functional relationships of depressive disorders and vegetative changes, as well as the quality of life in patients of arterial hypertension with cerebral disorders, have been studied insufficiently. In this work, an attempt has been made to analyze the severity of depressive disorders and their relationship with cerebral, vegetative disorders and quality of life in patients with arterial hypertension.

MATERIALS AND METHODS

150 patients (men — 50, women — 100, age 54.7±0.9 years) with Arterial Hypertension stage II who were on dispensary supervision with a general practitioner and received combined antihypertensive therapy with the achieved normal arterial blood pressure. Depending on the severity of depressive disorders on the scale of HADS, the patients were divided into 3 groups: the first group consisted of 113 patients with no depressive disorders (age 52.8±1.5 years), second — 27 patients (age 57.1±1.5 years) with subclinical depression, the third — 10 patients (age — 60,6±1,5 years) with clinical signs of depression.

All patients underwent general clinical examination. The neurological status was assessed, and the testing was carried out using the questionnaire of the HADS scale [3]. The HADS anxiety and depression scale includes 7 questions on anxiety and 7 questions on depression. Each answer corresponds to a certain number of points. The score was based on the result: 0–7 points — absence of authentically expressed symptoms of depression, 8–10 points — subclinical depression, 11 points and higher — clinically severe depression. To assess the quality of life, the SF-36 questionnaire was used, the items of which were grouped into eight scales : physical functioning (PF), role activity (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), emotional state (RE) and mental health (MH). The scores of each scale range between 0 and 100, where 100 represents total health.The scales are grouped into two indicators: the "physical component of health" (1 to 4 scales) and the "psychological component of health" (5 to 8 scales) [4]. Evaluation of the autonomic nervous system was carried out according to the Kerdo index and a questionnaire to identify vegetative changes (Wayne AM, 1998) [5]. So, if the Kerdo index is zero, then it

characterizes the vegetative equilibrium. The Kerdo index is less than zero indicating the predominance of parasympathetic influences (vagotonia), and with a significant deviation - hypervagotony. The Kerdo index is greater than zero, indicating a predominance of sympathetic influences (sympathicotony), with a significant positive value — hypersympathicotony. According to the questionnaire of A.M. Wayne, with a score above 15, was diagnosed with autonomic dystonia. The collected data were accumulated in the Excel 2003 table and processed using the statistical functions of this application. The results of measuring the values of individual variables are presented in the form of an average of the arithmetic and standard deviations (M±s); the confidence in the difference in mean values was estimated using the nonparametric Kruskal-Wallis criterion. To determine the dependencies between the parameters studied, a correlation analysis was performed using the Spearman coefficient of linear correlation [6, 7].

RESULTS

Among patients in Group 1 (men — 46, women — 67), blood pressure was 134.6±16.9/81.8±11.8 mm Hg. The level of depression on the HADS scale was 3.5±2.1 points. There were no cerebral disorders in 19 (16.8%) patients, initial manifestations of cerebral blood flow insufficiency (CBFI) were recorded in 27 (23.9%), Discirculatory Encephalopathy (DE) of stage I and stage II in 67 (59.3%). In assessing the clinical signs of cerebral disorders, dizziness was detected in 40 (35.4%), headache in 72 (63.7%), noise and ringing in the ears — in 38 (33.6%), decreased memory and attention — in 72 (63.7%), sleep disturbance — in 50 (44.2%), fatigue — in 54 (47.8%) patients. At a neurological examination, 78 (69.0%) patients had irregularities in carrying out coordination tests (Romberg, palcoccus). In the evaluation of autonomic disorders, cardiovascular syndrome was detected in 44 (38,9%), respiratory distress syndrome in 39 (34,5%), abdominal syndrome in 51 (45,1%), sweating dysfunction in 67 (59,2%), thermoregulatory in 54 (47,8%), asthenic — in 39 (34,5%). The Kerdo index was minus 13.7±35.4 points. On the Wein scale, there were signs of vegetative dystonia (23.6±14.5 points) in 70 (61.9%) of the examined. In assessing the quality of life, the physical functioning (PF) was 81.0±18.9, the role function (RP) was 69.5±36.4 points, pain (BP) — 22.9±23.2 points, overall health (GH) — 58.7±16.7 points, viability (VT) — 62.0±19.1 points, social functioning (SF) — 68.6±20.1 points, emotional functioning (RE) — 72.1±35.8 points, psychological health (MH) — 68.9±16.7 points, physical component of health (PH) — 50.0±6.2 points, mental component of health (MH) — 46.7±9.0 points.

When carrying out the correlation analysis, there was a statistically significant inverse correlation of very weak force between the vegetative index according to the Wein's questionnaire and MH r = –0.27 (p <0.01) and RE r = –0.3 (p <0.05), the inverse of the weak force between the value of the Wein's questionnaire RP = –0.37 (p <0.01), the mean force line between the value of the Wayne questionnaire is BP r= 0.52 (p<0.01).

Thus, in patients with AH without clinical symptoms of depression, cerebral disorders were registered in 59.3%, which were combined with a vegetative regulation disorder and a decline in the quality of life, mainly due to overall health and vitality (VT).

In patients of the 2nd group (men — 3, women — 24), the blood pressure level was 137.4±20.1/84.4±12.8 mm Hg. The level of depression on the HADS scale was 9.0±0.9 points. There were no cerebral disorders in 2 (7.4%) patients, cerebral blood flow insufficiency were registered in 2 (7.4%), DE of stages I and II — in 23 (85.2%). Compared with group 1, there was an increase in the frequency of cerebral complaints. Thus, dizziness was detected in 16 (59.3%), noise and ringing in the ears — in 20 (74.1%), decreased memory and attention — in 15 (55.6%), sleep disturbance — in 1 (3,7%), increased fatigue — in 19 (70.4%); headache — in 15 (55.6%) patients. Violations in the implementation of coordination samples (Romberg, palcoccus) were present in 25 (92.6%) patients. The vegetative disorders of this group were more common than among the patients of group 1, so cardiovascular syndrome was detected in 16 (59,2%), respiratory syndrome disorders in 14 (51,8%), abdominal — in 17 (62,9%), sweating dysfunction in 18 (66,7%), thermoregulatory — in 17 (62,9%), asthenic in 21 (77,8%). The Kerdo index was minus 20.9±22.3 points. According to the questionnaire of A.M. Wein 27 (100%) examined showed signs of vegetative dystonia (34.0±14.1 points, p=0.0111). In assessing the quality of life, the physical functioning (PF) was 64.4±22.9 points (1, 2 times less compared to group 1, p=0.0015), role function (RP), respectively — 24.0±29.6 points (2.9 times less than in group 1, p <0.0001) , pain (BP) — 40.0±21.0 points (1.7 times greater than group 1, p=0.006), overall health (GH) — 46.3±12.8 points (1.3 times less than in 1 group, p = 0.0023), viability (VT) — 44.6±15.3 points (1.4 times less than in compared with 1 group, p = 0.0003), social functioning (SF) — 52.9±21.6 points (1.3 times less than in group 1, p = 0.0054), emotional functioning (RE) — 30.8±39.9 points (2.3 times less than in the 1st group, p <0.0001), psychological health (MH) — 53.8±15.4 points (1.3 times less than in group 1, p=0.0003), physical health component

(PH) — 45.9±5.4 points (1.1 times less than group 1, p=0.0093), mental component of health (MH) — 37.5±8.9 points (1.2 times less than in group 1, p<0.0001).

When carrying out the correlation analysis, there was a statistically significant inverse correlation of the mean force between the vegetative index according to the Wein questionnaire and MH = –0.62 (p<0.01).

Thus, in patients of hypertension with pronounced subclinical depression, with an increase in cerebral disorders and non-vegetative disorders, a significant decrease in the quality of life was mainly due to emotional functioning (RE) and role functioning (RP).

In patients of the 3rd group (men — 1, women — 9), the blood pressure level was 138.8±11.8/81.0±9.9 mm Hg. The level of depression on the HADS scale was 12.5±1.3 points. Cerebral blood flow insufficiency was recorded in 1 (10.0%), DE of the first and second stages in 9 (90.0%). In assessing the clinical signs of cerebral disorders, dizziness was recorded in 9 (90.0%, p = 0.0007, test χ^2), noise and ringing in the ears — in 9 (90.0%, p <0.0001, test χ^2) of patients, headache — in 10 (100%, p = 0.0390, test χ^2), sleep disturbance 9 (90,0%, p = 0,0165, test χ^2), increased fatigue — in 7 (70,0%, p=0,0590, test χ^2), decreased memory and attention — in 10 (100%; p = 0.0186, test χ^2) of patients. Deviations in the performance of coordination samples (Romberg, palcoccus) were recorded in 10 (100%, p = 0.0067, test χ^2) patients. Among the vegetative disorders, cardiovascular syndrome was detected in 7 (70,0%, p = 0.0257, χ^2 test), respiratory distress syndrome - in 10 (100%, p = 0.0006, test χ^2), abdominal — in 7 (70, 0%), sweating disorders — in 8 (80,0%), thermoregulation — in 8 (80,0%, p = 0,0431, test χ^2), asthenic — in 10 (100%, p <0,0001 , test χ^2). The Kerdo index was minus 59.1±13.7 points. On the Wein scale there were signs of vegetative dystonia (49.0±10.8 points, p <0.0001 in relation to patients of group 1, p=0.0111 in relation to patients of group 2) in 10 (100%, p = 0.010, test χ^2). In the assessment of the quality of life, physical functioning (PF) was 52.0±22.5 points (1.5 times less than in group 1, p = 0.0005), role function (RP), respectively, 15.0±33.7 points (in 4.6 times less than in group 1, p = 0.0010), pain (BP) 54.0±15.8 points (2.3 times greater than group 1, p = 0.0007), overall health (GH) — 44.0±9.9 points (1.3 times less, n compared with 1 group, p = 0.0159), viability (VT) — 39.0±13.9 points (1.6 times less than in group 1, p = 0.0024), social functioning (SF) — 50.0±18.6 points (1.4 times less than in group 1, p = 0.0266), emotional functioning (RE) - 30.0±33.1 points (in 2.4 (p = 0,0137), psychological health (MH) — 48.0±18.6 points (1.4 times less than in the 1st group, p = 0.0050) , the physical component of health (PH) — 42.0±6.3 points (1.2 times less than in group 1; p = 0.0020), the mental health component (MH) is 37.0±8.2 points (1.3 times less than in group 1, p <0.0096).

When carrying out the correlation analysis, there was a statistically significant inverse correlation of high strength between the vegetative index according to the questionnaire of A.M. Wayne and PF r = –0.76 (p <0.01), RP r = –0.87 (p <0.01), the high-force line between the vegetative index according to the A.M. Wayne questionnaire and BP r = 0,9 (p<0.01).

Thus, in patients with AH, clinically pronounced depression is combined with severe cerebral, autonomic disorders and a significant decrease in the quality of life.

CONCLUSIONS

In patients with hypertension, despite the achieved target figures for blood pressure, with increasing depressive disorders, vegetative disorders are characterized by a predominance of parasympathetic tone, marked cerebral symptoms and a significant decrease in the quality of life, which must be taken into account when constructing individual rehabilitation programs.

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COMPLEX ASSESSMENT OF THE HEALTH STATUS OF CHERNOBYL NPP LIQUIDATORS BASED ON THE METHODS OF RADIOLOGICAL DIAGNOSTICS

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As is known, Chernobyl NPP liquidators were exposed to a complex of unfavorable factors, such as low doses of ionizing radiation (external and internal radiation), psycho-emotional stress, physical and psychic tension, exposure to certain chemical compounds, changes in the regimen of work, rest and nutrition. Some of these factors (incorporation of radionuclides, psycho-emotional stress, harmful working conditions), as well as smoking, alcohol use, have their influence on the liquidators even after the completion of the works in Chernobyl NPP. The majority of the aforementioned influences can be attributed to the risk factors for the emergence and maintenance of pathological processes in the digestive organs [1-9].

38 Chernobyl NPP liquidators were examined, whose age ranged from 52 to 67. Methods of the examination: scintigraphy of skeletal system, thyroid gland, liver and kidneys.

All the studies were conducted according to clinical indications, taking into account the complaints of the patients, blood and urine tests, as well as other methods of radiological diagnostics; all patients underwent ultrasound scan, as a screening test.

Radioisotope investigations were conducted based on program packages of IAEA, according to international protocols and adopted algorithms of choice of the "first line" method. Radioactive Tc-99m was used, with respective kits (Pyrfotech, DTPA, kolloid). In case of thyroid gland examination, radioactive Tc-99m was used without a kit. All studies were conducted on a "SPECT"– camera. The main goal is to early reveal the impaired function and the development of these impairments in dynamics, which creates conditions and justification for a choice of medical treatment in each specific case.

It is necessary to mention that, to date, there is no alternative for the radioisotope methods used in this work; the absence of alternatives is seen in the following stages: in the examination of the kidneys – the filtration phase, in the examination of the liver – the condition of the reticuloendothelial system ("Kupffer cells"), in the examination of the thyroid gland – the identification of "hot" and "cold" foci and/or developmental anomalies, in the examination of the skeletal system – the visualization of the bone marrow and the differentiation of bone pathology.

Based on the obtained data, it can be stated that the degree of the functional disturbance, revealed by the methods of radioisotope diagnostics, does not always correspond to the data of other clinico-

radiological changes, when assessing the degree of the functional disturbances of an organ or a system. This well-known fact is explained by methodological features of other methods (ultrasound, biochemical and other blood and urine tests); anatomical changes and shifts in biochemical and general analyses appear much later than the functional disturbances (6 months and more).

Methodologically, radioisotope investigations have a strictly targeted direction, as was mentioned above.

Reasoning from all the aforementioned, during the examination of Chernobyl NPP liquidators, the function of liver and spleen was measured (in case of viral and non-viral hepatitis), in the examination of the kidneys — the linear rate of secretion and the volume rate of filtration, the focality of the thyroid gland. With a complex combination of all radiation and non-radiation methods, the following patterns were revealed:

1. In case of disorders of the thyroid function, in 56–60% of patients renal pathology (predominantly — pyelites of different etiology) was revealed.
2. Enlargement and/or disturbance of the liver function had a certain directionality in relation to the involved segments and enlargement of the spleen with its activity. The latter depended on the etiopathogenesis of the disturbance of the reticuloendothelial system's function (viral or non-viral involvement, as well as hepatitis "B" and "C").
3. All examined liquidators had various pathologies of the musculoskeletal system, most often accompanied by thyroid pathology, by type of diffuse disorders of non-oncological genesis.
4. groups were analyzed:

Group I — hepatitis without focal and fatty changes. Characteristic features: increased contrast of the "cardial" section and a change in the 6th segment to 20–22%, enlargement of the 6th segment, without changes in the spleen.

Group II — hepatitis in combination with fibrosis and focal changes.

Characteristic features: enlargement of the right lobe of the liver, predominantly 6th, 7th and 8th segments. Minor enlargement of the left lobe of the liver, enlargement of the spleen (20–21%) and an increase in the contrast (20–25%); the ratio of the contrast of the liver and the spleen is 75/25%.

Group III — severe hepatitis with fibrotic changes.

Characteristic features: enalrgement of the 2 lobes of the liver (all segments, 60–65% decrease in the contrast, foci without a clear outline, enlarged (up to 50–55%) spleen, high contrast (60–65%)). The ratio of the contrast of the liver and the spleen is 40/60%.

Group IV — hepatic cirrhosis.

Characteristic features: small liver, minimal contrast — 30–35%. The spleen is increased in size, the activity is 80–81%. Besides the liver and the spleen, presence of radiopharmaceuticals is observed also in the vertebrae, bone marrow segments and is an absolute sign of cirrhotic changes of the liver, which is necessarily combined with a reduction in the liver size, with an increase in the spleen size and presence of a large number of fibrotic foci.

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A QUALITATIVE INQUIRY IN THE SOCIAL CONSTRUCTION OF CHRONIC ILLNESS. CASE STUDY ON DIABETES MELLITUS. DOCTORS' PERSPECTIVES

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ABSTRACT — The present paper is based on a secondary data analysis, and aims to identify the diabetologists' perspective on the relationship between the doctor and the patient in the (co)construction of the process of self-care of the chronic diabetic patient of type 1, in the context of the respect for the patient's autonomy, and of the (co)responsibility for the patient's state of health. The analysis starts from the data obtained within the project of exploratory research *Lifestyle and behaviour in health, for the chronic disease patient*, conducted by an interdisciplinary team in the program "Postdoctoral studies in the field of ethics of health-related policies", between 2012–2013, in a city in N.-E. area of Romania.
The data analysis method used is a qualitative one – the data-based constructionist theory – Grounded Theory, aiming at generating a model after following all the stages of inductive coding, specific for Grounded Theory, which may be the hypothesis for future research, that will validate the model.
The analysis shows the fact that the doctor-patient relationship is an important instance in the process of social construction of the idea of chronic disease, but also of the patient's autonomy in the process of self-care, while the responsibility for self-care is the result of a process of therapeutic education, on whose efficiency depends the state of well-being and the quality of life of the chronic patient.

KEYWORDS — ethical values; medical ethics; qualitative inquiry; social construction; chronic illness; Case study; diabetes mellitus; trust; medical sociology; public health

INTRODUCTION

The current article aims to answer the question "What is the role of the diabetologist doctor in the social construction of the autonomy and responsibility for the insulin-dependent, type 1 diabetic patient's health condition?". The discursive perspective analysed is that of diabetologist doctors. This study is based on

a secondary data analysis, obtained during the exploratory research "Lifestyle and behaviour in health, for the chronic disease patient", conducted by an interdisciplinary team in the program "Postdoctoral studies in the field of ethics of health-related policies".

The purpose of this research was to identify the mechanisms through which the responsibility for own health-condition and the autonomy [30] of the chronic patient are developed, in the process of care, at the interface with his family and the medical-social and religious institutions involved. The interest of the researchers was focused on the context specific for the diabetic disease, as a particular case of chronic disease, without limiting the research exclusively to this context.

SHORT CONTEXT OF HEALTH BEHAVIOUR OF PATIENTS WITH CHRONIC ILLNESSES

The health-related behaviour is a major issue of public health programs [1]; the health-related behaviour being connected to the decision of the autonomous individuals, who chose to responsibly act or not [2] in order to maintain their health state (health behaviour) [3];[28]; [1] in general, or as a response to a disease, especially a chronic one, which requires a particular lifestyle [3]. The benefits of an approach towards the chronic disease, based on respect for the patient's autonomy [4]; [5]; [6]; [7]; [9]; [10]; [12]; [13: 90-113]; [14: 17]; [15]; [16], the health-related behaviours of the individuals and their capacity of moral agent would, on one hand, be a part of their health-state improvement [17]; [18], and their quality of life, and on the other hand, of reducing costs [19]; [20] and lowering the pressure on the health system. The choice of type 1 insulin dependent diabetes in the context of studying the chronic patients' autonomy, and their responsibility for the their health-state is based on its incidence at global level and in Romania, the high costs for patients' care, but also the centrality of self-care in the management of the disease [21]. Kathryn Dean [22] defines self-care as being the fundamental level of health care in all societies [23]; [24]. The social construction of chronic disease is the analysis of the discursive particularities related to the health-state of different communicative agents involved in the process of care: patients, doctors, specialists, general medicine doctors, care institutions, families, etc [29]. One of the main axes of the social construction [25] of the idea of chronic disease is the doctor-patient relationship, the discourse of the doctors being the instance of social construction of the meaning offered to the term chronic disease. The phenomenon of medical life socialization drifts from the patients' internalization of the chronic health condition, taken from the discourse of caregivers, of which the most important role is that of doctors.

DATA COLLECTION

The data were collected in a city in the N.-E. area of Romania, between 2012–2013, through 5 focus group interviews with diabetologist doctors, general medicine doctors, insulin-dependent patients with type 1 diabetes and other persons involved in the process of care, and of 3 semi-structured individual interviews with patients. The sampling was achieved through the snow-ball method, the saturation of the sample being verified through the saturation grid. The selection criterion for the research sample was the involvement in the care/self-care of type 1 diabetes patient. The research was not considered gender-sensitive, which is why the interviewees' gender was not taken into account. For this article, we only analysed the diabetologist doctors' answers, the rest of the collected data being the object of other papers [26]; [27]; [32].

DATA ANALYSIS

The data analysis was conducted starting from the Grounded Theory methodology. This methodology aims to identify certain discursive categories, identified during the reading of the individual and group interviews, and applying certain three-step data coding processes: open coding — a first level of coding through which we identify keywords that give meaning according to the interviewees of the studied phenomenon; axial coding — aims to group the keywords in semantic categories; analytical coding — which aims at the relationships between the identified semantic categories; generating the model with exploratory nature — the conclusions of the model generated after following all the coding steps, representing hypotheses for future research, which will validate the model.

ABBREVIATIONS

[FG01.D2012] – focus group with Diabetologists

MAIN RESULTS

After conducting the inductive-type analysis, we have produced a series of semantic categories, relative to the perspective of the diabetologist doctors on the doctor-patient relationship in the context of supporting the construction of the type 1 diabetic chronic patient's self-care, whose process of construction we will not present in this article, due to limited editorial space. We will present the main semantic categories identified following the secondary data analysis obtained through focus group interview with diabetologist doctors [FG01.D2012].

The main inductive identified semantic categories were:

Normality and exceptional in the doctor's life. The clutter in the clinic was considered a leitmotif of the professional life of doctors — diabetologist specialists. Every day there is an exceptional situation, an emergency, a special case. *Each day there is an exceptional situation, or each person can be regarded as so.* With all these, the interviewed doctors couldn't describe the exceptional situations they have faced, precisely due to the exceptionality and uniqueness of each case. The chronic condition involves long-term care, and the patient's empowerment for self-care being *the diabetes, unfortunately, lasts — so to speak —, every day, for a lifetime*. The specific of chronic patient's medical care doesn't reside in the spectacular and imminent, like in the case of surgery, but in the tact and the art of convincing the patient to care for himself in order to lead an almost normal life, with the life expectancy and quality similar to the same-aged non-diabetic person. The exceptionality in the doctor's life is given by the choices he makes, both in the everyday life, and in specially chosen moment, such as changing the type of practice from the public system to the private on, for example. A feature of this category would be the everyday exceptional: *From a professional point of view, it wasn't special that we spent 5 years in the country-side, nor that we had a birth-house there and I was trembling... like so... when two twins were born*. The professional status of the doctor [8] is perceived as being exceptional, one of the diabetologists interviewed showing that in the decision of medical career choice, the *opinion of the group of equals* mattered, and who consider that *if you don't go to medicine, you are inferior*.

The experiences of the diabetologist doctor in the relationship with the chronically ill patient. The main element of the practice of diabetologists is to educate the patient for self-care. Their *participation* to self-care is essential. The therapeutic compliance, essential from the first phase of the disease, must be transformed in a therapeutic alliance, the doctor empowering the diabetic patient with the management of self-care. Another characteristic is the very high volume of patients, which leads to a certain level of automatism of the practice, considered to be beneficial by the interviewees. We make a clear distinction between the medical practice from the clinic of diabetology, where there is the necessary equipment and relatively enough time for the investigations conducted on the patient, and the medical practice in the polyclinic where it acts under the pressure of small time available at each meeting with the patient and the need for professional craftsmanship which involves the capacity to make a fast diagnosis and propose the necessary therapy (in our opinion, in the lack of certain investigation instruments, although the medical practice is less fit here).

Medicine as a vocation, not just a profession. The socialization of the doctor in the role of specialist is done both in the formal medical education system, and in the continuous one, as well as through the communication with other specialists in the field. When compared with the experience of practicing medicine in the country of origin, with that in other countries, we emphasize on the respect that the doctor, even debutant, is enjoying in the medical team, along with the technical-material equipment that the clinics have at their disposal. The experience of the international clinic is appreciated and recommended especially by debutant doctors. The acknowledged vocation of the doctor is helping people in distress. The choice of medical career is generally based on vocation, sometimes following the already existing tradition in the family, other time due to the *chance by accident*. Regarding the choice of the diabetologist specialty, the motivations discovered in the discourse of the interviewees targets the passion for nutrition, but also the complexity of the diabetology specialty among the clinical specialties. In all situations, however, the vocation is updated through practice and learning. The personal experience as diabetic chronic patient is also mentioned as a source of motivation for choosing the diabetologist career. The model of the experienced doctors is also very important, especially of professors and clinical chiefs. The satisfaction of the doctor is maximal when he managed to save a life through his work and due to his own experience: *you experience such a great joy when you saved that person's life (...). Nothing can compare with that*. In the care for chronic patients, the professional satisfaction of the doctor is connected to the *relationship with the patient*, the *therapeutic alliance* that was created, and the increase in the quality of life due to the chronic patient's involvement in self-care. Changing the beliefs and attitudes of the patient on the chronic (diabetic) disease is a source of professional satisfaction [11]. It is mentioned the special responsibility of the specialist doctor in the patients' care, especially when conducting practice in the clinic, where the doctor doesn't have the possibility of daily control of the patient's situation.

Portrait of the good professional. Patience in the relationship with the diabetic patient is one of the qualities of the good professional in diabetology. Due to the responsibility of the medical act, the doctor has the tendency to approach his relationship with

the patients in a paternalist way, trying to control all the therapeutic moments, even if this is impossible to achieve totally.

Limits of the system of care for the diabetic chronic patient. The main limitations of the system of care of the diabetic patient noticed by the doctors participating in the focus group, are: insufficient time with the patient, due to the small number of specialists compared to the number of patients, the lack of financial resources, both the patients' resources necessary for adopting the necessary lifestyle for self-care, but also the lack of resources in the medical system. The doctors' overload with cases may lead to a decrease in the quality of care. The lack of resources in the system is signalled despite the existence and functioning of a *National program of diabetes*, which provides for ensuring free insulin for all insulin-dependent patients, ensuring the necessary glucometers for self-care for this category of patients. Another limitation is strictly correlated with the financing of care and the doctor-patient relationship in case of diabetologist doctors. One doctor shows that he finds it impossible to go on strike and not sign the contract with the Health Insurance Company, since the lack of such a contract directly influences the patients whose insulin cannot be provided for free.

Particularities of the diabetic chronic disease. The particularities of the diabetic chronic disease requires an orderly lifestyle. *The patients must learn to live with the disease and not be dependent on the environment*. The intervention in the type 1 insulin-dependent diabetes patients are provided with, besides free insulin shots, also glucose measuring devices, glucometers and necessary tests. There are signalled situations in which the patients never use, or use incorrectly the measuring devices, which is considered a failure of the therapeutic education and an impossibility to develop certain options of management of self-care. The correct use and adequate self-care makes the diabetic patient be autonomous: express his moral agency, make decisions regarding his own health condition, and it also makes him responsible.

The dramatism of the chronic disease. For the patient suffering from a chronic disease, his condition may or may not be fully dramatic, based on the emotional burden projected on the disease, and the way in which he discursively develops his vision on his own health condition. At the time of the diagnosis, some patients go through real emotional shocks, being also noticed situations in which the patients feel stigmatized and excluded from the society. The lifestyle is the key for an almost normal life of the patients. Such examples of situations are also present in the specialists' discourse, when a good self-care management has led to a quality of life close to that of a normal person.

The medicalization of the patient's social life. The diabetic patient has a lifestyle that is adequate to the need for self-care, represented by the permanent measuring of glucose with the glucometer, and adapting the dosage of self-administered insulin. Also, the medical diet must also be strict in order to maintain the values of glucose within normal parameters. These conditioning lead to an increase in the medicalized dimension of the patient's social life, who tends to extend his self-care management from the elements that are strictly necessary for maintaining his health condition, to the most aspects of his social life. The patient should be involved — either while he is hospitalized after the diagnosis [31], or in the outpatient clinic — in courses of nutrition, glucose control, lifestyle, possible complications and avoiding them. These courses are available in certain university clinics in the country, but not in the region we have studied, the training activity being conducted by the medical nurses or interns.

It is also mentioned the need for a psychologist to participate in the therapeutic education of the diabetic person, at least in the first stages, when the patient is getting acquainted with the disease. A particularity of the life of the diabetic patient is represented by its spiritual dimension. If in the state of shock, many patients consider the illness as a result of divine punishment, in the stage of self-care, the spiritual practice can contribute to the tonus and trust of the patient, to the positive attitude and motivation for self-care. The role of support of the family is considered overwhelming for the efficiency of self-care of the diabetic patient. The local cultural model may lead, in certain situations, to the marginalization of the diabetic patient, who is considered guilty for his disease, being a risk for his family and the social environment, despite the fact that under the condition of an adequate treatment, the patient's life can be absolutely normal, including from the family and social-professional point of view.

THE MODEL OF THE SOCIAL CONSTRUCTION OF THE DIABETIC CHRONIC DISEASE FROM THE PERSPECTIVE OF THE DIABETOLOGIST DOCTORS' PERSPECTIVE

Analysing the results and their structuring into discursive categories, we could deduce, through successive induction processes, a series of statements which may constitute key elements of the descriptive model

of the social construction of diabetic chronic disease from the perspective of the diabetologist specialists:

- self-care of the chronic patient is of overwhelming importance in the therapeutic process, meant to maintain the patient's quality of life as closer to that of a healthy person;
- in the success of self-care, the doctor-patient therapeutic alliance is extremely important, the doctor being requested to prove a series of special communicative competences;
- the life of the diabetic patient suffers from an advanced process of medicalization, the medical model of the self-care management impinging on other aspects of the patient's life, including the family, professional or social one;
- the practice of medicine is, beyond the side of professions, an activity which requires a special vocation;
- the process of self-care is the framework in which the social construction of the autonomy and the diabetic patient's responsibility, both from the point of view of the social functionality, as well as of the moral (ethical) agency.

DISCUSSIONS

The requests concerning the ethics of research on human subjects were fulfilled, the research receiving the approval of the Commissions of Ethics in Research of the Gr. T. Popa University of Medicine and Pharmacy from Iasi, Romania. Being an exploratory research, based on qualitative data analysis, we don't talk about the data validity, but of the adequacy of the interpretative model created, as well as the potential of generalization widely. We consider that although the model is not a local one, through the particularities of the interviewed sample, there is a potential of generalization of the model, especially regarding the importance of self-care management, of the doctor-patient relationship in the construction of the therapeutic alliance. In order to increase the credibility of the analysis, the data interpretation involved the triangulation of the researchers involved in the process of coding and re-coding.

CONCLUSIONS

The doctor-patient relationship is an important instance in the process of social construction of the idea of chronic disease, but also the patient's autonomy in the process of self-care. The responsibility for self-care is the result of a process of therapeutic education, on whose efficiency, the well-being and quality of life of the diabetic patient depends on.

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THE PROBLEM OF SOCIAL ADAPTATION OF STUDENTS TO THE CONDITIONS OF TRAINING IN THE MEDICAL UNIVERSITY

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ABSTRACT — In the review article, the main approaches to the study of social adaptation of students to the conditions of study at a medical university are considered. Problems that hinder the successful adaptation of students were highlighted.

KEYWORDS — social adaptation, individual behavior, mental processes, sociocultural environment.

The question of social adaptation of students to training conditions in medical schools represents one of the major tasks which are investigated in sociology and psychology [1] now. There passes a large number of time before students adapt to new conditions of training. Besides, specifics of a technique and the organization of educational process in medical school, a big flow of information, lack of skill of independent work cause provokes emotional burning out that, most often, leads to disappointment in the choice of future profession [2].

According to many domestic researchers, social adaptation of the individual to educational activity also includes both biological, and social components. In opinion, V.V. Lagerev who has defined adaptation of students to training as "intensive and dynamic, multilateral and complex process of activity during which the person on the basis of the corresponding adaptation reactions develops steady skills of satisfaction of those requirements which are imposed to him during training and education in HIGHER EDUCATION INSTITUTIONS [5].

At the same time, according to some authors, in the beginning (on the first and second courses) there is an adaptation to the social environment of HIGHER EDUCATION INSTITUTION, and on older years to the chosen profession and specialty [3].

One of the major tasks which face medical schools in the course of training of specialists is creation of special psychological climate which has to minimize terms of social, psychological and cultural adaptation of students [3].

The idea of social and mental adaptation isn't new. She is investigated in works of prominent sociologists, psychoanalysts, interaktsionist and a number of the psychologists belonging to other directions of psychology [5].

In foreign science considerable distribution was gained by neobehaviouristic definition of adaptation which is used, for example, in a research of G. Ayzenk and his followers [1] who define adaptation doubly:

a) as a state in which need of the individual, on the one hand, and requirements of the environment — with another, are completely satisfied;

b) process by means of which this state (a condition of harmony) is reached. Interaktsionista, for example L. Filips, consider that all kinds of adaptation are caused by both intra mental, and environmental factors.

According to L. Phillips's opinion, the adaptability is expressed by two types of responses to influence of the environment:

a) the response to those social expectations which the personality meets (the researcher considers such adaptability expression of conformality);

b) the answer in specific sense at which adaptation doesn't come down just to adoption of social norms and happens flexibly and effectively at a meeting with new events.

At the same time events are given the direction, desirable for the personality. This second, specific understanding of adaptation contains the idea of activity. In this case the personality uses problem situations for realization of the aspirations, the purposes, claims [1].

Formation of positive psychological climate in group actively influences development of educational, scientific and creative skills of students [2]. Getting to the new social environment, many students can uncertainly become isolated, feel. On this background there is a number of problems which in essential degree influence results of training.

According to the sociological research Londadzhim Thierry which has defined that social adaptation represents a special form of social interactions as which parties the subject and object (environment) of adaptation act. Acquisition by subjects of new social experience through development of unusual, unusual situations which accompany different types of activity is result of this interaction. Social adaptation can provide *self-adjustment* of the personality on the due level of interaction with specific individuals, social groups, society in general, follows from individual inquiries and needs of the personality [4].

According to Mazitova, a factor which complicates sotsiobytovy adaptation of students is also the problem of a material and financial condition of foreign pupils. As their most part studies in the direction, the main source of existence for them is the grant which is paid by the government of their country (62,2% of respondents). Many students lack funds for satisfaction of the needs and requirements — 28,9% of respondents have said to us that they aren't satisfied with the financial position [5].

In a sociological research of Sukhova, it was revealed that for students representatives of non-European cultures the level of complexity of adaptation, in general, is higher, than for European students. The research has shown a significant gap between these groups of students both in the sphere of educational activity, and in spheres communicative and the general social (daily) the practician of interaction. It is connected with various level of flexibility, features of culture (mentality), a shortcoming habitual (traditional) the practician and the examples of behavior acquired by the student in the homeland. So, representatives of neighboring countries and Russia are distinguished by lack of high level of mobility and flexibility in familiarizing with the German sociocultural environment. The factor of group identification which interferes with their full integration into the accepting society is characteristic of students of non-European cultures, along with a notable language barrier. The special complexity of language adaptation is noted by the foreign students studying in Russia, pointing to unavailability of local community to interact in language of the international communication — English [7].

Adaptation process can be considered at various levels of his course, i.e. at the levels of the interpersonal relations, individual behavior, basic mental functions, psychophysiological regulation, physiological mechanisms of ensuring activity, a functional reserve of an organism, health. As considers, F.B. Berezin, at the individual in this row plays an important role mental adaptation, substantially exerting impact on adaptation processes which are carried out at other levels [8].

Y.A. Aleksandrovsky has considered mental adaptation as result of activity of complete self-governed system, which is provided activity of the person at the level of *operational rest*, allows him not only most optimum to resist to various natural and social factors, but also actively and to affect purposefully them".

Further studying of social adaptation of students of medical schools can be interesting not only to teachers of higher education institution, but also to teachers of school, and can be continued for the purpose of practical use in process of management of quality of education.

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ANALYSIS OF MEDICO-ECONOMIC EFFICIENCY OF DENTAL CARE PROVIDED BY HEALTH INSUARANCE PROGRAM

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The aim

of this work was to calculate health and economic efficiency of dental care provided by Health Insuarance Program to adults with rehabilitation of the oral cavity.

Methods

In this study we used the method of clinico-economic analysis.

THE RESULTS OF THE STUDY

indicate that in the structure of morbidity by the appealability of the adult population in the dental clinic, the largest share is caries and its complications — 96.3%, diseases of periodontal tissues correspond to 3.6% and diseases of the oral mucosa — 0.3%. The indicator of the population's appeal for dental care is 506.4 per 1000. 94.8% of the population need sanitation in the oral cavity, 31.6% of the adult population are being sanitized from the number of people in need. The indices show that 2082.68 teeth were cured and 515.29 teeth were removed in 1000 people (table 1, table 2).

During the sanation 1.2 teeth, afflicted with caries, was registered at each patient. Complications of caries among the adult population are 0.85 teeth (pulpitis, periodontitis, to be treated) and 0.52 teeth to be removed. In one visit, dentists, therapists, surgeons, physiotherapists are 8.43 services. To sanitize the oral cavity of 1000 adults in case of tooth decay with caries and its complications took 2908.48 visits, 27424.45 services, 30244.89 standard conventional units (SCU) [1].

The greatest number of services, including visits, falls on one patient with periodontitis of teeth — 14.96, followed by services rendered to a patient with pulpitis of teeth — 7.03, then — with deep caries — 2.57, middle caries — 18.75, superficial — 1.00, the initial caries in the clinic is not diagnosed.

On average, complete treatment (removal) of one tooth had to 1.12 visits, 10.56 services and 11.64 SCU.

The greatest number of visits is required for the treatment (removal) of the tooth, damaged by periodontitis — 1.68, and in case of treatment, completed by the imposition of a seal, there are 2.40 visits, and ended by removal — 0.99. A significant difference is observed in the number of services, which, with conservative treatment of periodontitis, is 24.83±0.86, and when removed — 5.62±0.27, there is also a difference in the labor costs of dentists, which is equal to 29.63±0.82 SCU and 6.17±0.28 SCU (at removal).

To complete the sanation of the oral cavity of 1000 patients (when the tooth is damaged by caries and its complications) 2082.68 seals were applied, including surface caries — 294.16, medium — 451.20, deep — 452.82, pulpitis — 427.29, periodontitis — 457.21. [2]

The structure of the seals is dominated, made of a composite of Russian origin, which makes up slightly

Table 1. *The indicators illustrate the volume and types of dental care provided to the adult population in the defeat of teeth caries*

The indicators		Surface caries		Medium caries		Deep caries	
		services	SCU	services	SCU	services	SCU
1	Reception dentist, primary	157.66	158.1	219.15	222.41	171.04	171.58
2	Total visits	160.0	159.77	232.14	232.16	246.36	228.07
3	Total services	831.14	784.79	1643.36	1531.06	2320.69	2517.26
4	Total services, including visits	991.14	944.56	1875.50	1763.22	2567.05	2745.33
5	Total seals	294.16	-	451.20	-	452.82	-
6	Teeth removed	-	-	-	-	-	-
7	Services in 1 visit	5.20	-	7.08	-	9.32	-
8	Visits for treatment of 1 tooth (seals + delete)	0.54	-	0.51	-	0.54	-
9	For a complete treatment of 1 tooth (services, SCU)	3.37	3.21	4.16	3.91	5.67	6.06
10	SCU on 1 service	-	0.95	-	0.94	-	1.07

Table 2. *The indicators illustrate the volume and types of dental care provided to the adult population in the defeat of teeth caries complications (per 1000 sanitized)*

The indicators		Pulpitis		Periodontitis	
		services	SCU	services	SCU
1	Reception dentist, primary	219.32	219.32	445.06	445.06
2	Total visits	697.14	577.68	1572.84	1294.95
3	Total services	6329.04	7416.11	13391.74	15503.04
4	Total services, including visits	7026.18	7993.79	14964.58	16797.99
5	Total seals	427.29	-	457.21	-
6	Teeth removed	36.35	-	478.64	-
7	Services in 1 visit	9.08	-	8.51	-
8	Visits for treatment of 1 tooth (seals + delete)	1.50	-	1.68	-
9	For a complete treatment of 1 tooth (services, SCU)	15.14	17.23	15.99	17.95
10	SCU on 1 service	-	1.14	-	1.12

more than half of all the seals — 51.75%, mostly «Silicin» and «Silidont». Then follows the seals made of imported composite — 48.19%, mainly «Compolight» and «Herculite», cement seals of the import make only 0.06%.

Ratio of the number of teeth treated for uncomplicated caries to the number of teeth with complicated caries is 1.36:1.0 at sanitized patients. The average number of teeth treated in one visit in sanitized patients is 15.8%.

Evaluating the medical effectiveness of treatment provided with tooth decay caries, should be noted that preventive measures for the adult population are extremely rare. Complications of caries developing in 36.81±0.85% of the cases, 884.5 teeth affected by pulpitis and periodontitis (per 1000 sanitized) was removed 58.26% (515.29) of the tooth.

X-ray control revealed a low quality of root canal filling — only 18.3% of single-root teeth and 4.8% of multi-root teeth were satisfactorily obturated. The expert integrated assessment (out of five criteria), which characterizes the quality of 630 seals supplied in the dental clinic, indicates that, on average 31.11 ± 1.84% of the seals were performed with disorders, combining several defects (mobility, development of secondary caries , cleavage of the seals and others), 46.67% need to be replaced (Figure 1).

X-ray control revealed a low quality of root canal filling - only 18.3% of single-root teeth and 4.8% of multi-root teeth were satisfactorily obturated.

Supposed reasons for poor quality of endodontic treatment may be a low level of professional skill, financial support or non-compliance with technology. In most cases, it is necessary to note the absence in the

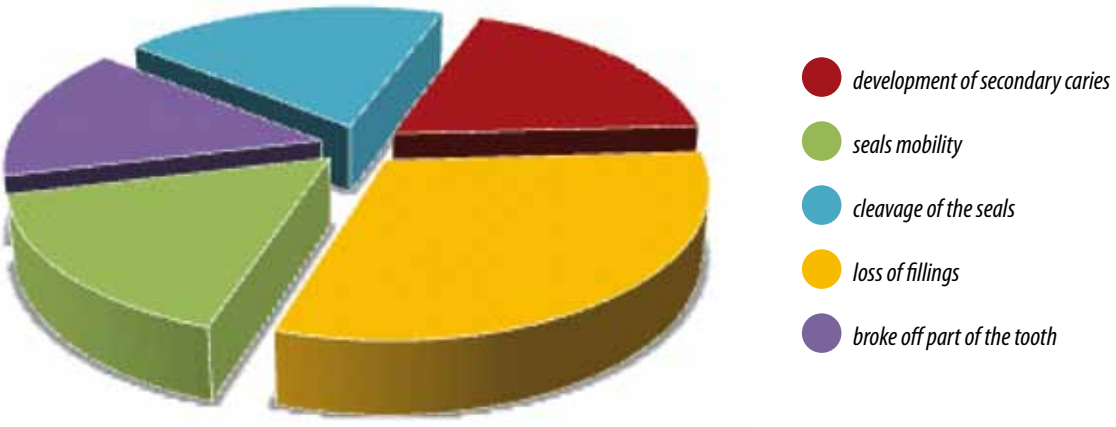

Fig. 1. *Disadvantages of the seals*

medical card of dental patient data description x-ray examination. This fact indicates not only to the absence of X-ray diagnostics, but also about the absence of X-ray-quality control of the performed endodontic treatment. [3]

On the basis of the study we would like to note, that when preparing plan for the development and performance of «Dental clinic №3», Astrakhan, it is important to consider the proposed indicators. These indicators reflect the types, the structure and volume of dental care provided during oral sanitation of the adult population, the algorithms for analyzing medical efficacy in the rehabilitation of the oral cavity. Also reflect the analysis of economic efficiency the renovation of the oral cavity of the adult population and carrying out individual primary prevention.

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METHODOLOGICAL APPROACHES TO THE DEVELOPMENT OF THE NURSE-LEADER'S WORKPLACE

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Currently, an effective solution to the problem of selection of nursing staff requires the develop-ment of scientifically based models of nursing jobs that provide selection, evaluation and place-ment of staff on a single methodological basis. An expert assessment of the nursing staff made it possible to form a workplace model of the nurse-leader.
The model of the nurse-leader's workplace, in our opinion, includes 14 elements that represent the qualitative and quantitative characteristics of the workplace.

The aim

of this work analysis of the elements of the workplace and create a model workplace of the nurse-leader.

Methods

In this study we used the methods of sociological survey and non-parametric statistics

THE RESULTS OF THE STUDY

As a result of the analysis, we found that the 835 respondents (92%) give the advantage to the female sex. 77% of respondents selected the range from 30 to 40 years, as like as optimum age for the nurse-leader. According to 65% of specialists, the family status of the nurse-leader does not matter, as well as the social status (724 respondents — 81%).

The appearance of the nurse-leader should necessarily be, in most cases, charming (as noted by 500 representatives of nursing staff — 56%). Work experience is the most important criterion of the level of skill of the worker. 547 respondents noted that professional experience of the nurse-leader should be more than 10 years (61%).

Professional knowledge is the basis of effective activity of each leader. The most important in HR-management and in the organization of work of medical workers, according to respondents, are: knowledge in the field of psychology (812 respondents — 89%), management (788 respondents — 87%), legislation (748 respondents — 83%), pedagogy (724 respondents — 81%), knowledge of the economy, the relationship of ethics (necessary for 700 respondents — 78%), knowledge of modern models of nursing care (indicated 692 respondents — 76%).

Professional skills are also important for the nurse-leader, since in most cases she has to act as an expert, which also implies elements of practical professional activity.

The most necessary practical skills were noted: skills of working with people (772 respondents — 85%), development of training programs for nurses (indicated 796 respondents — 88%), using standards of nursing care (717 nurses — 79%), conducting methodical work (624 respondents — 69%)), determining the quality of nursing care (618 respondents — 68%), scheduling (indicated 592 respondents — 65%).

Most managers select employees, assessing them according to their education. The employer should

study the duration and content of education, its compliance with the work. The nurse-leader in the opinion of 844 respondents should have a higher education in the specialty of *nursing*, qualification *manager* (94%); on specialty: *general medicine*, qualification *paramedic*» (indicated 646 people, 73%); on the specialty of *nursing*, qualification *nurse* (549 specialists of the nursing staff indicated that is 61%). [1]

It is also necessary for the nurse-leader to improve the qualifications, at faculties of higher nursing education of medical schools (812 respondents — 89%) and in management schools (432 respondents — 49%).

A significant role in determining the model of the workplace of the nurse-leader playing her personal characteristics. This group of indicators is determined by a wide range of personal qualities and subjective in their perception.

The main problem is the lack of direct observations of the properties of the person. Of the human qualities, the most preferable are: justice (823 respondents — 91%), honesty (782 respondents — 86%), kindness (725 respondents — 81%), attentiveness and punctuality (705 respondents — 78%), integrity and responsibility (672 respondents — 74%), responsiveness (654 respondents — 72%), tolerance (624 — 69%), optimism (indicated by 552 respondents — 63%).

When determining the quality of the nurse-leader were noted: the ability to listen people (it is important for 812 respondents — 89%), organization (it is necessary in the opinion of 750 re-spondents — 83%), the ability to complete the task to the end (relevant for 724 respondents — 80%), breadth of horizons (important for 695 respondents — 77%), diplomacy (680 respondents — 75% noted), ability to see the prospect (625 respondents — 69%), efficiency (popular among 620 respondents — 68%), purposefulness and executive (599 respondents — 66%), communication skills (indicated 690 respondents — 76%), discipline and hard work (695 respondents — 77%). Personality psychology plays a special role in the activities of any leader, especially the female leader. [2]

From the point of view of women, who make up about 95% of the nursing staff who have an education in *nursing*, *medicine*, the extrovert must be the predominant type of personality (698 representatives of the nursing profession — 77%).

By temperament — the first place was given to sanguine (728 respondents — 81%), and 842 respondents — 93% — without any doubt noted the high level of intelligence.

The health and efficiency of nursing staff is gradually becoming one of the important factors contributing to the effective operation of the clinic.

The performance of functional duties by the nurse-leader requires from her, quite often, good physical preparation and the presence of potential health, both physical and mental.

According to our results, only 423 (48%) of able-bodied sisters-leaders can call themselves healthy people, and 719 (79%) are almost healthy.

For some specialists, the health and efficiency of the nurse-leader does not matter (78 respondents — 9%).

Hobbies are for any person an original characteristic of his inner world, his preferences and tastes, which leaves an imprint on the business side of the life of the individual. The first place among the proposed variants of hobbies was taken by literature (690 respondents — 76%), the second — art in the form of painting and music (540 respondents — 60%), the third — theater and cinema (popular in 505 respondents — 55%) (Fig. 1).

The organization of work of the nurse-leader is reported to want to be better and more comfortable.

On wages, attention was drawn to receive a percentage of profits for paid medical services (said 590 of the respondents — 65%).

The most common social benefits that should be used by the nurse-leader, according to respondents, were: payment of branded clothing (indicated 578 respondents — 61%), compensation of for food expenses (said 515 respondents — 56%) and material assistance (necessary in the opinion of the 429 respondents — 49%).

The most important social guarantees for the nurse-leader were: annual leave (said 859 respondents — 95%), sick pay (indicated 815 respondents — 90%), benefit in case of death (important for 782 respondents — 87%) and benefits in case of dismissal for staff reduction (relevant for 727 respondents — 80%). [3]

Thus, the model of the nurse-leader's workplace is the next portrait.

This is a specialist female, age from 31 to 40 years, with marital status as social is not important; preferably charming appearance, fair, decent and educated, not devoid of kindness, punctual and attentive; at the helm is enough, benefit from sanguine with a high level of intelligence who has sufficient knowledge in psychology, management, law and pedagogy; possess practical skills in working with people in development programs for nurses; respectively with tertiary education, raising the qualification as nursing and management; owning quite literary in knowledge, having the opportunity to receive a percentage of profits for paid medical services; in addition, to pay for branded clothing and to have social security on annual leave, paid sick leave and receive ben-efits in the event of dismissal for redundancy.

Fig 1. *The main elements of the model nurse-leader's workplace*

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SOCIO-HYGIENIC FEATURES OF BREAST CANCER IN THE SOUTH OF THE RUSSIAN FAR EAST

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In recent decades, the world has seen a significant increase in women's cancer, among which breast cancer (BC) is the main one [1, 2]. In Russia, the incidence of breast cancer is also rising irresistibly upward [3]. A number of authors note the impact of social shocks, leading to stress on the occurrence of BC. Patients with oncological diseases in 39.3% experienced the influence of chronic psycho-emotional stress. In some cases, deterioration of living conditions, including hygiene, is also capable of causing stress, leading to a pathology in a person. [4, 5].

Such stressful conditions among the population were marked in the period of socio-political and financial-economic crises, when the established traditions and way of life collapsed. In the Russian Federation such periods were observed in 1991 (the collapse of the USSR), in 1998 (default), from 2008 to 2009 (the economic crisis) and in the period from 2014 to 2016. (economic crisis and sanctions).

The first period was characterized by social collapse: by the closure of most enterprises, the destruction of collective agriculture, unrestrained price increases, hyperinflation, and, as a result, by the catastrophic impoverishment of people and unemployment, that did not occur in the USSR. During this period, there was also an unprecedented increase in crime, a massive violation of human rights, separatism, nationalism and inter-ethnic strife. All these led to a catastrophic decline in the quality and standard of living, including the deterioration of hygiene standards, a sharp change in the diet — a decrease in the quality of food, derivation of surrogates, substitutes, previously absent in food in the USSR. Subsequent two economic crises were also characterized by a decline in the standard of living in all spheres of the life of a citizen of Russia, which also led to a deep psycho-emotional stress. Only the last crisis did not lead to social stress even in decline of general standard of living in population.

We investigated the interrelationship between these phenomena in the Russian Far East, in view of the significant difference from the central regions of Russia in terms of socio-economic and sanitary-hygienic living conditions.

We used data of the State Statistical Service and hospital register's statistic data and the cancer registry of the Primorsky Regional Oncological dispensary.

As a result, it was found out, that socio-economic crises had a significant effect on the development of breast tumors. The incidence corresponds to the trend in this time interval. Mortality has a pronounced dependence, in particular in the post-crisis period in the Far East RF.

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FEATURES OF MEDICAL CARE IN THE CONDITIONS OF OIL EXPLORATION AND PRODUCTION IN THE EXTREME NORTH

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INTRODUCTION

The Arctic is defined as a natural extreme zone, which places high demands on the adaptive capabilities of the body. The Far North is a territory that exceeds several European states. At the bottom of the Arctic Ocean is almost 20% of the world's oil reserves and 30%of gas reserves [2]. He is characterized by extreme climatic conditions, a quarter of all foreign exchange earnings to the state budget of Russia comes from this region. Every year, 20% of the world's and 90% of Russian gas and oil are produced. Moreover, the Far North is not only a powerful raw material base of the country today, it is also a kind of guarantor for the energy security of the state for many years to come: here is concentrated a quarter of all the world's proven reserves of natural gas and oil. At this point, changes can be rapid and unexpected, often causing a switch to very different ecosystem types. Many of these triggers for change are amenable to management, suggesting that our choice of policies in the coming decades will substantially influence the ecological and societal consequences of current climatic change [9].

To preserve the human potential, we need deep knowledge and experience in studying the fundamental specific northern problems, identifying the prospects for socio-economic development of the North and the Arctic, which is inextricably linked with the problems of health care in conditions of shift, seasonal and permanent jobs [5]. The effectiveness of human labor in the Far North is largely determined by the degree of its adaptation to external conditions of activity, to social and environmental factors. Therefore among researchers [8] it is axiomatically considered that the foremost pragmatic goals of studying the mechanisms of psychological adaptation to work in the Arctic are prediction of the dynamics of adaptation to existing conditions there and the implementation of an external correction of this process with a view to optimizing it.

Deficiency of the workforce in the conditions of the Far North against the backdrop of a professional high-intensity load significantly exceeding the standard for normal working conditions, create the prerequisites for violations in the psychoemotional sphere and accompany the development of psychosomatic pathology in workers [4]. In addition, the complex of natural factors of the Far North has a pronounced negative effect on the physical and mental state of a person, called the "polar tension" syndrome [3]. The human body is adversely affected by: low temperatures in combination with strong winds, short cold summers, high humidity, the presence of peculiar periods of polar night and polar day, lack of solar radiation, geomagnetic activity, sudden changes in atmospheric pressure, eating habits, prolonged exposure to enclosed spaces and etc.

All this dictates the immediate development of urgent legislative measures of medical care for workers in the oil and gas industry.

RESULTS

Nowadays, in indigenous populations of the North and Siberia lower indicators ofpsychic health are registered. The evidence ofthis occurrence is high mortality due to external causes and significant prevalence of alcoholism. The high level of suicide among indigenous children and adolescents reflects extreme social troubles.

Problematic for the northern territories are the presence of natural focal infections and zooanthroposes; peculiarities of nutrition, the way of life of the population and the ecological situation, since in regions equal to the Far North, a peculiar microelement composition of soil and water is noted, which in turn also requires analysis and study.

Life and work in the harsh conditions of the North is accompanied by an increase in functional loads on the body, thereby creating a greater risk of

impairment or loss of health. The climate of the North presents high demands on the human body, especially in the initial period of stay in unusual environmental conditions. The shortcomings in the healthcare system itself in the Far North, the health management system of the northern territories, functioning in difficult social conditions amid the changes in the regulatory framework and health management, the practical elimination of the system of centralized provision of health care facilities with medical equipment and medicines, medicines and budget cuts.

The respiratory disease-related mortality rates in the majority of Russian Northern regions were much higher compared to the national average.

According to McMahon BJ, Bruce MG, Koch A, Goodman KJ, Tsukanov V, Mulvad G, Borresen ML, Sacco F, Barrett D, Westby S, Parkinson AJ. (2016) Helicobacter pylori infection is a major cause of peptic ulcer and is also associated with chronic gastritis, mucosa-associated lymphoid tissue (MALT) lymphoma, and adenocarcinoma of the stomach [7]. Guidelines have been developed in the United States and Europe (areas with low prevalence) for the diagnosis and management of this infection, including the recommendation to 'test and treat' those with dyspepsia. A group of international experts performed a targeted literature review and formulated an expert opinion for evidenced-based benefits and harms for screening and treatment of H. pylori in high-prevalence countries [7]. They concluded that in Arctic countries where H. pylori prevalence exceeds 60%, treatment of persons with H. pylori infection should be limited only to instances where there is strong evidence of direct benefit in reduction of morbidity and mortality, associated peptic ulcer disease and MALT lymphoma and that the test-and-treat strategy may not be beneficial for those with dyspepsia.

Maslov L. (2015) and his co-authors was showed that in the case of indigenous people, dyslipidemia, which leads to diseases of the heart and vessels, develops less often. Habitation within the polar circle increases cardiovascular mortality rate and particularly increases mortality as a result of coronary events. The main reason of elevation of mortality from these diseases is a dyslipidemia which developed more among alien population residing long time in Far North. Dyslipidemia is less found among aboriginal population of Arctic Circle keeping traditional way of life and respectively it is low rate of mortality from coronary heart disease [6]. Bruklich NA, Nersesian EG, Tsitronov ES, et al. (2013) noted that high mortality in the North is observed due to pancreatonecrosis. This can be related to the peculiarities of nutrition in the North [1].

CONCLUSION

It is necessary to continue to carry out scientific research aimed at creating not only new equipment and technologies for prospecting, exploring and developing oil and gas fields on the shelves of the Arctic seas, in the zones of year-round ice, but also to study the influence of the specifics of the Far North on the human body. The strategy of further development and preservation of the polar regions is related to the need to solve tactical problems related to the preservation of the health of people living in the North today. This is the second and third generation of alien inhabitants of circumpolar regions — people who have moved to the North in recent decades, as well as indigenous populations of high latitudes.

The actual stage of development of public health rendering of specialized medical care is based on principles of generality, accessibility, addressness, qualitativeness, and effectiveness. However, the problem of rendering specialized medical care to population is one of most critical targets in district centers and requires immediate solution. The organization of reanimation counseling center, maintenance of remote monitoring of newborns and development of telemedicine and means of sanitary aviation play main role in supporting accessibility of high-tech medical care in conditions of this region. The revealed regional distinctions regarding the prevalence of, and mortality from, chronic respiratory diseases should be taken into consideration when designing integrated programs for chronic noncommunicable disease prevention in theseregions.

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FETAL TETRALOGY OF FALLOT

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ABSTRACT — Tetralogy of Fallot (ToF) is a common form of congenital heart disease (CHD). Frequency of occurrence is 1/3600 live births and 3,5–7% of infants with CHD. TOF is 5% to 10% of all congenital heart disease. Our database has included 112 cases of ToF in 2013–2016. Definition of fetal ToF was attempted from multiple ultrasound scan planes. Initial fetal echocardiograms were obtained between 12 and 39 weeks of gestation (m = 24.5 weeks). In all cases there was postnatal examination by echocardiography, angiography, surgery or autopsy. Prenatal diagnosis was confirmed in 100%. The termination of pregnance took place in 5 cases.
107 cases have been subjected cardiac surgery in our center and survival rate was 97%.

Tetralogy of Fallot (ToF) is a common form of congenital heart disease (CHD). ToF includes dextraposition of aorta, aortic ventricular septum defect, right ventricular outflow obstruction and hypertrophy of right ventricle in postnatal period. We will not have hypertrophy of right ventricle before birth, fetal right ventricle is larger, left ventricle is normal. Frequency of occurrence is 1/3600 live births and 3,5–7% of infants with CHD. ToF is 5% to 10% of all congenital heart diseases [2].

Classification of ToF

- Pale form (absent or minimum of right ventricular outflow obstruction);
- Classic form (middle and strong pulmonary stenosis);
- Extreme form (Atretic pulmonary valve);
- TF with absent pulmonary valve syndrom.

RVOT obstruction in ToF occur at following levels [1, 2, 3].

- 1. Infundibular stenosis 45%;
- 2. Pulmonary valve stenosis 10%;
- 3. Valvular and infundibular combination in 30%;
- 4. Atretic pulmonary valve in 15%.

Concomitant intracardial pathology:
25% of ToF associated with right aortic arch, 5% of ToF have anomalous coronary arteries, 2% of TOF are associated with atrioventricular septal defect.

Extracardial pathology:
trachea-esophageal fistula, cleft lip, abdominal wall defects, venrticulomegaly, renal anomalies [4,6].

Chromosome complement are 22q11deletion, trisomy 21, trisomy 13, trisomy 18.

Morphology

Anterior craniocaudal or cephalad deviation of the insertion of the muscular outlet septum torgether with hypotrophy of trabeculations on the infundibular free wall constitute the essential features of ToF. Instead of nestling berween the anterior and posterior limbs of the trabecula septomarginalis, the outlet septum is displaced and typically fuses with the anterior limb. This brings the aorta over the ventricular septum so that it has a biventricular origin and accounts for the malalignment ventricular septal defect. The displaced outlet septum, torgether with the trabeculations of the parietal or free wall, produce muscular sub-valvar right ventricular outlet obstruction [2].

HEMODYNAMICS

Due to overriding, aorta receives blood from both right ventricle and left ventricle. Ventricular sep-

tal defect (VSD) is nonrestrictive meaning no gradient across VSD. Pressure difference between in heart's cavieties is 10-15 mm Hg before the birth. There is the general circulation and lungs do not function. ToF is compensated before the birth.

After the birth ToF is cyanotic CHD. RV preferentially ejects into arota because of infundibular stenosis. Hypoxemia took place because took place the infundibular pulmonary stenosis.

MATERIALS AND METHODS

Our database was reviewed for cases with a diagnosis of ToF seen between 2013–2016. There were 112 cases of ToF.

Definition of fetal ToF was attempted from multiple scan planes including basic views: four-chamber view, five-chamber view, long-axis view of left and right ventricle, short view of aortic valve, and, three vessel view. (Fig. 1–8).

Doppler color flow mapping and pulsed Doppler interrogation were used to facilitate identification of great vessel relationship, location and severity of ventricular outflow obstruction and the measurement of maximal pulmonary velocity.

Methods of the echocardiographic identification of ToF were postnatal examination by echocardiography, angiography, surgery or autopsy. Initial fetal echocardiograms were obtained between 12 and 39 weeks of gestation (m = 24.5 weeks).

RESULTS

There were 112 cases of ToF, including : ToF with: middle pulnomary stenosis — 75, strong stenosis of PA — 27, extreme form — ToF and atresia of pulnonary artery – 1, ToF with absent pulmonary valve syndrom — 9.

The level of pulmonary obstruction was determined according to the next formula (supplement 1).

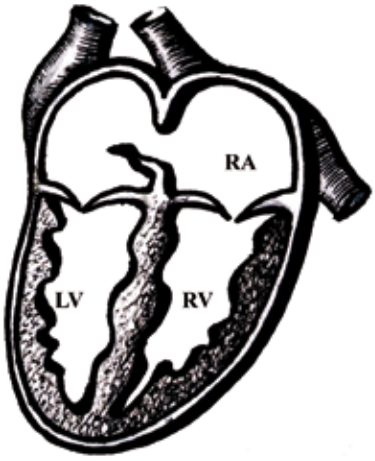


Fig.1A. four chamber view

Fig. 1B. 22 week of gestation

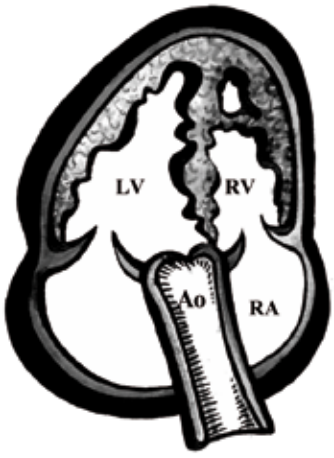


Fig. 2A. Five chamber view

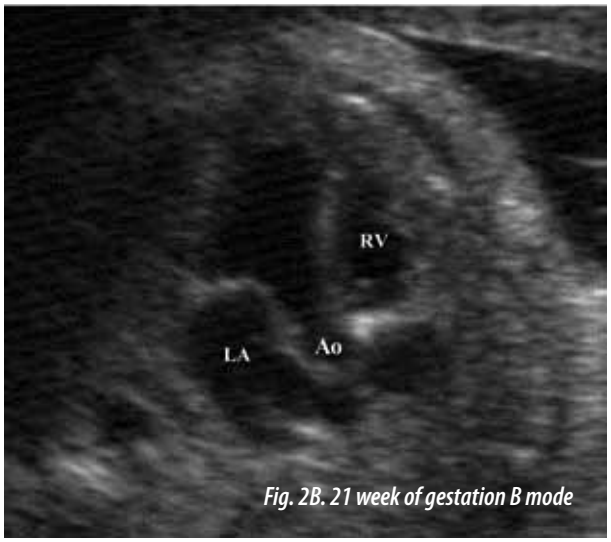


Fig. 2B. 21 week of gestation B mode

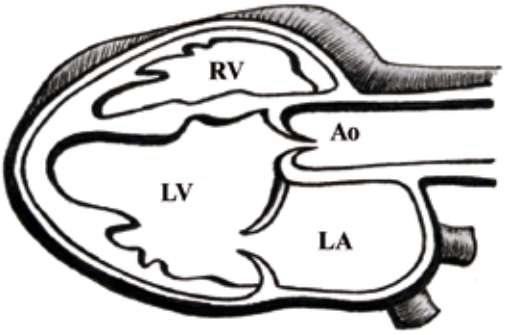


Fig. 3A. *LV outlet tract*

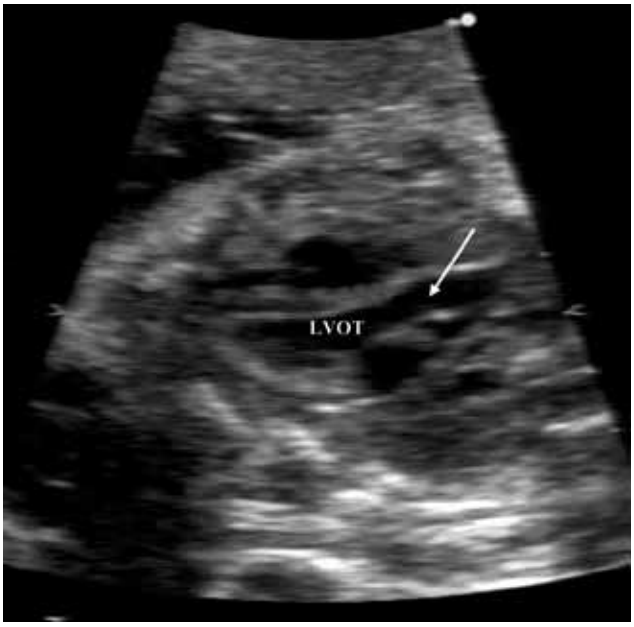


Fig. 3B. *20 week of gestation, B mode*

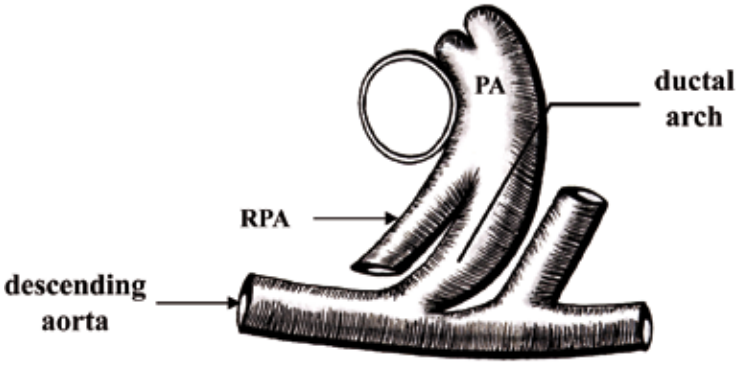


Fig. 4A. *Ductal arch*

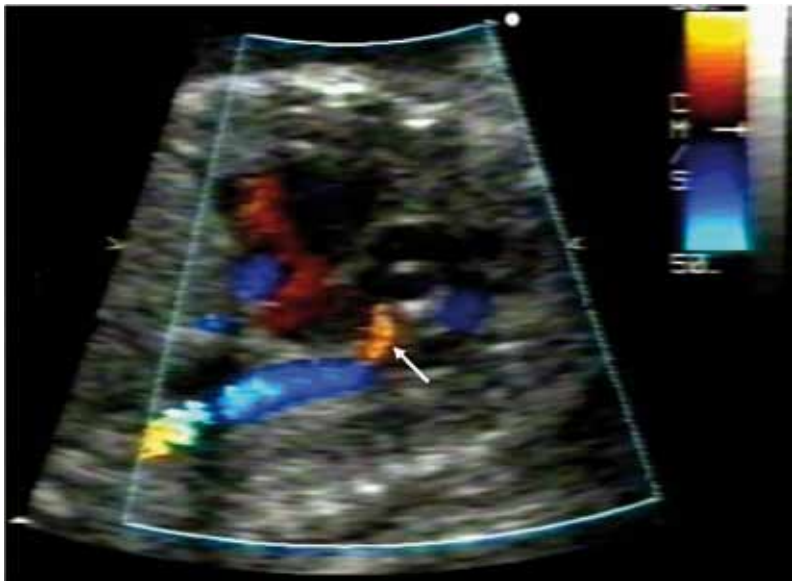


Fig. 4bB. *Color Doppler mapping. Modified aortic arch projection showing the aorta throughout. The arrow indicates the open arterial duct, which connects with the descending aorta*

Regress of pulmonary artery growth from middle pulmonary stenosis to strong pulmonary stenosis took place in 10 cases between 26–34 weeks of gestation. There were 6 cases of ToF with middle stenosis pulmonary artery and atrioventricular septal defect, 5 cases of ToF with severe pulmonary stenosis and face's, abdominal's and renal anomalies . There was chromocome abberation (Down syndrome) in one case.

Postnatal verification took place in all cases. Prenatal diagnosis was confirmed in 100%.

All patients with ToF were offered the cardiosurgerist, genetic's specialist. The delivery of all babies with this CHD was in specialized maternity hospitals. The method of delivery was determined by odstetric and somatic status of pregnant women.

The termination of pregnance took place in 5 cases. There were cases of ToF with severe pulmonary stenosis and extracardial pathology.

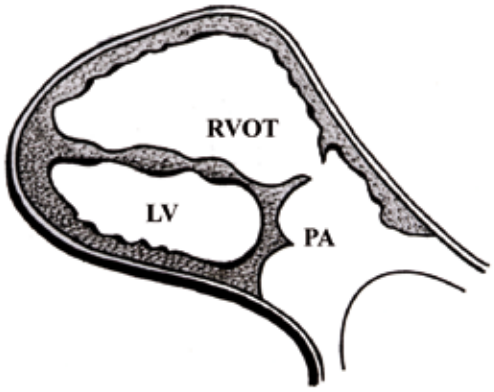


Fig. 5A. *Long axis view of the right ventricle*

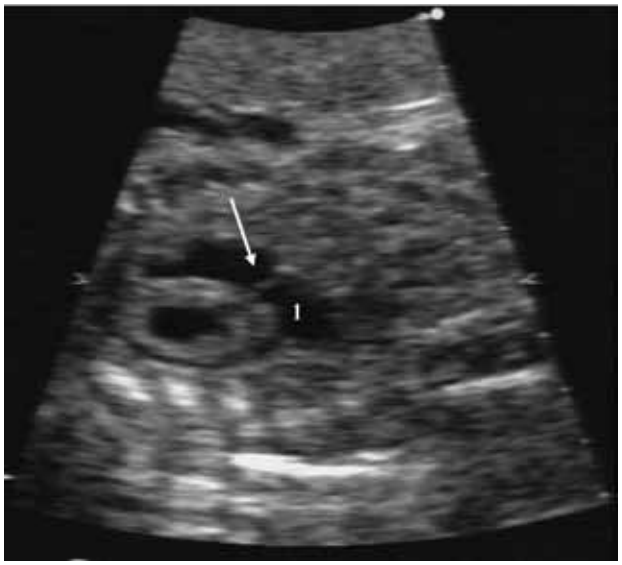


Fig. 5B. *19 week of gestation, B mode*

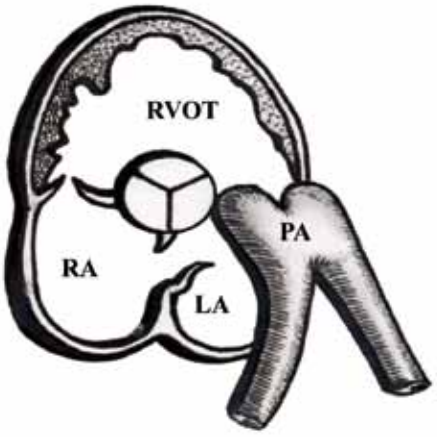


Fig. 6A. *Short axis view of the aortic valve*

Fig. 6B. *20 week of gestation, wB mode*

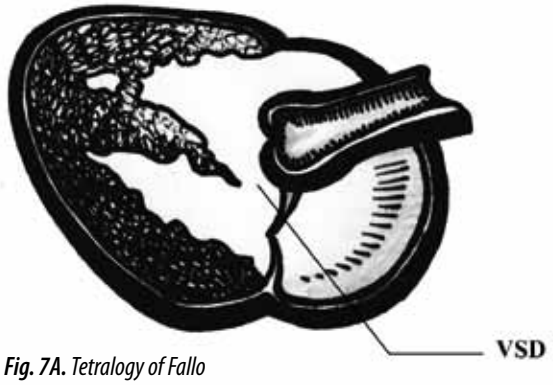


Fig. 7A. *Tetralogy of Fallo*

Fig. 7B. *31 week of gestation, Power Doppler Mode*

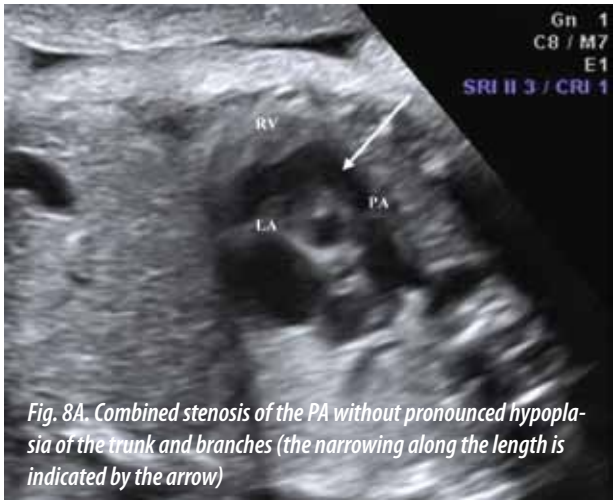


Fig. 8A. Combined stenosis of the PA without pronounced hypoplasia of the trunk and branches (the narrowing along the length is indicated by the arrow)

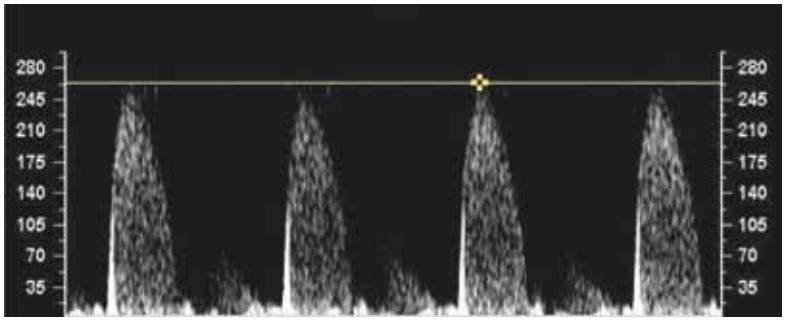
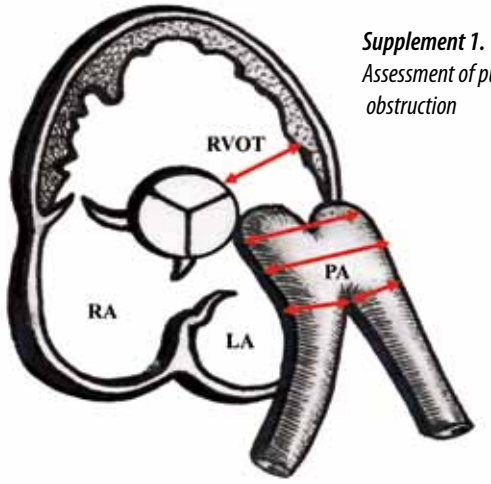


Fig. 8B. *34 week of gestation, Pulsed-wave dopplerography*



Supplement 1.
Assessment of pulmonary obstruction

Short-axis view of the aortic valve. Measurements of pulmonary levels: RV outlet tract, pulmonary valve, mean pulmonary artery, right, left pulmonary arteries for comparison with the rate of gestation
*[D PA measurement. (mm) / D PA coome. AG (mm)] * 100%*

Middle obstruction < 75% vs normal parameters AG ;
Strong obstruction 75–50% vs normal parameters AG
Severe obstruction 50–25%; vs normal parameters AG
Critical obstruction >25% vs normal parameters AG

107 cases have been subjected cardiac surgery in our center and survival rate was 97% . There were isolated form of ToF.

DISCUSSION

Tetralogy of Fallot is a common prenatal diagnosis. Prenatal detectability of this CHD was excellent. But very important to know anatomical details of ToF in every case.

Postnatal prognosis was determined by level and power of pulmonary's stenosis and presence of a combined pathology. The most cases in our cohort had middle stenosis of PA (66,9%) in the same time all cases of atrioventricular septal defect took place in this group. The severe form of TF were isolated heart pathology. Respectively , it was no simple to evaluate the postnatal prognosis in every case.

Our data showed , when the diagnosis of ToF was made in utero, karyotype , detailed anatomical survey and detailed general ultrasound scrinning should be offered in every case. It was important to do the monitoring pulmonary artery growth in fetal life and look for associated extracardiac anomalies throughout pregnance.

Expert review of anatomy of ToF, elimination of combined pathology was positive background for successful surgical repair. Our Center had good experience of ToF's surgical repair. Survival rate was 98% in 10 years after surgical repair during 1 year after birth [1].

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DIFFERENTIAL DIAGNOSTIC CRITERIA OF KIDNEY INJURY DUE TO LEPTOSPIROSIS

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ABSTRACT — Kidney injury in leptospirosis is a leading pathogenetic mechanism, due to development of degenerative changes in the tubular apparatus. A number of natural focal infections have similar pathognomonic symptoms that make it difficult to conduct differential diagnosis and provide timely ethiopathogenetic treatment. The article highlights the differential diagnostic criteria of kidney damage at leptospirosis, gives clinical examples.

KEYWORDS — leptospirosis, kidney damage, differential diagnostic criteria

INTRODUCTION

Almost all infectious diseases affected by severe fever and an intoxication syndrome are characterized by moderate proteinuria (within 0.3 g/l), caused by an increased permeability of the vascular wall [1, 3, 4, 7, 8].

There are a number of infectious diseases in which renal damage is the leading pathogenetic mechanism that often determines its outcome: malaria, hemorrhagic fever with a renal syndrome (HFRS), and leptospirosis [2, 5, 6].

At leptospirosis, there is a degenerative process in the epithelium of the tubular apparatus — a diffuse nephrosis in combination with hemolysis. This is a characteristic sign of leptospirosis, which occurs with necrosis of glomerular epithelial cells and the main membrane, followed by the involvement of renal tubules in the process [2, 5, 6]. In the first days of clinical manifestations, degenerative and necrotic changes develop in the affected organs and tissues, including the epithelium of the renal tubules. In some patients at the height of the disease, leptospira begin to accumulate,

multiply in the convoluted tubules of the kidneys and be excreted from the body with urine. Patients develop signs of acute renal failure, characterized by oligoanuria and uremic coma: diuresis decreases to 500 ml per day or less, proteinuria increases in the urine; there is an increase of the amount of leukocytes, erythrocytes, and cylinders in the urine sediment, and of the level of nitrogen-containing substances in blood. There is a decrease in both the secretory and excretory functions of the kidneys. Oliguria can change for anuria. The peculiarity of acute renal failure at leptospirosis is the absence of edema and arterial hypertension.

The aim of the study:
to estimate the incidence and single out differential diagnostic criteria of urinary tract involvement in leptospirosis.

METHODS

We made a clinical epidemiological analysis of 25 cases of leptospirosis of icterohemorrhagic form. The diagnosis of leptospirosis was confirmed by appropriate serological reactions and PCR diagnostics. The study involved patients aged 18 to 65 years. The majority of the cases were men of working age — 76%. More than half of those who developed leptospirosis were rural residents — 56%.

RESULTS

While collecting epidemiological anamnesis, we found out that the majority of patients with leptospirosis (76%) had a percutaneous mechanism of infection through the outer covers, contaminated water being the main factor of transmission of infection — when swimming in water tanks, fishing and hunting. Leptospirosis was registered mainly in the summer period (68%) with a maximum incidence rate in August (36%), although some cases were registered throughout the year.

In the initial period of the disease, the observed patients with leptospirosis often had a body temperature above 39,1° C, in 12% of cases — above 40° C. In 64% of cases, the temperature curve was remittent; a constant type of temperature curve was registered in every fifth patient; in single cases, with a severe disease, there was a double-wave fever.

The duration of the febrile period against the background of the antibiotic therapy was an average of 11.4 days. From the first days of the disease, the increase in body temperature in the patients observed was accompanied by severe symptoms of intoxication. All patients with leptospirosis complained of general weakness (100%), headache of a diffuse nature (92%).

We noted the development of renal syndrome in 12 patients with leptospirosis — 48%. Patients complained of pain in the lumbar region (48%), Pasternatsky symptom was positive in 10 patients (40%). In 9 patients (36%) there was a decreased urination. Anuria developed in 1 patient (4%) with a severe course of leptospirosis, which ended in a lethal outcome. Typical changes in urine were in 13 patients (52%): mild proteinuria, leukocyturia, hyaline and granular cylinders. An increased level of nitrogen-containing compounds was registered in the blood of these patients. The increase in creatinine was registered in each patient with the renal syndrome, the highest values were observed on the 7–8th day of the disease from 280 μmol/l at a moderate form to 517 μmol/l at a severe form. The level of urea was also increased — mean value was 12.0 mmol/l.

In severe leptospirosis, patients developed an acute medical emergency — acute renal failure. In the pathogenesis of renal insufficiency at this infection, the DIC-syndrome, intravascular hemolysis in combination with anemia and thrombocytopenia, and the metastatic spreading of pathogens to the tubular epithelium are important.

Clinically, it results in the development of acute nephrotic syndrome, manifested by proteinuria, edema and anuria.

Patient K., aged 64, resident of Astrakhan, was admitted to the Department of the Regional Infectious Clinical Hospital on September 26, 6 days after the onset of the disease with the directional diagnosis of *fever of unclear etiology*.

On admission he complained of weakness and fatigue, marked pain below waist, nausea, vomiting.

From the anamnesis: acute onset on the 29th of September, he felt weakness, body temperature increased to 39° C. At the same time, there was a darkening of the urine. The next two days he was running a fever of up to 39° C, suffered weakness, headache, severe muscle pain — the patient had difficulty walking around the room. He mentioned a single vomiting. Later, pain in the abdomen was becoming more intense and it acquired a permanent character; there was a twice repeated vomiting, jaundice on the skin, the reddish color of urine.

Epidemiological data — two weeks before the disease the patient went fishing to lakes in the Volga delta.

On examination — the condition is severe. The patient is running a fever, fragile. The face is hyperemic, sclero conjunctivitis is obvious (subscleral hemorrhages are revealed). The skin is icteric. On the skin of the body there is an abundant spotted and small-point rash of pinkish-red color.

In the lungs breathing is harsh. Respiratory rate is 24 per 1 min. Heart sounds are muffled, rhythmic. Pulse is 74 beats per minute. Arterial blood pressure is 120/60 mm Hg. Abdominal palpation is painful in all departments. Hepatosplenomegaly. Urination is seldom, in small quantities, urine is red. There are no meningitis signs.

Diagnosis: leptospirosis, an icterohemorrhagic form, severe course.

In the general blood test there is leukocytosis 16 · 10/ l, platelets — 24 thousand.

As clinically indicated, the patient was transferred to the intensive care unit.

The following day the patient's condition worsened. The jaundice increased. There was shortness of breath; weakened breathing, rhonchi crackles in the lungs. Respiratory rate was 30–32 per 1 min. Pulse — 88 beats per minute. Arterial blood pressure was 140/70 mm Hg. There was severe hepatosplenomegaly, oliguria, bleeding in places of injections. In the general blood test there was an increase in leukocytosis, stab shift, platelets — 36 · 10/l. The total bilirubin of blood was 107 μmol/l. In the coagulogram: fibrinogen B ++++, hypercoagulation. In the analysis of urine according to Nechiporenko: erythrocytes were 17500, leukocytes — 13500. The patient has registered complications of the underlying disease — acute renal failure, DIC syndrome, two-sided pneumonia.

From 29.09 — there is no fever, the symptoms of acute renal failure are increasing, the DIC syndrome is progressing, the patient is in sopor. Lumbar puncture was performed. In cerebrospinal fluid: cytosis — 57 cells 11 neutrophils, 46 lymphocytes, protein 0.75%, Pandy's reaction is weakly positive.

In dynamics: the patient's condition worsens, tachycardia is 120 per 1min, arterial blood pressure is 170/80 mm Hg, dyspnea is 40 per minute. Acrocyanosis. The skin is intensely icteric. The patient is transferred to the artificial lung ventilation. Coma I. Along the gastric tube — 200.0 of coffee-ground vomit.

On the 5th of October the condition is extremely serious. Coma IV. Hypothermia. Diffuse cyanosis. Pulse is 52 beats per minute, threadlike. Blood pressure is 80/50. At 15 o'clock there is cardiac arrest, resuscitation measures are without a positive result. Death was ascertained.

The diagnosis of leptospirosis was confirmed serologically by leptospira microagglutination Testing and lysis test with the serogroup of Icterohaemorragica 1/200, grippotyphosae 1/400.

CONCLUSIONS

kidney injury in leptospirosis is caused both by direct damaging action of the pathogen on the tubular apparatus of the kidneys, and indirectly as a result of hemolysis of red blood cells. Differential diagnostic criteria of leptospirosis are the absence of edema and arterial hypertension on the background of proteinuria of varying severity.

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UNTERSUCHUNGEN ZUR WIRKUNG EINER EIGENREFLEXION KÖRPEREIGENER ELEKTROMAGNETISCHER WELLEN AUF DEN FUNKTIONSZUSTAND DER MIKROZIRKULATION MITTELS EINER SPEZIELLEN HAUTAUFLAGE

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EINLEITUNG UND AUFGABENSTELLUNG

Es ist heute allgemein anerkannt, dass eine große Reihe von Erkrankungen durch Störungen der lokalen Durchblutungsregulation hervorgerufen wird oder dass Limitationen der Durchblutungsregulation das Krankheitsgeschehen mit eigner Dynamik begleiten [6, 15].

Die Mikrozirkulation des menschlichen Blutkreislaufes betrifft alle Transportvorgänge zwischen Blut und Gewebezellen, welche im Bereich von Blutgefäßen mit Durchmessern kleiner als 100 µm realisiert werden.

Sie ist daher der funktionell wichtigste Teil des Blutkreislaufes, da hier nicht nur der Stoffaustausch zwischen dem Blut und den Körperzellen stattfindet sondern zugleich ist hier auch der Ort, an dem die ersten Schritte immunologischer Reaktionen ablaufen [6, 15, 17, 18, 19].

Störungen der Mikrozirkulation bedeuten immer Einschränkungen oder gar Störungen von Zellfunktionen und Organfunktionen – bis hin zum Zelltod. Ohne adäquate Mitbeteiligung der Mikrozirkulation sind kein Genesungs-Prozess, kein restitutiver Vorgang und keine vollständige Regeneration möglich. Damit ergibt sich die große prophylaktische und protektive Bedeutung einer therapierelevanten Beeinflussung bei limitierter bzw. gestörter Mikrozirkulation [4, 5, 6 –15].

Nach derzeitigem Kenntnisstand stehen bei der lokalen Durchblutungsregulation die Vasomotionsphänomene der großkalibrigen und der kleinkalibrigen Arteriolenabschnitte im Vordergrund. Während die Durchflussregulation durch die nerval und/oder humoral angesteuerten Diameterperiodizitäten realisiert wird, erfolgt in den kleinkalibrigen Arteriolen eine spontane, autorhythmische Vasomotion. Auf diese Weise wird die stoffwechseladäquate Anpassung der Durchblutung, also der Verteilungszustand des Plasma-Blutzell-Gemisches in den kapillären Netzwerken, gewährleistet. Hierbei spielt die schubspannungsabhängige endothelvermittelte arterioläre Tonusregulation via Stickstoffmonoxyd eine herausragende Rolle.

Neben diesen Mechanismen sind sehr wahrscheinlich auch noch andere Mechanismen beteiligt, die bisher nur unzureichend erforscht sind (molekularbiologische Vorgänge, Kanäle, Membranphänomene u.a.m.) [2–19].

Betrachtet man die von der Körperoberfläche an die Umgebung abgestrahlte Energie (hauptsächlich eine elektromagnetische Welle im Infrarot-Bereich), so enthält diese Wärmestrahlung, welche eine zusammengesetzte Welle darstellt, Informationen der Zellaktivitäten jener Gewebestrukturen, aus denen sie durch Konvektion und Konduktion sowie Strahlung abgeführt wird. Das Amplituden-Frequenz-Spektrum dieser zusammengesetzten Welle ist somit nicht nur ein Indikator des Gewebefunktionszustandes, sondern

es liegt auch die Möglichkeit nahe durch Reflexion der körpereigenen Strahlung eine Beeinflussung von Regulationsmechanismen zu bewirken — im Sinn einer Eigenstimulierung. Im Mittelpunkt der Betrachtung stehen hierbei aussagefähige Merkmale der lokalen Durchblutungsregulation.

Von dieser Hypothese ausgehend ist eine mehrschichtige Hautauflage (Testprodukt) empirisch entwickelt worden, dem die Erfinder einen gewissen Eigenstimulierungseffekt zugeschrieben haben.*

Im Rahmen von GCP-konformen klinischen Untersuchungen war an geeigneten Stichproben mit validen Messverfahren anhand repräsentativer Merkmale zu prüfen, ob und in welchen Ausmaß mit Hilfe einer speziellen Auflage zur Rückreflexion körpereigener Strahlung eine medizinisch relevante Wirkung auf die Mikrozirkulation zu erzielen ist.

MATERIAL UND METHODEN

Die Abbildung 1 zeigt den Schichtenaufbau des Testproduktes und seine Anordnung auf der Hautoberfläche (Durchmesser ca. 3 cm, lokale Anwendung).

Zur allgemeinen klinischen Prüfung wurden 4 Untersuchungsreihen durchgeführt. Anwendung des Testproduktes als Schuheinlage.

Als validiertes Messverfahren auf höchstem technischen Standard diente die kombinierte Weißlichtspektroskopie und die Laser-DOPPLER-Mikroflussmessung (System LEA, D). Simultane Messwerterhebungen alle 20 ms in 2 Eindringtiefen (ca. 2 mm — subkutane Mikrogefäß-Netzwerke, ca. 6–8 mm Mikrogefäße in der Skelettmuskulatur).

Angaben zur Validierung sind der Literatur zu entnehmen. [2, 6–16, 20, 21]

Als Messorte wurden der linke Knöchelbereich und die linke Wade ausgewählt (mikrovaskuläre Netzwerke in der Subkutis und in der Skelettmuskulatur).

Die untersuchten Merkmale waren :
- Venolenseitige Sauerstoffausschöpfung ΔpO_2.
- Strömungsfluss der roten Blutzellen Q_{RBC}.

Alle Probanden wurden einer leichten 60-minütigen Laufbandbelastung unterzogen.

Die Messungen erfolgten zu definierten Messzeitpunkten :
- a – Erhebung der Ausgangswerte.
- b – Unmittelbar nach 60-minütiger Laufbandbelastung.
- c – 15 Minuten nach dem Ende der Laufbandbelastung.
- d – 30 Minuten nach dem Ende der Laufbandbelastung.

Die jeweiligen Stichproben wurden zufällig (Zufallsgenerator) in 2 gleichgroße Teilstichproben unterteilt :

Kontrolle (Placebo-Schuheinlage).

Verum (Anwendung des Testproduktes).

Zur statistischen Prüfung der ermittelten Messdaten fand der WILCOXON-Rangsummentest Anwendung (alpha = 5%). Die Angaben für die kritischen Werte von T wurden der gültigen Standard-Literatur entnommen [1].

1. Untersuchungsreihe

Untersuchung einer weitgehend homogenen Gesamtstichprobe aus 32 männlichen und weiblichen untrainierten Probanden (hausärztlich ohne pathol. Befund, infekt- und stressexponiert), die in 2 gleichgroße Teilstichproben mit jeweils gleichen Anteilen männlicher und weiblicher Probanden unterteilt wurde (Kontrolle, Verum).

Die Konstitutionsdaten der Probanden zeigt Tabelle 1:

2. Untersuchungsreihe

Untersuchung einer Gesamtstichprobe aus 32 männlichen und weiblichen untrainierten Probanden mit Diabetes mellitus Typ II (Diabetes eingestellt, keine oder nur geringe Insulin-Medikation, Diät und Bewegungstherapie verordnet, infekt- und stressexponiert, sonst hausärztlich ohne pathol. Befund), die in 2 gleichgroße Teilstichproben mit jeweils gleichen Anteilen männlicher und weiblicher Probanden unterteilt wurde (Kontrolle, Verum).

Die Konstitutionsdaten der Probanden zeigt Tabelle 2:

3. Untersuchungsreihe

Untersuchung einer weitgehend homogenen Gesamtstichprobe aus 16 männlichen und weiblichen untrainierten Probanden (infekt- und stressexponiert, hausärztlich ohne pathol. Befund).

An diesen Probanden wurde verblindet ein intraindividueller Vergleich vorgenommen (zeitlicher Abstand zwischen Kontrolle und Verum 7 Tage).

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Die Konstitutionsdaten der Probanden zeigt Tabelle 3:

4. Untersuchungsreihe

Untersuchung einer Gesamtstichprobe aus 24 männlichen und weiblichen untrainierten Probanden mit Diabetes mellitus Typ II (Diabetes eingestellt, keine oder nur geringe Insulin-Medikation, Diät und Bewegungstherapie verordnet, infekt- und stressexponiert, sonst hausärztlich ohne pathol. Befund), die in 2 gleichgroße Teilstichproben mit jeweils gleichen Anteilen männlicher und weiblicher Probanden unterteilt wurde (Kontrolle, Verum).

Das Testprodukt bzw. das Placebo wurde in einem Zeitraum von 7 Tagen mit einer speziellen Haltevorrichtung Tag und Nacht getragen

Jeden Tag erfolgte eine 60-minütige leichte Laufbandbelastung.

Die täglichen Messzeitpunkte waren :

0. Tag (Ausgangswerte), 1. bis 7. Tag (stets zur gleichen Uhrzeit und jeweils 1 Stunde nach Laufbandbelastung).

Die Konstitutionsdaten der Probanden zeigt Tabelle 4:

Zur Wundheilung wurden 2 Untersuchungsreihen durchgeführt. Anwendung des Testproduktes auf einer kliniküblichen Wundauflage.

Im Rahmen einer GCP-konformen (placebokontrollierten) Untersuchungsreihe wurde eine Stichprobe aus 28 männlichen und weiblichen Patienten (hausärztlich ohne pathol. Befund) untersucht, bei denen eine Naevus-Entfernung vorgenommen wurde (Brust- und Bauchbereich). Die Länge des O.P.-Schnittes betrug 3 bis 4 cm. Die Stichprobe wurde zufällig in 2 gleichgroße Teilstichproben mit jeweils gleichen Anteilen männlicher und weiblicher Probanden unterteilt (Kontrolle, Verum).

Kontrolle: Kliniküblliche Wundversorgung ohne Testprodukt auf der Wundauflage.

Verum: Kliniküblliche Wundversorgung mit Testprodukt auf der Wundauflage.

Die Konstitutionsdaten der Patienten waren : ~ 45 Jahre, ~ 75 kg, ~ 174 cm.

Gemessen wurde die venolenseitige Sauerstoffausschöpfung (kombinierte Weißlichtspektroskopie und Laser DOPPLER-Mikroflußmessung) in den subkutanen Mikrogefäßnetzwerken 3 bis 4 mm vom Schnittrand (Wundrand) entfernt und im Abstand von ca. 5 cm vom Wundrand im unverletzten Hautgewebe

Die Messungen wurden zu folgenden Messzeitpunkten vorgenommen:

0. d — unmittelbar nach dem chirurgischen Eingriff, nachfolgend täglich vom 1. bis zum 10. Tag.

Bestimmt wurde die Differenz der Merkmalbeträge zwischen dem Wundrand und dem unverletzten Hautgewebe.

Eine weitere Untersuchungsreihe diente der Beurteilung der Narbengüte.

Untersucht wurde eine Stichprobe aus 24 männlichen Probanden im Alter von 50 bis 60 Jahren mit leichtem Diabetes mellitus Typ II (eingestellt) nach operativer Naevus-Entfernung, die zufällig in 2 gleichgroße Teilstichproben unterteilt wurde :

Kontrolle (kliniküblliche Wundbehandlung ohne Testprodukt).

Verum (kliniküblliche Wundbehandlung mit Testprodukt, Anwendung des Testproduktes bis zum 10. Tag nach O.P. auf der kliniküblichen Wundauflage).

Als Messverfahren zur Beurteilung der Narbengüte am 60. Tag nach O.P. dienten die spezifische Auflichtmikroskopie mit computergestützter Bildverarbeitung (Referenz Perthometer) und die Oberflächenthermogrammometrie mittels cholesterinischer Flüssigkristallgemische gem. internationalem Standard [3]. Gemessen wurden zentral im Narbengewebe (rote Narbe) und im unverletzten Hautgewebe der gleichen Region im Abstand von 6 cm vom Narbenrand folgende Merkmale:

Maximale Rautiefe Rmax.

Oberflächliche Hauttemperatur T.

Die statistische Auswertung der Messdaten erfolgte mit dem WILCOXON-Rangsummentest (alpha = 5%).

ERGEBNISSE DER ALLGEMEINEN KLINISCHEN PRÜFUNG

Die Tabellen 5 und 6 sowie 7 und 8 informieren über die ermittelten Messdaten zur venolenseitigen Sauerstoffausschöpfung und zum Strömungsfluss der roten Blutzellen in beiden Targetregionen der 1. Untersuchungsreihe (Probanden ohne pathol. Befund).

Bei allen erhobenen Messdaten treten signifikante Merkmalunterschiede zwischen den Ausgangswerten und den nachfolgende Messzeitpunkten auf.

Als Abbildungen 2 und 3 sind die Messdaten für die Merkmale venolenseitige Sauerstoffausschöpfung ΔpO_2 und Strömungsfluss der roten Blutzellen Q_{RBC} zur 2. Untersuchungsreihe in beiden Targetregionen zusammengefasst (Patienten mit Diabetes mellitus Typ II). Bei allen Merkmalen treten in beiden Targetregionen signifikante Merkmalunterschiede zwischen

Tabelle 1. *Konstitutionsdaten der Probanden bei der 1. Untersuchungsreihe*

	Geschlecht m / w	Alter (Jahre)	Körperlänge	Körpermasse (kg)	BMI
Mittelwert	16 m / 16 w	39,3	175,3	77,6	25,3
Stand.abw.		2,40	2,68	2,12	0,47

Tabelle 2. *Konstitutionsdaten der Probanden bei der 2. Untersuchungsreihe*

	Geschlecht m / w	Alter (Jahre)	Körperlänge (cm)	Körpermasse (kg)	BMI
Mittelwert	16 m / 16 w	54,4	174,3	84,4	27,8
Stand.abw.		4,47	3,79	5,44	1,66

Tabelle 3. *Konstitutionsdaten der Probanden bei der 3. Untersuchungsreihe*

	Geschlecht m / w	Alter (Jahre)	Körperlänge (cm)	Körpermasse (kg)	BMI
Mittelwert	8 m / 8 w	47,8	175,5	77,3	25,1
Stand.abw.		4,61	4,86	4,32	0,54

Tabelle 4. *Konstitutionsdaten der Probanden bei der 4. Untersuchungsreihe*

	Geschlecht m / w	Alter (Jahre)	Körperlänge (cm)	Körpermasse (kg)	BMI
Mittelwert	12 m / 12 w	50,3	176,0	77,9	25,2
Stand.abw.		4,16	3,73	4,22	1,29

Tabelle 5. *Messdaten der 1. Untersuchungsreihe zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 in der linken Knöchelregion*

Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten Messzeitpunkte:

a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

Knöchel / Subkutis — Kontrolle

	a	b	c	d
Mittelwert	0	-3,6	-3,5	-3,3
Stand.abw.	0	3,80	3,66	3,49

Knöchel / Subkutis — Verum

	a	b	c	d
Mittelwert	0	15,9	5,9	3,4
Stand.abw.	0	5,33	2,32	2,64

Knöchel / Muskel — Kontrolle

	a	b	c	d
Mittelwert	0	-4,1	-3,8	-3,5
Stand.abw.	0	4,98	4,81	4,52

Knöchel / Muskel — Verum

	a	b	c	d
Mittelwert	0	-3,6	-3,5	-3,3
Stand.abw.	0	3,80	3,66	3,49

Tabelle 6. *Messdaten der 1. Untersuchungsreihe zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 in der linken Wade*

Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

Wade / Subkutis — Kontrolle

	a	b	c	d
Mittelwert	0	-5,9	-5,5	-5,0
Stand.abw.	0	1,45	1,44	1,37

Wade / Subkutis — Verum

	a	b	c	d
Mittelwert	0	4,8	3,2	2,0
Stand.abw.	0	2,02	1,68	1,29

Wade / Muskel — Kontrolle

	a	b	c	d
Mittelwert	0	-5,5	-5,0	-4,5
Stand.abw.	0	1,64	1,68	1,70

Wade / Muskel — Verum

	a	b	c	d
Mittelwert	0	15,1	6,8	4,1
Stand.abw.	0	4,73	2,33	1,86

den Ausgangswerten und den nachfolgende Messzeitpunkten auf.

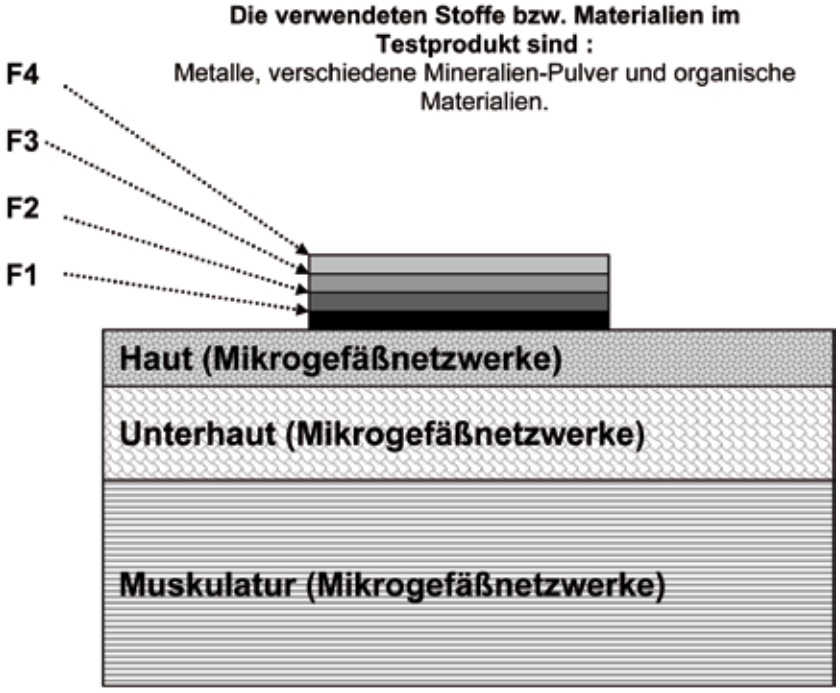
Ausgewählte Messergebnisse des intraindividuellen Vergleiches (3. Untersuchungsreihe) für die Merkmale venolenseitige Sauerstoffausschöpfung ΔpO_2 und Strömungsfluss der roten Blutzellen Q_{RBC} in der Knöchelregion zeigen die Abbildungen 4 und 5, wobei signifikante Merkmalunterschiede zwischen den Ausgangswerten und den nachfolgenden Messzeitpunkte ermittelt werden.

Die erhobenen Messdaten zur 4. Untersuchungsreihe (7-tägige Anwendung des Testproduktes) zeigen die Abbildungen 6 und 7. Signifikante Merkmalunterschiede zwischen der Kontrolle und der Verum-Gruppe treten bei allen untersuchten Merkmalen bereits ab dem 1. Tag auf und sind bis zum 7. Tag nachweisbar.

ERGEBNISSE ZUR WUNDHEILUNG

In dieser Untersuchungsreihe wurde in einem Zeitintervall von 10 Tagen im Abstand von 3 bis 4 mm vom Schnittrand entfernt die venolenseitige Sauerstoffausschöpfung ΔpO_2 in der Haut gemessen und gleichzeitig im Abstand von 5 cm im unverletzten Hautgewebe. Unmittelbar nach dem operativen Eingriff (0. Tag) wurde die Differenz der Messdaten aus beiden Hautregionen gleich 100% gesetzt. Somit würde eine Differenz von 0% bedeuten, dass kein Unterschied der Merkmalbeträge zwischen Wundrand und umgebenden unverletzten Hautgewebe besteht. Die Abbildung 8 zeigt die ermittelten Messdaten. Bereits ab dem 1. Tag treten signifikante Unterschiede zwischen Kontrolle und Verum auf. Am 10. Tag beträgt die Differenz in der Kontroll-Gruppe 37,1%, in der Verum-Gruppe dagegen nur noch 13,4%.

In einer weiteren Untersuchungsreihe wurde die Narbengüte am 60. Tag nach dem operativen Eingriff untersucht (rote Narbe). Gemessen wurden die Merkmale maximale Rautiefe ΔRmax gem. DIN; angegeben als prozentuale Differenz im Vergleich mit dem im umgebenden Hautgewebe ermittelten Wert, welcher gleich 100% gesetzt wurde. Ferner wurde die oberflächliche Hauttemperatur ΔT bestimmt; angegeben als Differenz in °C mit dem umgebenden Hautgewebe. Die Messdaten sind als Tabelle 8 angegeben. Bei beiden untersuchten Merkmalen unterscheiden sich die Messdaten von Kontrolle und Verum signifikant voneinander.



F1 – Basisfolie und Klebeschicht.
F2 – Organischer Halbleiter db-21.
F3 – Schutzfolie.
F4 – Abschlussfolie mit Schutzschicht (Verguß oder transparente Folie).

Abb. 1.

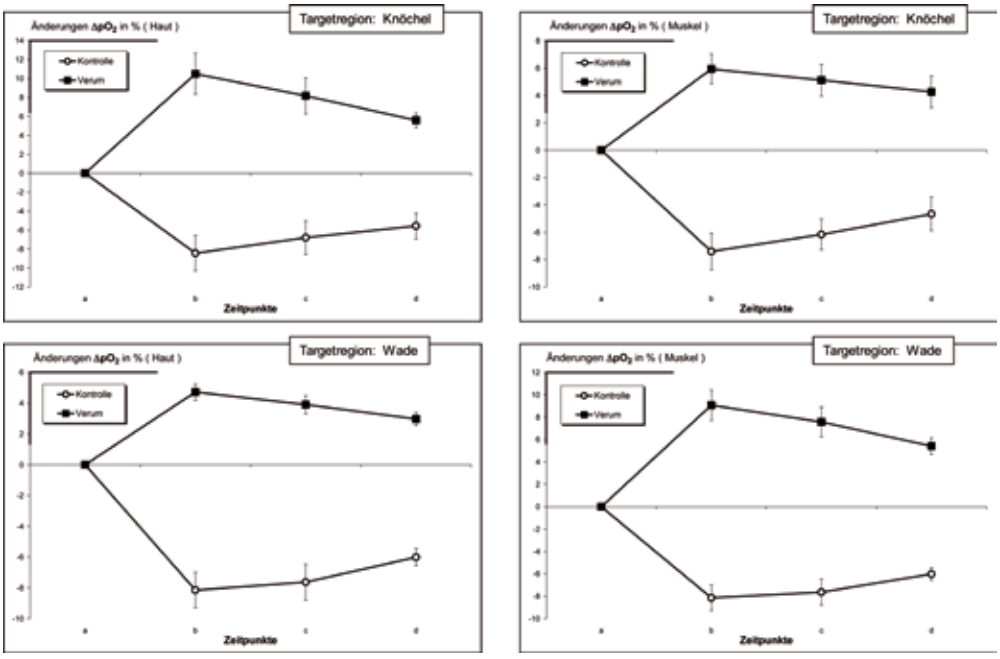


Abb. 2. *Schichtenaufbau des Testobjektes und Anordnung des Testobjektes auf der Hautoberfläche (schematisch)*

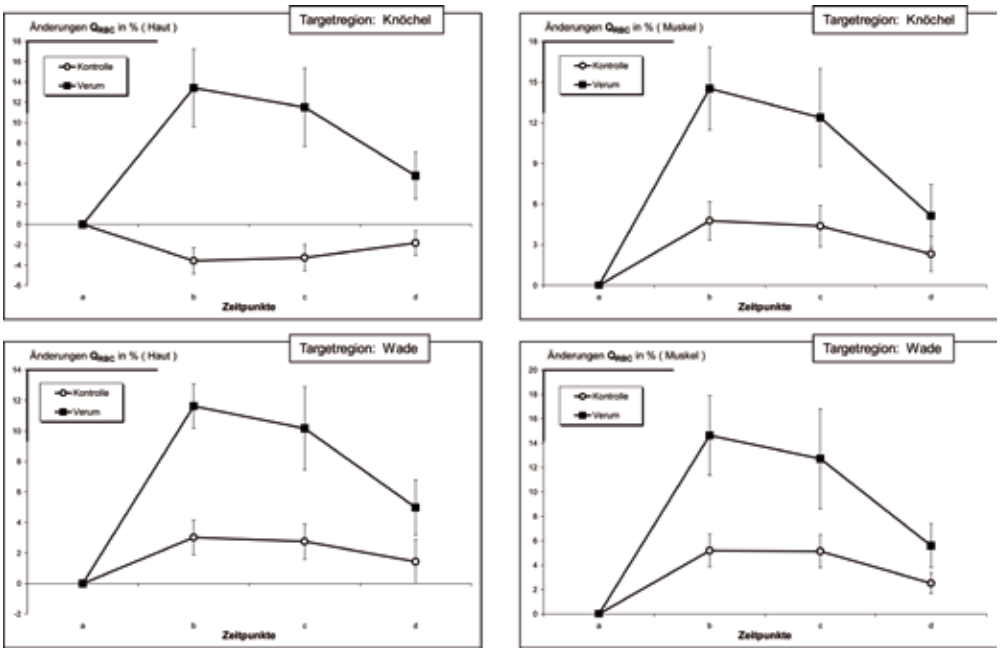


Abb. 3. *Zusammenfassung der Messdaten der 2. Untersuchungsreihe zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 in der linken Knöchelregion und in der linken Wade (Mittelwerte und Standardabweichungen) Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten*

Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

DISKUSSION

Betrachtet man die Ergebnisse der allgemeinen klinischen Prüfungen (Untersuchungsreihen 1 bis 4) so treten deutliche signifikante Unterschiede zwischen Kontrolle und Verum zutage. Die Anwendung des Testproduktes bewirkte Verbesserungen des Funktionszustandes der Mikrozirkulation in der Subkutis und in der Skelettmuskulatur in der untersuchten Knöchelregion und in der Wade.

Die nachgewiesenen Wirkungen des Testproduktes sprechen für eine Eigenstimulierung des wichtigsten lokalen Regulationsmechanismus der Organdurchblutung, der spontanen auto-rhythmischen Vasomotion arteriolärer Mikrogefäße. Hierfür stehen die Befunde zur venolenseitigen Sauerstoffausschöpfung und zum Strömungsfluss der roten Blutzellen. Die vom Testprodukt in das Gewebe rückgestrahlte Welle ist offensichtlich so konfiguriert, dass sie einen physiologischen Reiz auf diesen Regulationsmechanismus ausübt. Ob auch andere (intrazelluläre) Phänomene mitbeteiligt sind, ist nach derzeitigem Kenntnisstand nicht zu beurteilen.

Die Untersuchungen erfolgten in der Knöchelregion der unteren Extremitäten, die eine bevorzugte Gewebe-Region bei der Entstehung und Ausprägung von Durchblutungsstörungen ist (insbesondere bei Patienten mit Diabetes mellitus Typ II – aber auch bei Personen, die besonderen körperlichen Belastungen ausgesetzt sind). Ferner wurde die Wadenregion untersucht, die bei der Laufbandbelastung gewissen Beanspruchungen ausgesetzt war. Somit ist eine kreislaufphysiologische und stoffwechselbezogene Bewertung der Messresultate gegeben [3, 6, 15, 17, 18, 19].

Dem Testprodukt kann im Fall gravierender Erkrankungen wegen der hierfür nicht ausreichenden Beträge der Merkmaländerungen keine causaltherapeutische Wirksamkeit zugesprochen werden, wohl aber ist das Testprodukt geeignet als ergänzende Maßnahme zu anerkannten Behandlungsmaßnahmen eingesetzt werden (zur Prophylaxe und Protektion, Steigerung des therapeutischen Erfolges etablierter Behandlungsmaßnahmen).

Die festgestellten Wirkungen des Testobjektes erlauben eine Empfehlung für folgende Anwendungsgebiete :

Zur Prophylaxe, insbesondere bei beruflich exponierten Personen (Nässe, Kälte usw.), im Sport und bei vornehmlich älteren Menschen mit limitierter Regulation der Durchblutung u.a.m.

Zur Leistungssteigerung bei körperlichen Belastungen.

Adjuvant-therapeutisch zur Optimierung des therapeutischen Erfolges etablierter medizinischer Behandlungsmethoden (z.B. zur Unterstützung der Bewegungstherapie bei Personen mit Diabetes mellitus Typ II).

Die prophylaktische und adjuvant-therapeutische Bedeutung einer Anwendung des Testproduktes betrifft die bessere Anpassung der Mikrozirkulation an sich ändernde Stoffwechselbedürfnisse, die Stärkung

Tabelle 7 *Messdaten der 1. Untersuchungsreihe zum Merkmal Strömungsfluss der roten Blutzellen Q_{RBC} in der linken Knöchelregion*

Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

Knöchel / Subkutis — Kontrolle

	a	b	c	d
Mittelwert	0	1,4	1,2	1,4
Stand.abw.	0	0,86	0,81	1,61

Knöchel / Subkutis — Verum

	a	b	c	d
Mittelwert	0	26,1	9,6	5,2
Stand.abw.	0	8,86	4,30	2,21

Knöchel / Muskel — Kontrolle

	a	b	c	d
Mittelwert	0	2,8	2,5	2,3
Stand.abw.	0	1,09	1,12	1,06

Knöchel / Muskel — Verum

	a	b	c	d
Mittelwert	0	21,9	8,4	4,5
Stand.abw.	0	9,27	2,82	2,05

Tabelle 8. *Messdaten der 1. Untersuchungsreihe zum Merkmal Strömungsfluss der roten Blutzellen Q_{RBC} in der linken Wade*

Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

Wade / Subkutis — Kontrolle

	a	b	c	d
Mittelwert	0	3,1	2,9	2,6
Stand.abw.	0	0,83	0,88	0,93

Wade / Subkutis — Verum

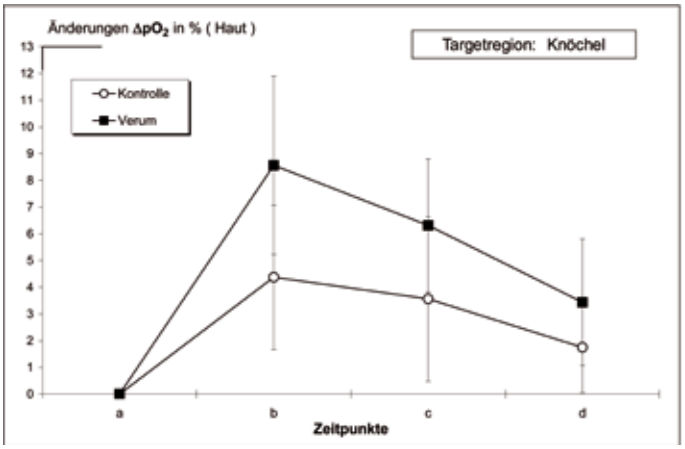
	a	b	c	d
Mittelwert	0	21,0	8,3	4,5
Stand.abw.	0	8,33	2,81	2,12

Wade / Muskel — Kontrolle

	a	b	c	d
Mittelwert	0	4,4	4,0	3,4
Stand.abw.	0	0,92	1,02	0,99

Wade / Muskel — Verum

	a	b	c	d
Mittelwert	0	26,3	10,0	5,6
Stand.abw.	0	7,94	4,27	2,29



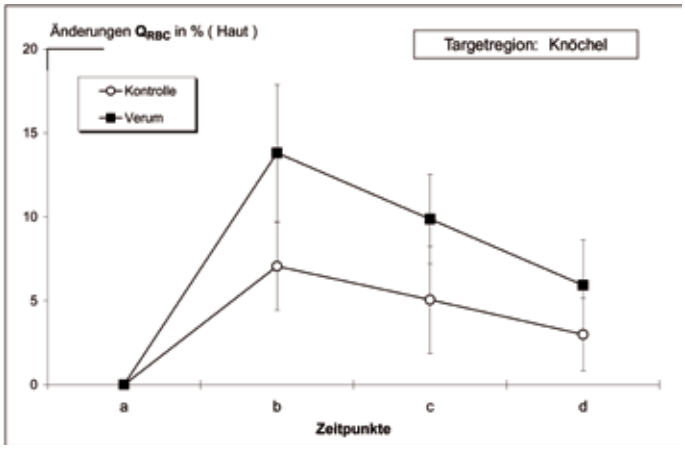


Abb. 4. *Zusammenfassung der Messdaten der 3. Untersuchungsreihe zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 in der linken Knöchelregion (Subkutis). (Mittelwerte und Standardabweichungen) Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten*
Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

Abb. 5. *Zusammenfassung der Messdaten der 3. Untersuchungsreihe zum Merkmal Strömungsfluss der roten Blutzellen Q_{RBC} in der linken Knöchelregion (Subkutis). (Mittelwerte und Standardabweichungen) Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten*
Messzeitpunkte:
a — Erhebung der Ausgangswerte.
b — Unmittelbar nach 60-minütiger Laufbandbelastung.
c — 15 Minuten nach dem Ende der Laufbandbelastung.
d — 30 Minuten nach dem Ende der Laufbandbelastung.

der Regulierung des Wärmehaushaltes, eine Minderung der Infektanfälligkeit bzw. gestärkte Infektabwehr und damit in gewissen Grenzen eine höhere Lebensqualität und Leistungsfähigkeit.

Die Untersuchungsresultate zeigen des Weiteren, dass bei Anwendung des Testobjektes auf klinikü-blichen Wundauflagen in einem gewissen Ausmaß ein günstiger Einfluss auf die Wundheilung ausgeübt werden kann. Es konnte nachgewiesen werden, dass sehr wahrscheinlich ein fördernder Einfluss auf die Neubildung von Mikrogefäßen am Wundrand (in der entzündlichen Phase der Wundheilung) erzielt werden kann, wofür die Messdaten zur venolenseitigen Sauerstoffausschöpfung sprechen. Des Weiteren wirkt sich eine Anwendung des Testproduktes auf den späteren Zustand der Narbengüte aus (glattere Hautoberfläche und bessere Temperaturregulation).

Das Testprodukt ist somit auch zur Steigerung des therapeutischen Erfolges als Ergänzung zu etablierten Wundheilungsbehandlungen bei verzögerter oder gestörter Wundheilung geeignet, wofür eine Anordnung des Testproduktes auf handelsüblichen Wundauflagen empfohlen wird.

Somit ergibt sich eine Reihe von Anwendungsoptionen:

Als Schuheinlage.

Das Testprodukt kann im Rahmen der Bewegungstherapie bei Patienten mit Diabetes mellitus Typ II eingesetzt werden.

Des Weiteren kann es einen Beitrag leisten zur Vermeidung von Ermüdungsbrüchen (z.B. im Fußbereich) – bei beruflich besonders exponierten Personen, bei Rehabilitanden, im Sport, bei Soldaten u.a.

In der (Schutz-) Kleidung (Weste, Jacke, Handschuhe u.a.).

Für beruflich exponierte Personen, Sportler (z.B. Wintersport) u.a.

Verwendung in Schlafsystemen (Unterlage, Decken u.a.).

Als Ergänzung der klinikü̈blichen Behandlungsmaßnahmen bei normaler und vor allem bei gestörter Wundheilung ist ein Einsatz des Testproduktes Erfolg versprechend (auf handels-üblichen Wundauflagen bzw. –verbänden angebracht oder als eigene Wundauflage/Pflaster).

Abschließende Bemerkungen:

Für die Betrachtung der Wirkungen des Testobjektes stehen die Gesetzmäßigkeiten der Wechselwirkungen von Wellen und Materie im Vordergrund – die Wechselwirkungen von körpereigener Strahlung und Testobjekt. Die „Quellen“ der körpereigenen

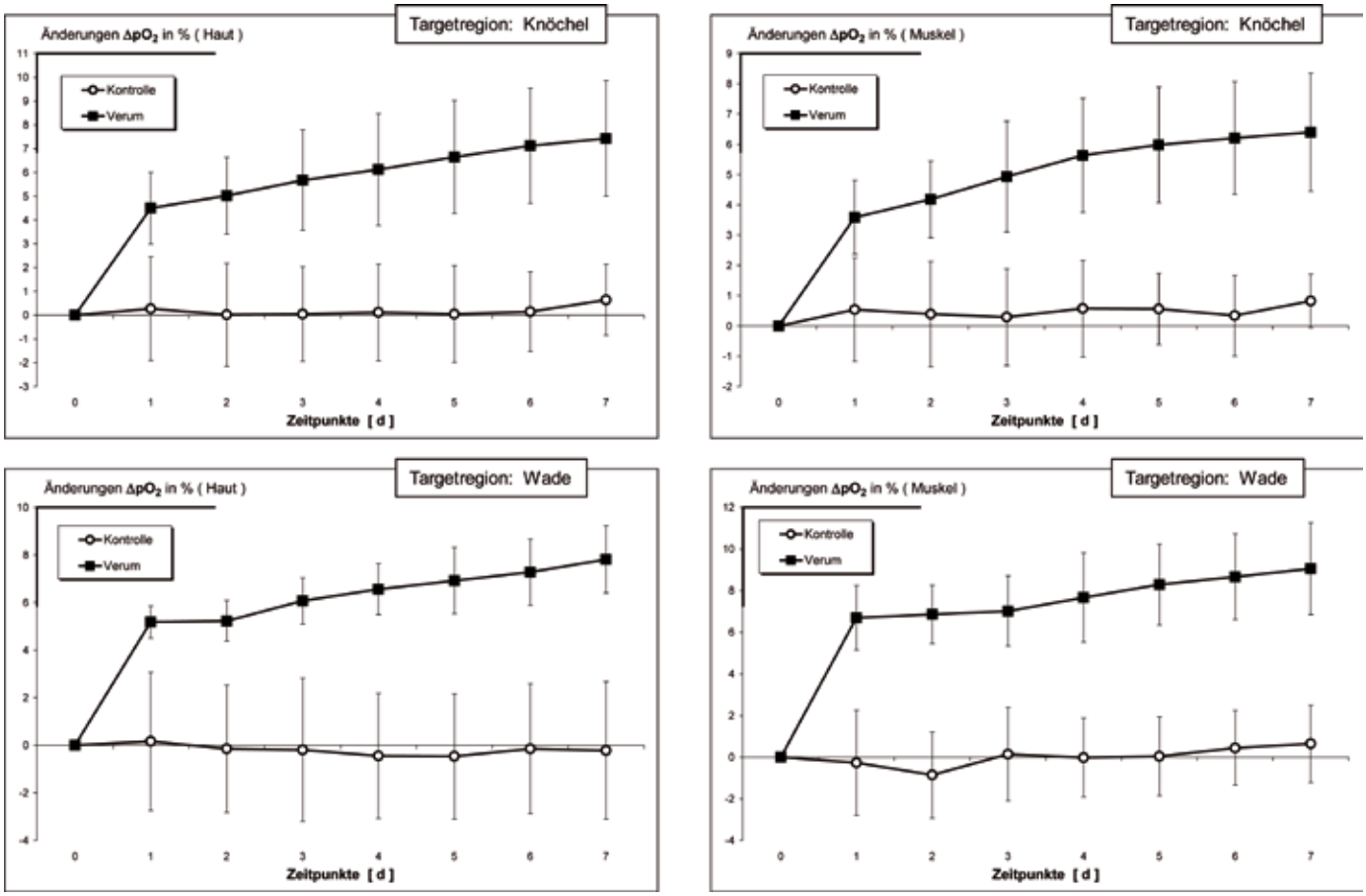


Abb. 6. *Zusammenfassung der Messdaten der 4. Untersuchungsreihe zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 in der linken Knöchelregion und in der linken Wade (Mittelwerte und Standardabweichungen) Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten Messzeitpunkte:*
0. Tag (Ausgangswerte), 1. bis 7. Tag

Strahlung, die von der Hautoberfläche an die Umgebung abgegeben wird sind: Aktivitäten des Nervensystems, bestimmte Aktivitäten der Körperzellen, Aktivitäten der glatten Muskelzellen, welche die Gefäßwände (hier der kleineren) Blutgefäße umgeben u.a. Hierbei handelt es sich um verschiedene elektromagnetische Wellen (Transversalwellen), die von der Hautoberfläche überwiegend als sog. Wärmestrahlung abgegeben werden. An jeder Grenzfläche bzw. Grenzschicht des Testproduktes (F1 bis F4 in Abbildung 1) betreffen diese Wechselwirkungen folgende physikalische Gesetzmäßigkeiten, welche die vom Testprodukt in das Gewebe zurückgestrahlte Energie determinieren : Reflexion, Streuung, Beugung, Brechung, Absorption von Energie (Energieumwandlungen) sowie Interferenzen (Auslöschung, Verstärkung) der verschiedenen Wellenlängenanteile der elektromagnetischen Welle. Von Interesse ist ferner, dass es sich bei der Schicht F2 in der Abbildung 1 nach Angaben des Herstellers um einen organischen Halbleiter handelt (Organischer Halbleiter db-21).

Die ins Gewebe rückgestrahlte Welle ist somit hinsichtlich der Frequenzen, Wellenlängen und Phasenverschiebungen ihrer Anteile von jenen Wellenanteilen etwas verschieden, welche vom Körpergewebe abgestrahlt wurden. Die vom Körper abgestrahlte elektromagnetische Welle stellt ebenso wie die rückgestrahlte Welle ein Gemisch verschiedener Spektralanteile dar.

Hierzu besteht noch enormer Forschungsbedarf. Es ist daher derzeit noch nicht möglich den nachgewiesenen Wirkungen des Testproduktes eindeutige, naturwissenschaftlich begründete Erklärungen zuzuordnen.

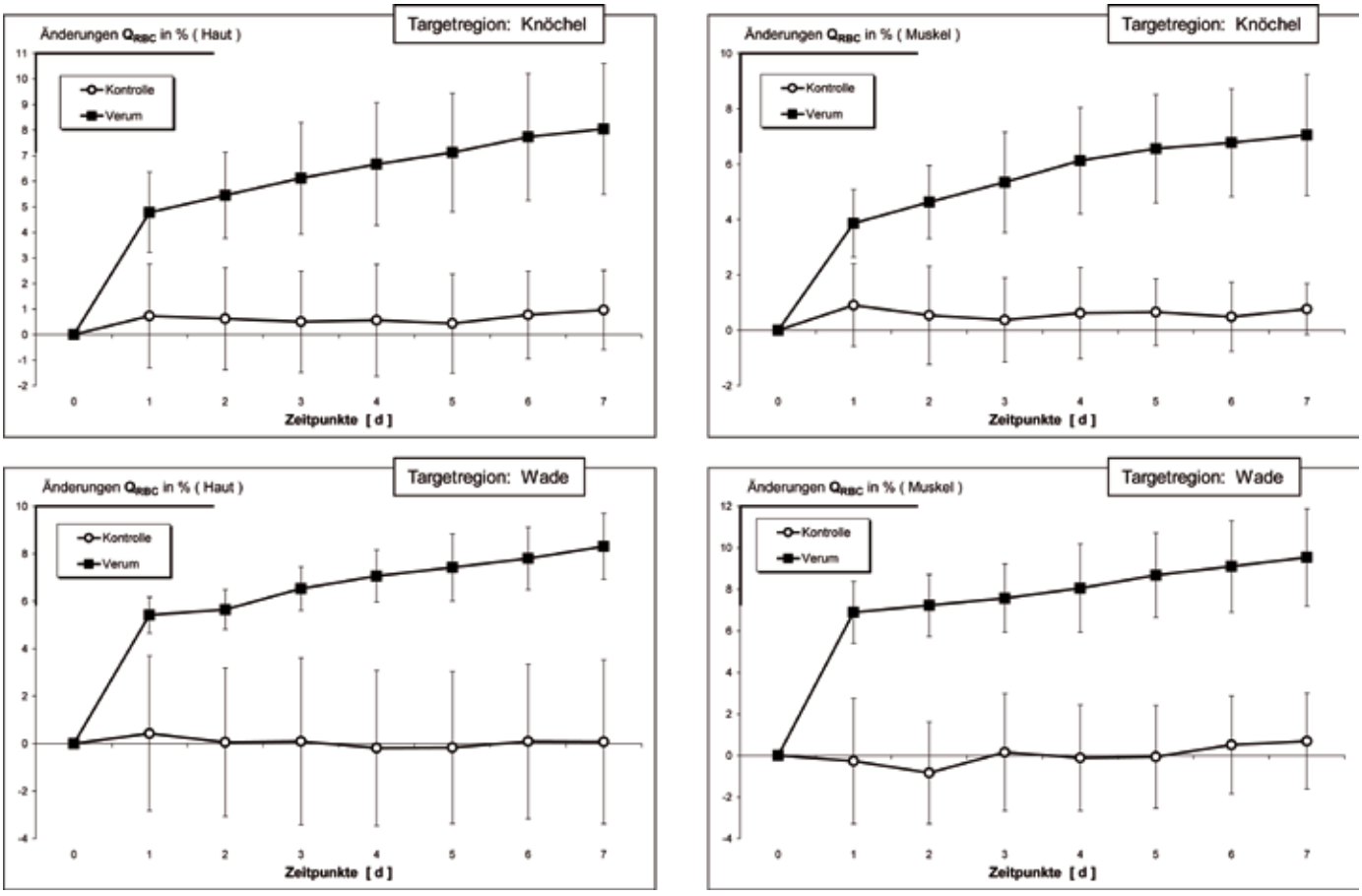


Abb. 7. *Zusammenfassung der Messdaten der 4. Untersuchungsreihe zum Merkmal Strömungsfluss der roten Blutzellen Q_{RBC} in der linken Knöchelregion und in der linken Wade (Mittelwerte und Standardabweichungen) Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten*
Messzeitpunkte:
0. Tag (Ausgangswerte), 1. bis 7. Tag

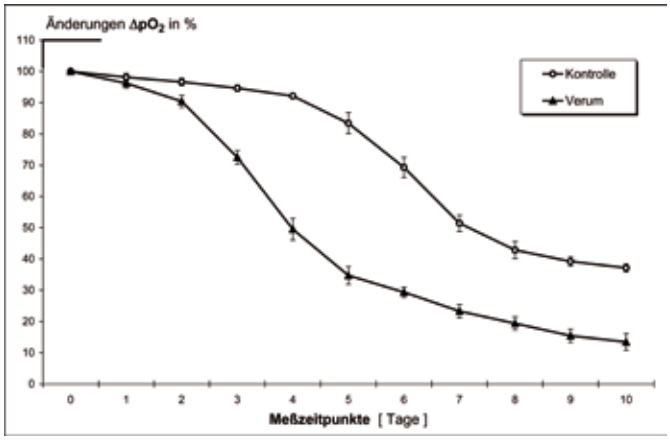


Abb. 8. *Zusammenfassung der Messdaten zum Merkmal venolenseitige Sauerstoffausschöpfung ΔpO_2 als Differenz zwischen Wundrand und unverletztem umgebenden Hautgewebe (Mittelwerte und Standardabweichungen) Die Differenz der Messdaten am 0.Tag (unmittelbar nach dem operativen Eingriff) wurde gleich 100% gesetzt. Angabe als prozentuale Änderungen im Vergleich mit den Ausgangswerten*
Abszisse: Messzeitpunkte 0. Tag (Ausgangswerte), 1. bis 7. Tag

Tabelle 9. *Messdaten zum Merkmal maximale Rautiefe ΔRmax (prozentuale Differenz im Vergleich mit dem im umgebenden Hautgewebe ermittelten Wert, welcher gleich 100% gesetzt wurde) bei der Kontroll-Gruppe und bei der Verum-Gruppe (Mittelwerte und Standardabweichungen).*

	Kontrolle	Verum
Mittelwert	133,1	126,4
Standardabweichung	6,02	4,44

Messdaten zum Merkmal oberflächliche Hauttemperatur ΔT (Differenz in °C zwischen umgebenden unverletzten Hautgewebe und Narbengewebe) bei der Kontroll-Gruppe und bei der Verum-Gruppe (Mittelwerte und Standardabweichungen).

	Kontrolle	Verum
Mittelwert	- 0,6° C	- 0,5° C
Standardabweichung	0,14	0,15

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APTAMERS AS A METHOD OF CORRECTION OF HEMOSTASIS DISORDERS UNDER THE INFLUENCE OF ANTHROPOGENIC FACTORS

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ABSTRACT — Currently, in the treatment of disorders of the hemostasis system, either anticoagulants, or thrombolytics, or antiaggregants, are used. They are used not only separately, but also in various combinations, depending on the patient's condition and clinical indications, which increases the burden on the body. Direct thrombin inhibitors are a promising class of antithrombotic drugs. A corrective effect on the hemostasis of the DNA aptamer, thrombin inhibitor, RE31 was studied after inhalation of natural gas on 62 white mongrel rats. The positive influence of the DNA-aptamer RE31 on the parameters of hemostasis was determined, and in the later periods of exposure to hydrogen sulfide-containing gas the changes after the use of the aptamer statistically significantly differed from those in the control groups. It was also determined that, in comparison with groups exposed to inhalation without subsequent correction, differences in parameters of haemostasis after passage through the vascular system of the lungs were more pronounced in groups of animals treated with the aptamer.

KEYWORDS — laptamer, thrombin, experiment, lungs, hemostasis, natural gas.

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Repeated attempts have been made to penetrate into the essence of the mechanisms of clotting of blood and to select the appropriate arsenal of drugs for the prevention and treatment of such complications. Currently, clinicians use either anticoagulants that inhibit the formation of fibrin (heparin and its derivatives, indirect anticoagulants, direct thrombin inhibitors) or thrombolytics, whose action is directed to the activation of the fibrinolytic blood system and the dissolution of the thrombus (streptokinase, urokinase, tissue plasminogen activator) or antiplatelet agents that inhibit platelet aggregation (aspirin, thienopyridines-ticlid and plavix, Ihib-IIIa glycoprotein antagonists). However, the available preparations for correction of the hemostasis process with a tendency (or presence) of thrombosis are not without drawbacks. The problem of hemostasis requires finding an inhibitor of thrombin, which would be specific in the process of blood clotting, would not cause an allergic reaction, through which it is possible to effectively control this process. The study of DNA-aptamers of thrombin inhibitors is very relevant and promising in terms of the possible use of research results in the development of a set of preventive and curative measures in environmentally harmful production, as well as in patients with bronchopulmonary pathology.

The purpose of the research was to determine the degree of the corrective effect of the DNA-aptamer on changes in the components of the hemostasis system against the background of chronic inhalation of hydrogen sulfide-containing gas.

MATERIALS AND METHODS

The experiment was performed on 62 white mongrel male rats in the autumn-winter period. The content of rats in the vivarium corresponded to international standards [6]. Animals were divided into control and four experimental groups, depending on the duration of the gas inhalation period. The model of gas intoxication was created by placing in the seed chambers, a volume of 200 liters with a controlled composition of an air-gas mixture of 3.4±0.3 mg/m^3 concentration by hydrogen sulfide. Animals were in these conditions for 4 hours, every 5 working days a week. The individuals of the control group were placed in the chamber in a similar time mode, but with the usual air composition. After preliminary narcotization with sodium thiopental (40 mg/kg), by opening the abdominal cavity, the blood for examination was taken from the inferior vena cava, that is, before entering the pulmonary system, and from the abdominal aorta, that is, after circulation in the pulmonary vascular system, volumes of 1.5 ml per disposable insulin syringes with sodium citrate (9:1). Manipulations with the blood being studied were performed according to the recommendations of Z.S. Barkagan and A.P. Momot [1]. Changes in the platelet and coagulation units of the hemostasis system, anticoagulant plasma activity and the state of the fibrinolytic system were recorded with the help of the "Technology – Standard" (Barnaul) kits. The number of platelets was calculated using a light microscope in the Goriaev chamber.

RESULTS OF THE RESEARCH

We have studied the effect on the hemostasis system of the DNA aptamer – RE31. When calculating the number of platelets, no special changes were detected. In the right department, their number was 782±16.7 · 10^9/l, in the left — 789±18.5 · 10^9/l. The induced platelet aggregation in the right part was 21.6±0.4 sec, in the left part — 21.0±0.7 sec. In the study of activated partial thromboplastin time (APTT) after the action of the aptamer, it reached a value in the right part of 29.2±0.9 sec, in the left part it increased to 29.6±0.78 sec, respectively. In the study of prothrombin time, the value in the right part was 28.6±1.5 sec, in the left part it was 29.2±1.7 sec, respectively. Corresponding changes were registered in relation to other studied indicators. Thrombin time in the right part was 36.7±1.0 sec, in the left — 37.4±1.4 sec. The concentration of fibrinogen after application of the aptamer in the right part was 1.58±0.06 g/l, in the left — 1.54±0.05 g/l. And the last parameter was the content of soluble fibrin-monomer complexes. In the right part, their amount reached 2.8±0.06 mg/dl, in the left — 2.7±0.11 mg/dl, respectively. When studying the properties of this aptamer in the control group of animals, we found its favorable pharmacological properties in relation to the parameters of hemostasis. When studying the effect on the hemostasis system of the DNA aptamer – RE31 after 30 days of experimental treatment: APTT in the right part reached a value of 27.4±1.25 sec, in the left part it was 27.6±1.6 sec, respectively. In the study of prothrombin time, the value in the right part was 29.6±1.4 sec, in the left part it was 30.3±1.5 sec. Corresponding changes were registered in relation to other studied indicators. The thrombin time in the right part was 33.9±1.2 sec, in the left 34.5±1.1 sec, respectively. The concentration of fibrinogen in the right part was 1.7±0.09 g/l, in the left — 1.66±0.07 g/l. Adhesive-aggregation function of platelets in the right part of 22.7±1.0 sec, in the left — 22.3±0.9 sec. The number of platelets in the right and left sections was 818±24.4 · 10^9/l and 831±22.6 · 10^9/l, respectively. The content of soluble fibrin-monomer complexes in the right part reached 2.4±0.07 mg/dl, in the left 2.5±0.08 mg/dl, respectively. When introducing the DNA aptamer — RE31 against the backdrop of a 60-day exposure to natural gas, the following changes were recorded. When studying APTT in the right part, it reached 22.7±1.4 sec, in the left part — 22.4±1.7 sec, respectively. In the study of prothrombin time, the value in the right part was 26.6±1.2 sec, in the left part it was 26.9±1.3 sec, respectively. The thrombin time in the right part was 31.2±0.9 sec, in the left part — 31.8±0.7 sec, respectively. The concentration of fibrinogen in the right ventricle was 1.74±0.13 g/l, in the aorta — 1.7±0.1 g/l. Adhesive-aggregation function of platelets in the right part was 22.9±1.1 sec, in the left section — 23.1±1.2 sec, their number in the right and left divisions was respectively 825±26.2 · 10^9/l and 826±20.7 · 10^9/l. The content of soluble fibrin-monomer complexes — in the right part reached 2.7±0.08 mg/dl, in the left — 2.7±0.13 mg/dl, respectively. When introducing the DNA aptamer (RE31) against the backdrop of 90-day exposure to natural gas, the following changes were recorded. In the right part, when studying APTT, it reached a value of 21.4±1.3 sec. In the study of prothrombin time, the value of 22.8±0.8 sec was determined, respectively. The thrombin time was 27.1±1.1 sec. The concentration of fibrinogen was 1.78±0.18 g/l. Adhesive-aggregation function of platelets was 23.4±1.3 sec, their number was 807±22.8 · 10^9/l. The content of soluble fibrin-monomer complexes reached 3.3±0.13 mg/dl, respectively. When studying blood taken from the aorta, after the introduction of RE31: APTT reached a value of 20.9±1.0 sec. In the study of prothrombin time, a value of 22.4±0.9 sec was determined, respectively. Corresponding changes were registered in

relation to other studied indicators. The thrombin time was 27.3±0.9 sec. The concentration of fibrinogen was 1.79±0.08 g/l. Adhesive-aggregation function of platelets was 23.8±1.0 sec, their number was 782±18.5 · 10^9/l. The content of soluble fibrin-monomer complexes reached 3.4±0.15 mg/dl, respectively. When introducing the DNA-aptamer (RE31) against the background of 120-day exposure to natural gas, the following changes in blood from the right ventricle were recorded. In determining the APTT, it reached a value of 17.6±0.9 sec. In the study of prothrombin time, a value of 19.3±0.9 sec was determined, respectively. The thrombin time was 24.4±1.3 sec. The concentration of fibrinogen was 1.8±0.14 g/l. Adhesive-aggregation function of platelets was 24.6±1.2 sec, their number was 757±16.8 · 10^9/l. The content of soluble fibrin-monomer complexes reached 3.8±0.1 mg/dl, respectively. In the study of blood taken from the aorta, the following indices were recorded: APTT after 120 days of experimental exposure reached a value of 17.2±0.7 sec. In the study of prothrombin time, a value of 18.8±0.7 sec was determined. Corresponding changes were registered in relation to other studied indicators. The thrombin time was -24.0±1.2 sec, respectively. The concentration of fibrinogen was 1.82±0.12 g/l. Adhesive-aggregation function of platelets was 25.2±1.4 sec, their number was 760±21.2 · 10^9/l. The content of soluble fibrin-monomer complexes reached 4.0±0.18 mg/dl, respectively.

Thus, the positive influence of the DNA-aptamer RE31 on the parameters of hemostasis was determined, and after 90 and 120 days of chronic exposure to hydrogen sulfide-containing gas, the changes after application of the aptamer were distinct and statistically significantly different from those in the control groups. It was also determined that in the groups of animals that received the aptamer, differences in hemostasis parameters after passing through the vascular system of the lungs were more pronounced compared to the groups subjected to inhalation without subsequent correction. This indicates a decrease in the load on the enzyme systems of the lungs in the background of the application of RE31 and the improvement of lung function for the purification and correction of components of the hemostasis system.

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THE POSSIBILITIES OF MRI-DIAGNOSTICS IN EARLY DETECTION OF SECONDARY FOCAL LESIONS OF THE LIVER

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Introduction. According to the resources [1,2] the liver is one of the organs which is often damaged by the secondary metastatic lesions, particularly when primarily localized in unpaired organs of abdominal cavity, in mammary gland and in lungs. The early detection of the problem makes it possible to use the appropriate methods of therapy.

Aim. To improve the diagnostic possibilities of the early detection of the secondary inflexible liver lesion with the help of the contrastive magnetic resonance scanning (MRI).

Resources and methodology. 82 patients with primary oncological pathology outside of the liver were examined. All the patients had the ultrasound diagnostics of the abdominal organs and MRI (by Magnetom Aera, Siemens, with the magnetic field strength in 1,5T) of the abdominal organs with dynamic contrastive strengthening (the contrastive substance is tomovist); the record of MRI examination includes: T2 COR, T2 AX, T2 fatsat AX, T2 fatsat AX Trigger, T1 Precontrast, T1 arterial, T1 portal, T1 AX FAT SAT Starvibe, T1 Vibe delay, T1 Vibe COR delay.

Research results. The Ultrasound and MRI diagnostics of the abdominal organs, particularly the liver, were done to 82 patients with primary oncologic pathology outside of the liver. After the results of the Ultrasound diagnostics of the liver 14 patients (17%) had single and multiple secondary liver neoplasms, after the results of MRI diagnostics with contrastive strengthening 6 patients had single sections of pathological defeat and 12 patients had multiple secondary neoplasms (total 22%). According to the results of the Ultrasound diagnostics among these patients in 4 cases the focal lesion wasn't found, and according to the MRI diagnostics – the volumetric neoplasms of the liver were found.

Conclusion. The Method of MRI scanning with contrastive strengthening is the most effective in the diagnosis of the early detection of the secondary focal liver lesion.

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THE DYNAMICS OF CHANGES IN ENDOTHELIAL FUNCTION IN PATIENTS WITH IMPLANTATION OF SINGLE-CHAMBER PACEMAKER

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Endothelial function (EF) plays an important role in maintaining adequate blood flow in vital organs such as the brain, myocardium, liver. The deterioration of endothelial function observed in patients with various disorders of AV conduction. Main treatment is to install a permanent pacemaker (PP) in these conduction disturbances. Implantation single chamber PP (66,3%) is the main distribution at present in Russia. Setting PP leads to ventricular dyssynchrony influencing the magnitude of cardiac output (CO) (1, 2). It is known that endothelial function is provided adequate shear stress, with a decrease of SV, the extent of recent changes, and is likely to reduce the EF.

Aims. To estimate the initial state of endothelial function and its change with the installation of single-chamber pacemaker after 2 months.

Materials and methods. The study included 20 patients with an average age of 70.1 ± 12.9 years, with the presence of AV blockade II–III degree, which implanted a single chamber PP. Exclusion criteria from the study were: large-focal myocardial damage, atrial fibrillation, cardiomyopathy, congenital and acquired heart defects. The brachial artery (BA) was studied by ultrasonic duplex scanning on the unit 690 Toshiba–Aplio XG (Japan). Patients were mangalica test with assessment of endothelium-dependent vasodilation (dilatation) according to the classical method before surgery and 2 months after implantation PP.

The results obtained. Assessment of the internal diameter of the BA revealed that the source he was 3.74±0.65 mm, after implantation of PP after 2 months, the diameter decreased to 3.53±0.8 mm. The decrease in the sectional area of the BA were also noted. It was 0,14±0,05 cm^2 source , and was 0.1±0,04 cm^2 after 2 months , indicating a decline of 28.57%. Perhaps these changes in the internal diameter of the vessel, the cross sectional area testified about the decrease in cardiac left ventricular ejection, which was accompanied by a reflex contraction of the lumen of the vessel. Maximum velocity (V_{max}) was estimated, which source made up 66.78± of 20.74 cm/sec, and increased to 73,96±14,53 cm/s after 2 months. This was due to the reduction of diameter and cross-sectional area of the BA.

Parameter endothelium dependent vasodilation was decreased as observed during the tests. So, setting the initial dilatation was 6.67±4,54% of patients, within 2 months of the specified parameter has decreased to 5.57±2.19%, signifying a deterioration of EF, associated probably with ventricular dyssynchrony.

Conclusions. The deterioration of endothelial function observed in patients with implantation of single-chamber PP, which is manifested by decrease in endothelium dependent vasodilatation. This decrease is probably connected with the change in CO, a decrease in shear stress, thereby reducing the diameter, cross-sectional area BA, which leads to an increase of maximum flow velocity.

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USE OF MUCOFALK IN COMPLEX THERAPY OF PATIENTS WITH CHRONIC KIDNEY DISEASE ON PERITONEAL DIALYSIS

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Today, chronic kidney disease (CKD) has been recognized as a pandemic of 21th century because of the high frequency of occurrence, the steady progressing course and the development of a large number of complications. Therapy of the terminal stage of CKD consists of renal replacement therapy (RRT) — dialysis and/or kidney transplantation — and treatment of medicines such as antihypertensive drugs, statins, calcium preparations, phosphate binding agents, ketoanalogs of essential amino acids. Nowadays, one of the promising areas of CKD therapy is considered drugs that normalize gut microbiota, such as pre-, pro-, sim-, syn-, metabiotics.

Aim of the study was to assess the effectiveness of the use of prebiotics Mucofalk for 1 month to nitrogen metabolism and gut microbiota of patients with CKD on peritoneal dialysis (PD).

Materials and methods. The study involved 60 patients who received PD, without severe concomitant somatic pathology, divided into 2 groups: the first group received Mucofalk in therapy, the second group received standard treatment comparable by sex and age (43.2±11,5 years). There were biochemical analysis of blood (urea, creatinine) and analysis of feces for gut microbiota by real-time polymerase chain reaction (PCR-RV) with fluorescent detection.

Results. Before the start of therapy, the mean creatinine of patients of the 1st group was 618±196 μmol/l, urea — 19,1±4,5 mmol / l, of the second group — 648±188 μmol/l and 18,8±4,7mM/L with p (DA) <0.001, after a month of treatment, the patients of the 1st group had a decrease in creatinine — 591±192 μmol/l, and urea — 18.0±4.0 mmol/l, and The 2nd tendency was observed to increase the creatinine — 665±186 μmol/l and urea — 21.3±4.8 mmol/l with p (DA) <0.001. When analyzing the gut microbiota as total bacterial mass (12.3 [11.9, 12.5] log CFU/L), *Lactobacillus spp.* (6.5 [5.6, 7.3] log CFU/l), *Bifidobacterium spp.* (8.5 [8.0, 9.8] log CFU/L), *E. coli* (7.0 [6.3, 7.6] log CFU/L), *E. coli enteropathogenic* (8.5 [8.3, 9.5] log CFU/L), *Enterobacter/ Citrobacter* (9.2 [8.6, 9.5] log CFU/L), *Cl. perfringens* (detection in 30% of patients), the initial values of which before the course of treatment were approximately the same in both groups. After a month of therapy, the patients of the 1st group had an improvement in the form of a decrease in the total bacterial mass (12.0 [11,6; 12,3] log CFU/L), *E. coli enteropathogenic* (5.5 [5.0, 6.0] log CFU/L), *Enterobacter/ Citrobacter* (5.2 [5.0, 5.9] log CFU/L), increase of *Lactobacillus spp.* (7.8 [7.6, 8.6] log CFU/L), *Bifidobacterium spp.* (9.7 [9.3, 10.3] log CFU/L) and *E. coli* (8.3 [7.8, 8.5] log CFU/L), the absence of *Cl. perfringens*, whereas the patients of the 2nd group for p (DA) <0.001. Thus, Mucofalk beneficially affects not only the state of gut microbiota but also the nitrogen metabolism.

Conclusions. Prebiotic Mukofalk is effective in the complex treatment of patients with CKD on PD and requires inclusion in the management of such patients.

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OPTIMIZATION OF THERAPEUTIC DRUG MONITORING FOR PATIENTS WITH HEART TRANSPLANTATION

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Everolimus is an immunosuppressant widely used in clinical practice for the prevention of transplant rejection in adult recipients. The narrow therapeutic range of concentrations and the high variability of the pharmacokinetic parameters of the drug require constant monitoring its blood concentration.

The purpose of the study was to develop reliable, selective, sensitive and reproducible technique for determining everolimus in human whole blood by high performance liquid chromatography (HPLC) method with mass spectrometric detection.

Materials and methods. The study was performed using a high performance liquid chromatograph "LC 1260 Infinity" (Agilent, USA) with mass spectrometric detector "TripleQuard 6460" and the ionization system "Agilen Jet Stream – electrospray" using pharmacological substances "Everolimus" and "Everolimus–d4".Calibration and control samples at 1; 3; 5; 7; 9; 11; 13; 15 ng/ml were prepared from whole blood of healthy donors by adding equal volumes of concentrated solutions of everolimus in methanol and Everolimus–d4 as internal standard, to the intact blood.

Results. At the stage of development of technique the sample preparation and implementation of the study protocol was picked up.

Chromatographic separation: the amount of input — 5 mcl; mobile phase: A — 100 mM ammonium formate solution in water containing 0.1% formic acid; B — 100 mM solution of ammonium formate in methanol containing 0.1% formic acid; isocratic — elution mode; flow rate — 0.4 ml/min.

Ass spectrometry Settings: Scan mode — MRM (monitoring given ion reactions), MRM transition"everolimus" — (975.6 - 908.5); MRM transition"everolimus–d4" — (979.6- 912.5).

Data processing: software — Agilent Technologies Mass Hunter B 07.00.

Validation of analytical methods is performed. To evaluate the selectivity of the method we analyzed intact blood sample not containing the analyte of 6 different sources. Sample preparation and sample analysis were performed in the conditions described above.

The inspection results are satisfactory, as the mass chromatograms had no peaks at specified crossings masses with signal/noise ratio greater than 3:1.

Evaluation of reproducibility is made basing on the results of model blood samples analysis at three concentration levels of 10 repetitions (reps required - not less than five). The coefficient of variation (RSD) for the lower limit concentration was — 9.2%; RSD for the average level of concentration was — 3.7%; RSD for a high level of concentration — 2.1%.

The sensitivity of the method was 0.3 ng/mL. The linear range of the method was 1–15 ng/mL, MSE> 0.999. The lower limit of detection — 1 ng/ml. Reproducibility, precision and accuracy is achieved over the entire range of concentrations. Concentration determination method is the method of internal standard.

The results of checking the correctness of the results have been declared admissible, since the measurement error was less than 15% and for the lower limit of quantification was not higher than 20%.

Thus, the characteristics of the technique correspond to the eligibility criteria of the validated bioanalytical method.

This technique has been successfully applied for the determination of everolimus in 50 whole blood samples from 10 patients.

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PATHOGENETIC APPROACH TO INTRA-ABDOMINAL HYPERTENSION MANAGEMENT IN CASE OF INTESTINAL OBSTRUCTION

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The aim of the research is to study functional disorders in patients with acute intestinal obstruction on different levels of intra-abdominal hypertension and to use the results of the study to perform the surgical treatment of such patients more effectively.

Materials and Methods. The clinical material includes the analysis of treatment results of 86 patients with adhesive and obturative acute intestinal obstruction (AIO). All the patients had laboratory and instrumental examinations, vegetative index of Kerdo and leukocyte index of intoxication were calculated, oncotic pressure and intra-abdominal pressure were measured. All the patients with obturative AIO underwent the surgery, 63% of the patients with adhesive AIO underwent the surgery and 37% of the patients received conservative treatment.

Results and Discussion. The evaluation of the vegetative status revealed that sympathetic influences dominated in all the patients with AIO at the time of hospitalization. This fact indicates the adequate activation of compensatory mechanisms in the body. There was approximately the same number of patients with vagotonia and eutonia. The abdominal obstruction caused the rise in intra-abdominal pressure and the development of paresis of the intestine, the appearance of exudate in the abdominal cavity and, as a consequence, hypoproteinemia. The most evident hypoproteinemia (59.8±2.5 g/l) was found in the patients with obturative AIO and it was considerably lower ($p<0.05$) in comparison with the patients with adhesive AIO (63.9±2.3 g/l). Consequently, AIO (19.8 ± 1.3 mm Hg) was reliably ($p<0.05$) lower in the patients with obturative AIO in comparison with the patients with adhesive AIO (25±1.2 mm Hg). So, the amount of exudate was reliably ($p <0.05$) increased (335.7±43.8 ml) in case of obturative AIO in comparison with adhesive AIO (157.4±29.4 ml). Hypoproteinemia and hypoionia contribute to water balance disorders, the development of hypovolemia, hypoperfusion, and a decrease in the rate of diuresis. In case of obturative AIO diuresis was below the norm (750±95.7 ml/day) in 34.4% of patients. In case of adhesive AIO diuresis was below the norm (800±129.4 ml/day) in 18.5% of the patients.

An important role in the growth of exudate and the disturbance of water metabolism in the body is played by the inflammation of the intestinal wall. Leukocyte index of intoxication in the patients with obturative AIO was reliably ($p<0.05$) higher (8.43) than in the patients with adhesive AIO (5.79). As a rule, the pathogenesis of system and organ dysfunctions is determined by intra-abdominal hypertension syndrome. The level of intra-abdominal tension increased above the norm (11.8±0.1 mm Hg) in 63% of the patients with adhesive IO, which was the reason for undergoing surgery. All the patients with obturative IO had the increased level of intra-abdominal tension (12.4±0.2 mm Hg) which indicates the first stage of intra-abdominal hypertension. Besides, 3.4% of the patients developed fecal peritonitis during the treatment.

Conclusion. Pathologic changes of organs and systems are most evident in case of obturative IO. It leads to the conclusion that the tactics of the treatment must include the early diagnostics of the pathology in the abdominal cavity when the level of intra-abdominal tension is measured and a prompt surgery is performed. But in case of adhesive AIO the tactics of conservative treatment must be the priority as pathological changes in the body are minimal and often caused by postoperative adhesion process.

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MATRIX METALLOPROTEINASE-9 (MMP-9) CORRELATES WITH THE DEGREE OF PAPILLARY THYROID CARCINOMA (PTC)

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In cancer research, behavior and prognosis matrix metalloproteinases (MMPs), a family of zinc-dependent endopeptidases with the capacity to degrade extracellular matrix proteins and basement membranes, is proved to play an important role in multiple stages of cancer progression and metastasis. [1]. Among the MMPs, a subset called gelatinase, consisting of MMP-2 (gelatinase A) and MMP-9 (gelatinase B), has gained the most attention of studies on the acquisition of invasive and metastatic tumor properties, as they could degrade collagen IV, which is the major component of the basement membrane.

In thyroid diseases, much evidence demonstrated that MMP-9 is overexpressed in thyroid carcinoma (TC), especially in PTC, when compared to the benign tumor and normal tissues, and the active MMP-9 contributes to the development and metastasis of TC [2, 3].

Considering above mentioned, we have studied 22 cases of PTC, among them 12 — was cases with soft tissue metastasis in the neck and 10 — multifocal with capsular invasion.

According histological (H&E) and immunohistochemical data, it was shown MMP-9 strong diffuse activity (expression) into tumor parenchyma with neck soft tissue metastasis versus of multinodular lesion showing only capsular invasion.

Statistic also suggest that MMp-9 is more appliable for accuracy diagnosis of metastatic activity of tumor cells and aggressive biological behavior.

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SKIN REACTION ON HPV INFECCHIONS

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Introduction. Despite the huge number of studies on HPV infection, the development of HPV prevention in women of different age groups, the issue of early detection of carcinogenesis in the structures of the female reproductive system have not been solved yet [1–9]. Moreover, 98% spontaneously recover without treatment HPV — infection suggest some speculative to get vaccinated, and the lack of comprehensive evidence that certain strains are more common against cancer of the cervix is more pathogenic than others. Not resolved the issue, on which the depth of contamination in the epithelial layer of the virus [15, 19]. Given that about 30% of women are infected and have symptoms of the virus-genital warts, the relevance of the study of mucosal immune homeostasis of the cervix is extremely high.

The purpose of the study. Our research is devoted to the study of immune homeostasis mucous membrane of the cervix of women and the interaction of cells with different cluster immune phagocytic level of differentiation in the transition zone of stratified squamous epithelium of the cervix in a single-layer cylindrical.

Methods. The paper material used mucous membrane of the cervix in women aged 18 to 78 years. For clinical and patient consent is extracted material lining the cervix against papilloma warts. Additionally performed PCR-reaction to the identification and proof of strains of HPV. Immunohistochemistry to detect CD4, CD8, CD10, CD68, CD163, CD204 made phenotyping of immune cells and analyzed their quantitative relations, especially the topography of immune cells in PVH. Studied for comparison composition and topography immunocytes with PVH human skin. Analysis of the results was performed using a microscope Olympus BX51, illustrations derived from the digital camera CD x 25, the statistical treatment of the material is produced using proprietary software by Olympus.

Results and discussion. We found that in the lamina propria mucosa of the cervical canal and papillary dermis identified CD phenotypes: CD4, CD8, CD10, CD68, CD163, CD204. We observed that infection with papilloma CD68 antigen presenting cells are identified in large numbers only in the lamina propria of the mucous membrane, and completely absent in the epithelial plate. This indicates that the papilloma infection one of the key moments in the pathogenesis of dysgenesis and disruption recovery reservoir may be a perversion antigen presentation and subsequent immune cell interactions [10, 13, 20].

Conclusion. The mucous membrane of the cervix and the human skin with PVH violation stroke physiological regulation and the appearance of growths in the form of warts and genital warts due to a violation of antigen presentation CD68, their position in the underlying epithelium, connective tissue and the complete lack of epithelial layers. Our data are consistent with the data of other authors [11, 12, 14, 16–18].

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LEFT VENTRICULAR STIFFNESS AND CENTRAL BLOOD PRESSURE IN PATIENTS WITH DIASTOLIC DYSFUNCTION IN DIFFERENT AGE GROUPS

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Introduction. Heart failure is the world's most widespread cardiovascular disease. In recent years, many studies of pathophysiology of heart failure with preserved ejection fraction (HFpEF) were published. These studies show that that diastolic dysfunction (DD) and arterial wall stiffness play an important role in the development of HFpEF [1,2].

Objective. To evaluate arterial wall stiffness, central blood pressure and myocardial relaxation and left ventricular (LV) filling pressure in patients with DD in different age groups.

Materials and Methods. 140 patients (61 male and 79 female), aged from 20 to 80 yrs (mean age 50.6±16.8 yrs), with arterial hypertension, obesity, diabetes mellitus and chronic renal disease were enrolled in the study. In all patients, echocardiography was performed to evaluate the DD. M-mode, B-mode, pulse wave Doppler and tissue Doppler were used to calculate the velocities and ratio of early and late LV diastolic filling (E/A), the ratio of early LV diastolic filling and diastolic mitral annulus velocity (E/e') and the amplitude of the aortic root excursion (cm). Oscillometry was performed to evaluate the central systolic blood pressure (cSBP), central pulse blood pressure (cPBP) and aortic augmentation index (Aix).

Results. The patients were divided into 6 age groups. The first group included 25 patients aged from 20 to 29 yrs (mean age 21.8±1.5 yrs). The second group included 12 patients aged from 30 to 39 yrs (mean age 356±2.6 yrs). The third group included 16 patients aged from 40 to 49 yrs (mean age 45.6±2.2 yrs). The fourth group included 31 patients aged from 50 to 59 yrs (mean age 54.4±2.6 yrs). The fifth group included 34 patients aged from 60 to 69 yrs (mean age 62.9±2.9 yrs), and the sixth group included 22 patients aged over 70 yrs (mean age 74.0±3.9 yrs). The results of the study illustrate that both mitral annulus velocity and aortic root excursion decrease with age. The velocity of e' in first and second groups was normal – 0.10±0.02 m/sec and 0.08±0.02 m/sec, resp., and the amplitude of the aortic root excursion was 1.3±0.2 m/sec и 1.1±0.2 m/sec, resp. The results in the following groups showed the progressive decrease of e' ($p<0.0001$): in the third and fourth groups, e' was 0.07±0.1 m/sec, in the fifth group – 0.06±0.01 m/sec, and in the sixth group – 0.05±0.01 m/sec. E/e' did not increase with age: in the first group, it was 6.8±1.5, in the second group – 10.7±2.5, in the third group – 12.3±2.5, in the fourth group – 10.6±2.9, in the fifth group – 13.3±2.2, and in the sixth group – 12.2±2.2. This may be explained by the fact that all patients had different stage of arterial hypertension. cSBP values progressively increased in all groups: in the first group, cSBP was 125.3±11 mmHg, in the second group – 125.2±11 mmHg, in the third group – 127.6±8.0 mmHg, in the fourth group – 128.9±9.0 mmHg, in the fifth group – 132.6±7.0 mmHg, and in the sixth group – 131.9±7.5 mmHg. There was no significant difference between cPBP values in different groups: in the first group, cPBP was 53.6±8.3 mmHg, in the second group – 56.3±8.5 mmHg, in the third group – 57.5±5.9 mmHg, in the fourth group – 61.0±7.3 mmHg, in the fifth group – 63.3±6.3 mmHg, and in the sixth group – 73.5±6.9 mmHg. Aortic Aix also progressively increased in each group. In the first group, it was -7.26±2.4%, in the second group – -5.3±2.1%, in the third group – -4.7±2.7%, in the fourth group – -1.9±0.9%, in the fifth group – -1.2±1.1%, and in the sixth group – -0.1±1.2% ($p<0.0001$).

Conclusion. The study shows that both central blood pressure and left ventricular myocardial stiffness increase with age.

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THE ROLE OF PREBIOTICS IN ENHANCING THE EFFECTIVENESS OF ANTIBIOTIC THERAPY FOR ACNE

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Acne is one of the most common diseases of human skin. Acne treatment is carried out depending on severity and include systemic and topical therapy, with correction of the concomitant symptoms of chronic diseases. Distinguish mild, moderate and severe and very severe acne. According to the National recommendations 2015 the first-line drugs in the treatment of severe and very severe form of acne are also systemic retinoids and drugs of the second and third lines of systemic antibacterial drugs. Side effects in the treatment of antibacterial drugs was observed in resistant P.acnes. and intestinal microbiota changes.

The aim of our work to study the effect of prebiotic (drug, Zakofalk) on the tolerability and efficacy of systemic antibiotic therapy of acne and prevent the development of antibioticassociated diarrhea (and/or dysbiosis) in the treatment of acne of different severity.

Materials and methods. The study involved 45 patients aged from 18 to 37 years, with acne of moderate severity, as confirmed by clinical, laboratory and instrumental methods of examination. All patients were divided into two groups: the core team (CT)-25 patients treated with basic therapy in the form of doxycycline 100 mg a day orally with a total duration of therapy 8 weeks on the background of the drug, Zakofalk in the dosage regimen 1 tab 3 times a day, and the comparison group (HS) of 20 persons receiving only basic therapy. Each group was conducted by physical examination before and after treatment: medical history, clinical analysis of blood (AS), blood biochemical parameters (total protein, C-reactive protein, ALT, AST, alkaline phosphatase, GGTP, amylase, lipase, glucose, total cholesterol), lipid profile, urine analysis, ultrasound examination of abdominal cavity organs, PCR of feces for dysbiosis. Clinical evaluation of acne therapy were conducted based on the following criteria: severity of erythema, infiltration on a 4-point scale (0 – none; 1 – mild; 2 – expressed; 3 – pronounced); index of the clinical course (severity index), as measured by 4-point system from 0 to 3 points (0 – the number of comedones, papulopustules to 5; 1 is the number of comedones and papulopustules from 5 to 10; 2 is the number of comedones and papulopustules – 10–20; 3 – the number of comedones and papulopustules more than 20). The sum of all the points expressed in the General account (OS), the maximum number is 9. The registration of all parameters was performed before treatment, then weekly until the end of therapy. The observation period for the patients was 8 weeks.

Results. After 8 weeks in both groups showed regression of the erythema, reaching the lowest values in all methods of treatment: EXHAUST from 2.4 to 0.6; in the HS – from 2.5 to 0.8 by the end of 8 weeks of treatment. Regression of the infiltration was more significant in patients in the OG: from 2.3 to 0.5 by the 8th week of treatment, whereas in HS to this date, and its value corresponded to 0.9. The number of inflammatory cells decreased significantly by week 8 in both groups: from 2.4 to 1.0 points; from 2.4 to 1.2 points. A more pronounced therapeutic effect was observed when combined treatment in the EXHAUST gas, the total score decreased from 7.35 to 2.6. In the treatment of antibiotic without the support of the above prebiotic dropped from 7.59 to 3.05. By the end of therapy in patients OG clinical recovery was observed in 65.0±7.8% of patients, significant improvement of 20.0±6.2%, improvement in 10,0±4,6%, without effect – 5,0±2,8%, Only a 5.0±2.8% of the cases were reported the ineffectiveness of treatment, which differed from the results of treatment in GS 7±1,8%. The drug is well tolerated by patients, there was no side effect during treatment. In the group of patients who received conventional therapy, the results were as follows: 54,5±10,4%, 13,7±9,2%, 22,7±10,8%, 9,1±1,8% accordingly, gradation. After 2 weeks of inclusion in the study with repeated survey and inspection of the syndrome of intestinal dyspepsia (bloating, rumbling; loose stools more than 3 times per day), induced the

holding of antibiotic therapy, was observed in 5 patients GS (40%), 3 (15%) of them during the first week of treatment refused further antibiotics. In the study of feces in the initial period is quite pronounced changes in the ratio of representatives of the intestinal microflora were revealed in most patients in both groups in the first place was a marked decrease in bifidobacteria and lactobacilli. After a course of antibiotikoterapii the patients, a significant increase in the number of bifidobacteria and lactobacilli and a significant decrease in the number of pathogenic and conditionally pathogenic bacteria. In the GS drew the attention of the inhibition of microbial growth of representatives of the normal intestinal microflora and an increase in the degree of intestinal dysbiosis.

Conclusions. Thus, the obtained data confirm the negative effect of standard antibiotic therapy of acne on the microbial composition of the intestines. The inclusion of prebiotics in the traditional method of acne treatment, allows to obtain a more pronounced therapeutic effect compared with using only the standard dermatological treatment regimens and achieve more severe patients adherence to treatment.

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OSTEOPATHIC CORRECTION AS A METHOD OF PREVENTION OF GALLSTONE DISEASE

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The aim of the study to study the effect of osteopathic influence on biomechanical and neural disorders and the functional state of the gallbladder in patients.

Materials and methods. Under observation, there were 68 patients with anomalies of the gallbladder and violation of colloidal stability of bile with prospective follow-up from 3 months to 12 months. The study group included 48 patients who underwent osteopathic diagnosis and treatment with frequency of 5–7 sessions. The comparison group consisted of 20 patients treated with the drugs ursodeoxycholic acid for 3 months. Ultrasonographic study was conducted on apparatus "Sonoline Prima LC" firm "Siemens" (Germany), working in real time, using sector and linear transducers 3.5 MHz and 7.5 MHz according to standard methods with the assessment of the size, shape, structure of gall bladder and liver before and after a course of osteopathic influence and homogeneity of bile.

The algorithm of osteopathic diagnosis. Osteopathic diagnosis includes the following tests: fascial listening (global, local), the definition of cranio — sacred synchronicity, the definition of mobility at the level of the cervical, thoracic, lumbar spine, sacrum, the definition of mobility of the thoracic and pelvic diaphragms, the definition of mobility and mailnote of the liver, gallbladder, stomach, duodenum, small intestine and colon, determining whether a voltage and/or pain at the level of the sphincter of Oddi, pyloric stomach, duodeno-analnogo sphincter, ileocecal valve, in the region of the gallbladder, in the course of the common bile duct.

The algorithm of osteopathic impact. In the treatment of patients with padkamenne stage with

cholelithiasis were used techniques of osteopathic correction: soft tissue, fascial, articulatory, visceral, cranial.

Almost all patients of the study group was performed to restore mobility at the level C0/C1, the thoracic diaphragm, correction of dysfunctions of the liver and biliary tract, mobilization of equipment in the small intestine.

Results The study found that all patients revealed functional abnormalities (somatic dysfunction) the global and regional level, including biomechanical, neural and psihofiziologic violations. Regional functional abnormalities manifested on the biomechanical level of the neck, thoracic and lumbar somatic and visceral disorders. At the background of osteopathic correction of dysfunctions were eliminated after a single and after a course of treatments. The results of ultrasound of the gall bladder in patients of the main group the size of the gallbladder accounted for a length of 7.5±1.6 cm, width of 3.3±0.8 cm, with the excesses of the body and neck of gallbladder, with honetmoon bile in the gallbladder different densities displace clots, not giving acoustic shadow. Patients in the comparison group, the size of the gallbladder was made along the length of 7.8±1.7 cm, width is 3.2 ±0.9 cm with the excesses of the body and neck of gallbladder, biliary suspension. At the background of osteopathic correction in patients with biliary sludge are available, the size of the gallbladder decreased compared to the initial length to 4.0±1.7 cm and width of 1.5 ±0.5 cm, the coefficient of discharge was more than 50%, indicating that the increase in contractility of the gall bladder and the effectiveness of treatments. Patients in the comparison group on the background of urotherapy was noted positive dynamics of clinical symptoms and disappearance of biliary sludge, gallbladder had a length of 7.9±1.8 cm and width of 3.4±0.9 cm Ratio emptying of the gallbladder after administration of choleretic Breakfast was less than 45%, indicating hypomotor function of the gallbladder. It follows that ursotherapy effective in biliary sludge, and has no effect on the contractile function of the gallbladder. Thus, integration of the osteopathic treatment in traditional allopathic system for the treatment of biliary disorders contributes to the normalization of the contractility and tone of the gall bladder that can form the basis of prevention of gallstones.

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THE EFFECTS OF REGENERATIVE THERAPY IN PATIENTS WITH CHRONIC HEPATITIS

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To date, the treatment of chronic hepatitis is actual issue of gastroenterology. Despite the development and use of modern medications, the question of progression of fibrosis and development of cirrhosis of the liver, is very serious.

We surveyed 100 patients NAFLD and autoimmune hepatitis. Patients were randomized in two groups. The control group received standard treatment, including drugs ademetionina at a dose of 400 mg/day, patients with autoimmune hepatitis continued immunosuppressive therapy with prednisolone at a dose of 30 mg/day. The study group in addition to basic therapy was carried out introduction the mononuclear fraction of umbilical cord blood from a rate of 1 million Cells per 1 kg of body weight. The follow-up was 12 months. To assess indicators of the effectiveness

of therapy, we have carried out the following studies: Clinical-sky analysis of blood, biochemical analysis of blood, morfologische and immuno-histochemically the study of liver biopsy spec-imens). Performance evaluation of Pro-was carried out using 1, 6, 12 months after the start of therapy.

The results of the study: In the study group experienced a more rapid normalization of syndrome of cytolysis ALT, AST is characterized by the presence of Las in the first month after initiation of therapy, complete normalization of the syndrome of cytolysis and cholestasis marked by a 3-month treatment. In the control group, normalization of indicators of cytolysis and cholestasis was noted by 6 months-TSU after the start of the hepatoprotective and pathogenetic therapy.

We have found that patients in the study group, characterized by the presence of is the increase in the number of T-helper cells (CD 3+, CD 4+) relative indicators-La, also, the reduction of T-cytotoxic lymphocytes, relative and absolute measures, a significant increase in IL-8 in sponta-neous and induced activity in the serum. In the study of liver biopsy specimens revealed a reduc-tion of CD3 T-lymphocytes, CD8 T lymphocytes, and CD68, an increase in T-lymphocytes, which indicates a lowering of inflammatory histio-lymphocytic infiltration of the liver tissue. In the HS from patients, there is maintaining the same level of these indicators, which indicates the degree of inflammation in the liver tissue.

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THE CONCEPT OF CARCINOGENESIS IN VIRAL CONTAMINATION

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Introduction. Despite numerous information on the biology of the virus, ways of infection, pathogenesis, clinical manifestations of infection, HPV infection, the nature and mechanisms of the development of the growth of the structures of the

skin that have been contaminated with the virus are still unknown, and it is also not proven that it is the papillomaviruses that produce starting substances for carcinogenesis [7, 9, 12].

Morphological identity is set against the backdrop of the developing cells of prolonged human papillomavirus infection (HPVI) human blasts skin tumors cells human blood smear, a patient with leukemia [1, 13]. Morphologically and immunohistochemically cells that populate the area damaged, apply to blood stem cells. It was showed dinamics changes structures of the skin on phone HPVI, characterized by the violation of the interaction between the epidermis and the underlying connective tissue, the destruction of the basement membrane, violation of the main differentiation of keratinocytes, the lack of perlatum and granular layers. It is concluded that the identification of progenitor cells in the human skin damage associated with violation of intercellular interactions in the epithelium-mesenchymal tissue [3, 11]. Increased proliferative activity, changing lives main keratinocytes, moving the Effector antigen presenting CD68 in contiguous to skin connective tissue, are inductors factors for migration stem cells leucocytes in area destruction of the skin. Disappearing not only property restitution keratinocyte and epithelial dependent differentiation of young blood. Migration not differentiation cells is the vector of the blood – zone of alteration of epithelial cells, but not vice versa [6, 10]. As a result of insufficient or no differentiation of progenitor blood cells in the epidermis and damage surrounding tissue starts to carcinogenesis. Offered an author's model of carcinogenesis, modifying model Correa (1990). Conclusions based on the results of the work are changing perceptions about the pathogenesis of cancer and provide a new strategy towards finding the earliest diagnosis of carcinogenesis [2, 5]. Also, precise mechanisms of damage to the skin and mucous membranes of human HPV, as well as the origin of tumor cells, have not been established [4]. Cambium of its own tissues, hich has lost the ability to differentiate into mature cells, or cells with a damaged oncogene genome, are the main open questions in the study of tumor cells [8]. Given the high infection rate of the population of HPV, as well as the high risk of cancer on the background of HPV contamination, the relevance of studying the features of the alteration of the skin with prolonged HPV infection is extremely high. We have studied the features of damage to human skin structures in chronic HPV infection in the dynamics of reparative regeneration. Skin biopsies were obtained in accordance with the Helsinki Declaration, fixed according to classical protocols and embedded in paraffin. Sliches and all further processing of the material were performed on the automated equipment of the laboratory of pathomorphology of the Medical University of Niigata (Japan). Identification of immunocompetent cells was carried out according to the same scheme, in spite of different antigen localization in cellular structures: membranes, lysosomes, Golgi complex. Immunohistochemical methods were used to determine CD68 and the intensity of proliferative processes in the epithelial plate was studied by using a marker on the Ki-67 gene protein. Antibodies were used at a dilution of 1:50 and 1:100. The material was analyzed using an Olympus-Bx82 microscope and a digital camera PDx25.

Results and its discussion. We have established that in chronic HPV infection with a disease duration of more than 2 years, in the age group over 45 years, in the skin of some patients after necroticisation of part of the epidermis, both on the surface and in the depth of papillomatous growths, infiltration of blood cells around the zone damage to the tissue. Depletion of CD68 in non-inflammatory papillomas with HPV is associated with a decrease in the level of MIP-3α and E-cadherins of keratinocytes, followed by migration to the inflammation zone of various subsets of DC and cytotoxic T cells. The total apoptosis in the prickly and basal layers of the epidermis is accompanied by an increase in the proliferative activity of basal keratinocytes, and then depletion of the regenerative potential. In addition, leukocyte infiltration, which when HPV infection before 2 years is observed only within the connective tissue of the dermis, is accompanied by its spread beyond the destroyed basement membrane to the epidermis up to the shiny and horny layers, replacing the layer of cambial cells of the epidermis.

Due to the death of keratinocytes of the basal layer and in the absence of differentiation and specialization of apoptotic cells of the spiky epidermis layer, only the shiny and horny layers are preserved, sometimes granular. When an inflammatory infiltrate appears under a shiny layer in combination with the destruction of the basal membrane of the epidermis and the death of basal and prickly cells, they are replaced by blood cells unable to differentiate into effector cells.

Given the tropicity of HPV to the cambial cells of the epidermis, we can conclude that the regenerative potential of stem keratinocytes is depleted, and keratinocyte production of inducers for the maturation of incoming young undifferentiated lymphocytes is stopped.

Therefore, we concluded that, possibly, the dying cambial cells of the epidermis could signal the migration of young undifferentiated blood cells to the area of skin damage, to close the defect, but without performing the function of the destroyed HPV structures.

Differentiation of these cells in the new conditions of contact interactions is absent, at the beginning of reparative regeneration they have only high proliferation - as an adaptation to the damaging effect of HPV. It should be noted that our data are consistent with the data of Susman S, Tomuleasa C, Soritau O, et al. (2012), who found similarity between colon cancer cells and blood cells in leukemia [15]. But these authors, like Warburg (1924) [14], suggested that it was the gene mutations that caused the cambial epithelial cells of the intestinal mucosa tissue to rearrange into cancerous cells. Our findings differ fundamentally from the conclusions of Susman S. et al. (2012), since we believe that the stem cell tumor is performed by blood stem cells as a result of the antigen presentation violation, the initiation of apoptosis of keratinocytes, and then adaptation to the physiological demand of tissue in conditions of impaired reparative regeneration. The absence of an epidermal factor in the differentiation of lymphocytes (ELDIF) in connection with the death of keratinocytes leads first to the appearance of blast cells in the area of damage, and later fibroblast-like cells appear that participate in the structuring of the developing cyst towards the tumor of a more dense tissue organization.

Conclusion. According to many authors, neoplastic transformation is a multi-step process associated with progressive accumulation of damage in DNA reparants in cambial tissue cells, as well as tumor suppressors, oncogenes, growth factors, cell surface receptors, and cell adhesion molecules. It is generally accepted that genetic instability, inactivation of oncosuppressive genes, overexpression of telomerase predispose to early carcinogenesis, while oncogen activation, expression of growth factors, cytokines and angiogenic factors lead to late tumor progression and invasion [8]. In our studies, data have been obtained confirming that in the connective tissue of the human skin in HPV infection the physiological regeneration algorithm, leading to the appearance of sprouting in the form of warts and condylomas, is violated, which is associated with a violation of the antigen presentation of CD68, their migration to the underlying connective tissue against the background of their complete absence in epithelial beds. Peculiarities of the distribution of effector immunocytes CD68 in HPV indicate a violation of antigen presentation in the structures of the human skin and subsequent reduction of control over physiological and reparative regeneration as a whole, which can lead to disruption of cellular interactions in the effector immunocyte system and initiation of the oncogenesis process in the structures of the skin. One of the causes of the disorder is that keratinocytes in the postnatal ontogenesis secrete the epidermal lymphocyte differentiation factor (ELDIF), which inhibits proliferation and stimulates differentiation, specialization and maturation in whole lymphocytes [13], which agrees with our conclusions about the origin of the tumor from young blood cells, migrating to the zone of damage as a result of changes in signals from damaged epithelial cells.

The foregoing allows us to modify the model of carcinogenesis according to P. Correa (1990). The process of oncogenesis in the presumed infectious etiology can be divided into 2 stages: Stage I — changes in local local immune homeostasis — increase in proliferative activity in the case of damaging effects of any etiology (microbial, carcinogenic, hormonal) — metaplasia — infiltration of effector cells of the keratinocyte damage zone — redistribution of APC — apoptosis — death of the cambium (point of no return) — destruction of the basal membrane; II — generalized process in the body — disorders in the hematopoiesis system and immunogenesis — migration of blood stem cells into the area of skin damage — secondary immunodeficiency.

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THE EPITHELIUM BARRIER OF THE GASTROINTESTINAL TRACT IN PATHOLOGY

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Introduction. We investigated *H. pylori* infection in children patients with gastrointestinal diseases in Vladivostok, Far Eastern Russia. In this study, we further investigated the role of *Helicobacter pylori* infection in lactase deficiency pathogenesis in children. In the pediatric fields, secondary and transient lactase deficiency was seen during clinical practice of different gastrointestinal diseases. Many previous studies have shown the mucosal conditions of small intestine and duodenum in secondary lactase deficiency; however, local immune responses in gastrointestinal tract have not been examined [1–10]. Especially, conditions of gastric mucosa and epithelium in different pathogenetic variants of lactase deficiency in infants and children under 3 years have not been well studied. In this study, we investigated roles of *H.pylori* infection and immune responses of gastric mucosa and epithelium in, pathogenetic aspects of lactase deficiency in children under 3 years.

Methods. Sixty-three pediatric patients (age: 5 months to 3 years) with different loss of weight in Regional Clinical Center of Maternity, Vladivostok, Russia, were also included during 2008–2011. All patients were diagnosed as lactase deficiency. Morphological changes of gastrointestinal mucosa were examined by endoscopy and dark field microscopy. *H. pylori* in biopsy specimens was detected by immunostaining. CD4-, CD8-, CD 68-, CD163-, or CD204-positive immune cells in the specimens were detected by immunostaining.

Results. In our previous study, 89.9% of patients (age, 15 to 80 years) were *H. pylori*-positive, regarding the virulence genotype of *H.pylori*, 79.4% were cagA-positive. As for EPIYA motif of cagA, ABC type was the most prevalent and accounted for 73.2%; ABCC type for 14.6%; AB or ABCCC type for 4.9%, and novel AAABC type for 2.4%. No ABD type was detected.

In this study, 95% of children under 3 years with secondary lactase deficiency were *H. pylori*-positive. We have established changes of immune cell; numbers and condition in cellular and humoral immunity according to clinical manifestations of this disease. Increase of proliferative activity of immune cells in epithelial layers and the cells without contact to epithelial wall in mucosa were found. Immunostaining showed the increase of immune cells positive for CD4, CDS, CD 68, CD163, and CD204 in gastrointestinal epithelium in *H. pylori*-positive lactase deficiency patients.

Discussion. In our previous study, *cagA*-positive *H. pylori* mainly belonged to Western type (EPYIA-ABC type) although Vladivostok is geographically located in East Asia.

Present study is the first investigation of lactase deficiency with H. pylori infection in children under 3 years in Vladivostok, Russia. Our data suggest mechanisms of pathogenicity of lactase deficiency under *H. pylori* infection. Our data are also useful for development of immune response algorithm during medication of those patients and for monitoring of morphological condition of gastrointestinal mucosa in children during various pathologic processes associated with malabsorption and lactase deficiency. Further investigation is required to reveal the exact mechanisms of lactase deficiency under *H. pylori* infection.

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THE ROLE OF THE CHANGES IN INTESTINAL MICROBIOTA AND MICROBIOTA EXOMETABOLITES IN THE DEVELOPMENT, COURSE AND PREVENTION OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Relevance. In recent years, non-alcoholic fatty liver disease (NAFLD) is of frequent occurrence and is diagnosed in 37.3% of the Russian population. One of the factors contributing to the development of NAFLD is a disturbance of the qualitative and quantitative composition of the intestinal flora — dysbiosis.

The objective of our study was to determine the effect of disturbances of intestinal micro flora and its metabolites on the development, course, and prevention of NAFLD.

Materials and methods. 25 overweight patients age 45,4±16.2 with NAFLD (with steatosis) were examined. There were included such methods as: questioning, inspection, assessment of life quality (SF-36), clinical and biochemical blood tests, Fibromaks-test, analysis of the metabolome of blood, bacteriological examination of the contents of the colon (PCR-RT), bioimpedance analysis of the component composition of the body and an ultrasound examination of the liver (SPD). All patients took "Gepagard Active": containing essential phospholipids, L-carnitine, and vitamin E. (Eurasian patent № 019268 from 28.02.14), 1 capsule 3 times a day during a meal for 3 months.

Results: All patients were found to have a microbial imbalance (dysbiosis of the colon), expressed as a significant decline in the proportion of Bacteroides. After treatment there was a significant increase from 11.3%±10,6 (media±CO) to 47.6%±28,8 of the total number of microorganisms ($p<0.0001$). It shows the ability of the drug to restore the microbial balance in the large intestine associated with excess body weight and the risk of systemic metabolic disorders. This fact proves the prebiotic effect of the drug (patent RF № 2571495 from 20.12.2015). Metabolic analysis of blood revealed 92 connections (4 connections are associated with the development of NAFLD). After therapy an overall increase in the number of metabolites in the blood was observed. It was achieved due to the mobilization of fatty acids from fat depots, and an increase of the activity of their oxidation in the liver, which was the result of activation of lipolysis in adipose tissue. The level of 3-oxopropionate acid in serum may be a marker of changes of microbial metabolism in the colon during the treatment. All the patients noted a decrease in body mass on average by 10.7%. In addition, the positive dynamics of clinical laboratory indicators was achieved.

Conclusion: All the patients with NAFLD suffered from dysbiosis associated with obesity and systematic metabolic disorders. Gepagard Active optimizes the qualitative and quantitative composition of microflora and its metabolites. It improves the quality of life and the condition of the liver. Furthermore, it reduces excess weight. All these suppress symptoms of NAFLD and prevents its progression.

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PLACE OF TUMOR NECROSIS FACTOR ALPHA AMONG ACUTE PHASE PARAMETERS OF INFLAMMATION IN NONALCOHOLIC FATTY LIVER DISEASE

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Introduction. According to the current model of the pathogenesis of nonalcoholic fatty liver disease (NAFLD), the systemic low-level inflammatory process is the basis of the disease progression, initially caused by macrophage infiltration of visceral adipose tissue [1, 2]. Timely recognition of inflammation is extremely important for the diagnosis of NAFLD, especially for differential diagnostics between its early forms — hepatosteatosis (HS) and steatohepatitis (SH), for the rationale therapy and the prognosis of the disease course [3, 4]. Laboratory markers of inflammation have a different sensitivity in the early forms of NAFLD [1] .

The aim of the study was comparative evaluation of the importance of traditional laboratory parameters of inflammation — leukocyte count, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), fibrinogen and the key proinflammatory cytokine tumor necrosis factor-alpha (TNF-α) in the early forms of NAFLD — in HS and SH.

Materials and methods. A total of 106 patients were examined: 33 — HS (18 — 54.5% of men, 15 — 45.5% of women, aged 52.3 ± 10.6 years) and 73 SH (50–68.5% of men and 23–31.5% of women, at the age of 47.2±11.0 years). The diagnosis of NAFLD was established on the basis of clinical and laboratory data, abdominal ultrasound results, and in some patients – on the histological study of liver biopsy specimens. The concentration of TNF-α in the blood was determined by the method of non-competitive ELISA using the «Human TNFα Platinum ELISA test system»("EBioscience", Austria) and «Sunrise» analyzer («Tecan», Switzerland). The control group consisted of 18 healthy persons: 9 men and 9 women aged 32.6±10.0 years. Statistic processing of the data was conducted with application of Wilcoxon-Mann-Whitney U criterion. Differences were significant at $p<0.05$.

Results. The level of leukocytes in HS was $5.9\pm1.2 \cdot 10^9$/l, in SH — $6.3 \pm 1.4 \cdot 10^9$/l ($p> 0.05$), both indicators did not differ from that in healthy individuals – $6.1\pm0.3 \cdot 10^9$/l ($p> 0.05$). The frequency of leukocyte level increase was higher than the reference value in HS in 3.0% of patients, in SH — in 12.3% of patients ($p< 0.05$).

The level of ESR in HS was 13.3±5.5 mm/h., in SH — 14.9±6.8 mm/h. ($p> 0.05$), and both indicators did not differ significantly from those in healthy subjects — 6.0±2.4 mm/h. ($p >0.05$). The frequency of ESR increase was higher than the reference ERS value in HS — in 21.2%, in SH — in 27.4% of patients ($p>0.05$).

The level of fibrinogen in HS was 3.0±1.2 g/l, in SH — 3.3 ± 0.7 g/L ($p> 0.05$), both indicators did not differ significantly from those in healthy subjects — 2,5 ± 0.5 g/l ($p>0.05$). The frequency of fibrinogen increase was higher than the reference fibrinogen value only in SH — in 13.7% of patients.

The CRP concentration in HS was 3.7±1.0 mg/l, in SH — 10.8±4.9 mg/l ($p <0.05$), both of which were significantly higher than those in healthy subjects — 1.5±0.5 mg/l ($p <0.01$). The frequency of CRP

increase was higher than the reference value in HS in 15.2%, in SH — in 50.7% of patients (p<0.05).

The concentration of TNF-α in HS was 6,0±1,8 pg/ml, in SH — 6,8±2,1 pg/ml (p> 0.05), both of which were significantly different from those in healthy individuals — 3,8±1,1 pg/ml (p <0.05). The frequency of TNF-α increase was higher than the reference value in HS in 63.6% and in SH — in 79.5% of patients (p<0.05).

Conclusion. Thus, TNF-α proved to be a more sensitive indicator of inflammation in comparison with the conventional markers of this syndrome - it significantly increased already at the stage of hepatosteatosis, allowing a timely forecast of the probability of the transformation of steatosis into steatohepatitis and justify therapy.

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FEATURES OF THE DAILY DYNAMICS OF BLOOD PRESSURE IN HYPERTENSIVE PATIENTS DEPENDING ON THE DEGREE OF HEPATIC ENCEPHALOPATHY DYSCIRCULATORY

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Despite the large number of works devoted to the study of the state of the brain in patients with essential hypertension (GB), up to the present time is not the influence of developing disorders of cerebral blood flow on the clinical course of arterial hypertension.

Aim: to study features of the dynamics of HELL during the day a patient of GB at different stages of development DE using the method of daily monitoring of blood pressure (ABPM).

Materials and methods: To address this goal were examined in 150 patients. The ratio of men and women was 53 (35%) : 97 (65%) people. The average age of patients was 58,3±4.7 years. The diagnosis of GB was established in accordance with National guidelines and the European society of cardiology. Thus, patients with HD stage I in the sample was absent, whereas the incidence of stage II hypertension was 75%, and GB III stage — 25%. The degree of AG was determined in accordance with the classification who/ish 1999. The result of the distribution of patients according to the severity of hypertension in 54 patients (26.3%) were identified with its 1 degree, and 74 (49.3%) and 2 in 22 (14.6%) — 3rd degree. Determination of the degree of TE were made based on the neurological examination, as well as analyses of the magnetic resonance imaging of the brain was performed in 12% of patients. Gradation of the severity of the DAE was based on the classification proposed by E. V. Schmidt et al. (1971), E. I. Gusev (1985), by E.I. Burtseva et al. (1993).

1 group comparison (n=45) included patients of stage II hypertension with TE 1 degree. 2 group (n=67) included patients with stage II hypertension and DE 2nd degree. 3 group (n=38), consisted of patients with stage II hypertension and DE 3rd degree. All patients of this group had a documented history of acute ischemic stroke or transient ischemic attack, prescription for at least 9 months. A control group included 30 practically healthy individuals of appropriate study groups by sex and age.

ABPM was carried out using the apparatus "shiller" daytime every 15–20 minutes a night and 30 minutes. Were analyzed: a) average values of systolic blood pressure (SBP) and diastolic blood pressure(DBP) over 24 h, day and night. B) blood pressure variability that represents an estimate of the variance of AD curve circadian rhythm. In) the daily index(SI) or the degree of reduce night blood pressure , defined as the percentage of the night in blood pressure to his daily indicators, highlighting the type of diurnal profile HELL. G) index of time PRESSURE(PI) — indicator of the load pressure on target organs, presented as the percentage of elevated BP measurements in excess of the accepted upper limit of normal(for day — 140/90, for a night of — 120/20 mm. Hg.MT) to the total number of registrations. D) pulse PRESSURE (PAD), diurnal and srednesrochnoi. This index is an independent risk factor for cardiovascular and Cerebro-vascular complications in HD patients, especially older than 60 years.

Survey results: in patients with GB and DE of 1 degree, in comparison with the control, there was a tendency to increased daily GARDEN and revealed the predominance of EVE's GARDEN on DBP (52% and 47%, respectively), the increase of variability of the SAD ($p<0.05$). When assessing the performance of daily monitoring in patients with GB, DE 2, sravneniju with 1 group, revealed a significant increase in the average GARDEN up to 162,4±12.5 mm. Hg.St., fluorescent GARDEN to 172,5±2,7 mm. Hg.St. night GARDEN to 162,3±2.3 mm Hg.St. and a decrease in the average value of C to 5,9±1.6, which reflected the predominant presence of diurnal profile of AD-type non-dipper($p<0.05$). In addition to this, there was an increase in the average values of the indicator of the load of the GARDEN more than 77% and DBP more than 60% in the daytime and at night. Special prognostic value in this group had a high value of blood pressure variability, which was significantly higher than in 1 and 3 groups. So, the variability of day the GARDEN was 17.4±2.3 mm Hg.St, and 1 and 3 groups is 15.3 and 14.7 mm of mercury. St. respectively. In addition, patients GB, DE of 2 degrees was detected the highest numbers of PAD during day and night time is 76.8 mm.RT.St and 76.2 mm of mercury. St. respectively. In patients with GB ДЭ3 extent the average figures of the daily Hell as a whole was comparable with that in group 2. At the same time, we observed a significant predominance of daytime and nighttime DBP more than 100 mm of mercury. St and the decrease in variability compared with the 2 groups. In addition, there was a high EVE in the GARDEN especially at night (over 80%) and the predominance of diurnal profile of AD non-dipper.

Conclusion: Thus, was to identify the relationship between the severity of DE in patients GB and ABPM parameters. The most significant indicators was the extent of the increase in a GARDEN, BP variability, PAD, EVE and the lack of blood pressure reduction at night. The growth changes of cerebral blood flow was noted to increase the AD load n and the target organs, especially the day and night GARDEN. An important feature revealed in patients of group 2 was the presence of the highest rates of PAD in the daytime and at night and blood pressure variability during daytime. The most severe degree of DE was characterized by the largest IV at night.

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CLINICAL AND X-RAY CHARACTERISTICS AND DYNAMICS OF DYSPLASTIC CHANGES IN THE BONE SYSTEM DURING ONTOGENESIS

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In the course of the study, the features of clinical data and radiographic changes in the osteoarticular system of 2078 children in different age periods from 7 days to 18 years were studied. Changes in the spine, joints of the lower extremities and long tubular bones were evaluated. Radiographs were performed in standard projections. MRI and CT studies were performed in 415 children to clarify the morphological changes in the spine and knee joints.

MATERIAL AND METHODS

According to the X-ray characteristics and age-dependent classification of the stages of the postnatal formation of the osteoarticular system by V.I. Sadofieva (1990), the data obtained were divided into 5 groups (Table 1).

RESULTS AND DISCUSSION

Out of 204 examined children of the first group, in 176 (86.3%), asymmetry of the head position was revealed, more often with a right tilt and a turn to the left, a paravertebral muscle strain in the cervical spine, a painful palpation reaction, a tendency to roll back the head and a low muscle tone of the upper and lower limbs. At X-ray examination, there was a lack of structural disturbances, a decrease in the posterior craniocerebral distance due to rotation of the occipital bone, lateralization of the lateral masses of the atlant.

In the second group of 238 children aged 11 months up to 4 years on the roentgenograms of the cervical spine, cervical lordosis was smoothed, kyphosis in the middle section (67%), asymmetry of the atlas's lateral masses (11%), incongruence of the joint at the level of C0–C1–C2 (71%), initial signs of hypermobility. Clinically, this determined the hypotension of the muscles of the lower extremities with the valgus of the knee joints, flat-valgus feet. The hypertension of the calf muscles is noted, the extension of the feet is limited

Table 1. *Distribution of children by age, sex and radiographic signs of functional and structural disorders (N 2078)*

Group	Age	Characteristics	male abs.%	female abs.%	total abs.%
1.	7 days to 10 months	Initial radiographic and functional characteristics of dysplastic development of the spinal column	96 (4,6%)	108 (5,2%)	204 (9,8%)
2.	11 months to 4 years	X-ray manifestations of asymmetry of articulation C1-C2, formation of kyphosis of middle spine	112 (5,4%)	126 (6%)	238 (11,4%)
3.	5–8 years	Initial signs of degenerative-dystrophic changes in the cervical and lumbar spine	231 (11,1%)	223 (10,7%)	454 (21,8%)
4.	9–14 years	Development of structural disorders of the spinal column and initial functional changes in the knee joints	277 (13,3%)	320 (15,4%)	597 (28,7%)
5.	9–14 years	Formation of fixed deformities of the osteoarticular system	223 (10,7%)	362 (17,4%)	585 (28,1%)
Total			939 (45,2%)	1139 54,8%)	2078 (100%)

and the tendency to walk on the toes is limited. In the cervical part, a disruption of rotation, stoop, lumbar hyperlordosis.

In the third group there were 454 children aged 5 to 8 years with dysplastic changes in the musculoskeletal system. Manifestations of pathology at this age were violations of posture, the emergence of vegetative and functional disorders, the growth of the clinic of vegetative-vascular disorders, the pathology of the hip joints in boys and functional disorders in the knee joints, more often in girls. On the roentgenograms of the cervical calving of the spine, degenerative-dystrophic changes of the spinal column, an increase in kyphosis in the middle sections of the cervical spine, deformation of the lateral masses of the atlant, clearly showed signs of incorrect development.

Radiation methods of diagnosis in 97 boys of the main group at the age of 5 to 8 years revealed osteochondropathy of the femoral heads. In 37 children (38.1%), the process was bilateral, otherwise there was a one-sided defeat. In girls, the frequent pathology of the lower limbs was a valgus set of knee joints with internal rotation of the shins and a flat-valgus deformation of the feet. The provoking factor was significant sports loads (training 5-6 times a week for 2–3 hours) and active growth during the period of physiological stretching.

In 597 adolescents aged 9 to 14 years, the main segments of the lesion were various parts of the spine, knee joints. Objectively there was an asthenic physique, a decrease in the muscular tonus of the upper and lower extremities, valgus deviation (10–15°), and internal rotation of the legs (up to 20°), flat-valgus stop, hypermobility of the peripheral joints. The posture has been broken due to the strengthened thoracic kyphosis and lumbar lordosis. Movement in the cervical spine was limited due to rotation in both directions (up to 20-30% of the normal volume of movement).

X-ray patterns in the cervical spine showed asymmetry of the C1–C2 articulation, Kimmery anomaly, saddle-shaped deformation of the atlas's lateral masses, kifosis of the middle section, platipondylia; an increase in kyphosis in the thoracic, scoliosis, wedge deformation of bodies D 6–9, narrowing of intervertebral spaces, subchondral sclerosis; in the lumbar spine, non-growth of the posterior arches L5 and S1, anomalies of tropism, hyperextension of the sacrum.

In the course of the study, radiological changes in the osseous and articular system of 585 adolescents aged 15 to 18 years were revealed. The majority of patients had signs of osteochondropathy of the spinal column, degenerative-dystrophic lesions of the cervical spine, instability of the structures of the knee joints, diseases and deformities of the feet. When X-ray diffraction of the cervical spine in children of the main group, asymmetry of the C1–C2 articulation, kifosing, initial degenerative antheliosis in the spinal-motor segments at the C2–C4 and C4–C6 levels, deformation of the vertebral bodies was found. In the thoracic spine, there are signs of osteochondropathy (Sheyerman-Mau disease) in boys. In the lumbar spine on radiographs and CT data, various diseases and anomalies were identified in the form of non-extension of the posterior arc of L5, scoliosis, and osteochondropathy.

The data presented indicate an increase in pathological structural changes in bone tissue during ontogenesis, increased functional disorders and their severity. As a rule, they have no tendency to self-correction, contributing to the early development of degenerative-dystrophic processes.

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SURGICAL CORRECTION OF DYSPLASTIC COXARTHROSIS AND ENDOPROSTHESIS REPLACEMENT BY APPLYING TITANIUM NICKELIDE IMPLANTS

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INTRODUCTION

Early incidence and rapid progression of advanced dysplastic coxarthrosis has become an emerging trend in modern orthopedics. High bilateral pathology frequency results in life expectancy degeneration and impairments, disabilities and handicaps and further social and psychological adaptation difficulties [2, 3, 6].

Increasing children dysplastic disease frequency of supporting-motor apparatus induces new challenging problems in children surgery — development of both critical pathways and therapeutic approaches for dysplastic hip joint diseases. This article presents the results of early arthroplasty of progressive coxarthrosis by endoprosthesis replacement of hip joint (acetabulofemoral joint), which previously were surgically operated by applying titanium nickelide implants [1, 5].

MATERIALS AND METHODS

Progressive and advanced coxarthrosis course with degenerated-dystrophic manifestations in the hip component and further in femoral head are described in the following clinical case.

Clinical case: 12-year-old patient B was hospitalized in Orthopedics Department, Tomsk University Clinic, 15.12.2008. In-patient history case №4123. On admittance: diagnosis — left dysplastic coxarthrosis 2 degree. Patient examination: limb shortening up to 2 cm., rapid fatigability when supporting on left lower limb and gait disorder – limbing on left leg. Positive Trendelenburg symptom. According to past medical history at 6 Legg-Calve-Perthes disease (LCP) with adverse outcome as hip joint (acetabulofemoral joint) deformation and further dysplastic deformation as dysplastic coxarthrosis. During child growth and development, secondary deformation in hip joint roof and hip head bone dislocation. No established care in Children Out-patient Department and only now the above-mentioned complaints are present in the

patient. Patient B. X-ray of dysplastic coxarthrosis on admittance (fig. 1).

X-ray examination results: dysplastic coxarthrosis 2 degree with hip head bone subluxation, underdeveloped left external acetabular roof edge. АИ — 55°, neck-shaft-angle 130°, left angle of antetorsion — 55°, Wiberg angle 5°, left coating ratio — 0.5, coating index — 4. Pain and discomfort in the left hip joint region occurred 4 months ago when the patient put on weight.

First stage involved operation: overacetabular osteotomy of iliac bone with modeled acetabular implant component of porous titanium nickelide. Body cast for 6 weeks. After removing plaster bandage — standard remedial treatment, including electrotherapy, massage, physiotherapy and Kinesio Taping. Four months after operation — graduated weight bearing on crutches; in five months — walking with cane; and in six months — full weight bearing on operated limb. Examination of patient in a year. Functional capacity of limb — complete rehabilitation, no complaints. Patient B. X-ray of hip joint (acetabulofemoral joint) — one year after operation (fig. 2).

X-ray examination showed formed biocomposite porous bone implant. Complete roof coating. No mobility symptoms of the implant.

Patient examination in 5 years after first applying in hospital and 4 years after first operation at the age of 17 — symptoms of advanced dysplastic coxarthrosis from proximal femoral bone. Patient complained of pronounced pain in hip under axial and static load. After planned hospitalization endoprosthesis replacement of operated joint was performed. In forming socket "bed" the surgical exploration of joint titanium nickelide implant and acetabulum companion revealed complete biointegration (bone tissue ingrowth) without signs of metallosis (which could be observed in most surgical exploration cases of other implants) (fig. 3).

After inserting implant cup and subtrochanteric osteotomy, prosthetic implant was fixed. It should be noted that hip stem component of prosthethic implant, supporting the main load, is from porous titanium nickelide, as a result of biointegration, prevents micromobility and periprosthetic fracture. Appearance of operative wound after complete prosthethic implant insertion (fig. 4).

Surgical wound is stitched layer-by-layer 10 days after operative treatment. After remedial treatment (electrotherapy, massage, physiotherapy and Kinesio Taping) the patient was allowed graduated weight bearing on crutches; in two months — walking with cane; and in three months — full weight bearing on operated limb. Examination of patient in a year. Functional capacity of limb- complete rehabilitation, no complaints. Patient B. X-ray of hip joint (acetabulofemoral joint) — one year after operation (fig. 5).

RESULTS AND DISCUSSION

X-ray examination showed formed biocomposite porous bone implant. This is good plastic and support material to form the socket "bed" for prosthethic implant. The endosteal response to porous hip component of prosthethic implant exhibits its biointegration.

According to Harris Hip Scope the results are 61 and 90 scores before and after the operations. According to Luboshyce–Mattis–Schwarzberg clinical scale the treatment outcome is 4.3 out 5, which could be considered to be a good result. Dynamic factor is more than 1, which corresponds to the parameter "improvement." Recommendation – case follow-up at orthopedist.

CONCLUSIONS

Significant and successful treatment results of dysplastic coxarthrosis only in the case if the surgical correction of advanced disease is in-time and even, to some extent, upstream surgery. This could be based more on patient complaints than on X-ray patterns, as soft tissue component of hip joint (acetabulofemoral joint) retains its elastic properties to the end of the first adolescence period. In the case of advance malignant current coxarthrosis and formed iliac dislocation without adequate load on the joint surfaces, mineral metabolism in joint components progressively decreases under osteodystrophy aggravation, which, in its turn, completes the progressive coxarthrosis pathway [3, 4, 6].

Rotating transposition of acetabulum is useless as this would not provide the congruence of hip joint (acetabulofemoral joint) components, especially under advanced dysplastic coxarthrosis. According to reference review data it has been noted that to the end of the first adolescence period the formation of he acetabulum is close to normal [3]. Patients, in the second adolescence period under severe acute dysplastic coxarthrosis, would probably show unacceptable results.

It is considered that the most appropriate method of modeling missing acetabular roof is osteotomy of iliac bone with acetabular implant component of porous titanium nickelide, which, in its turn, provides complete coating of hip head bone without affecting the epiphysial plate, reliable fixation of left external acetabular roof edge and improve bone regeneration within osteotomy region.

Graduated axial load during post-operation period improves osteointegration from the bone bed in the porous implant. Applying the above-mentioned correction method for children coxarthrosis the anatomical relationships of the hip joint (acetabulofemoral joint) are persistent This enhances possible further endoprosthesis replacement of hip joint (acetabulofemoral joint) after closing the epiphysial plate under favorable conditions,

Fig. 1. *Patient B. X-ray of dysplastic coxarthrosis on admittance*

Fig. 2. *Patient B. X-ray of hip joint (acetabulofemoral joint) — one year after operation*

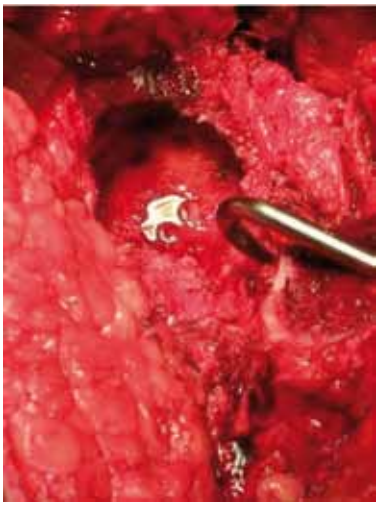

Fig. 3. *Surgical exploration of titanium nickelide implant and acetabulum companion when inserting prosthethic cup implant*

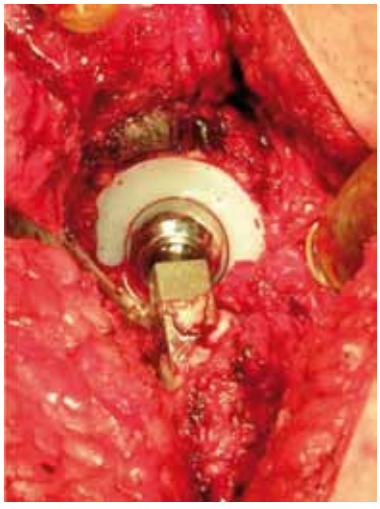

Fig. 4. *Appearance of operative wound after complete prosthethic implant insertion*

Fig. 5. *Patient B. X-ray of hip joint (acetabulofemoral joint) — one year after operation*

only if there are no severe formed deformations of the hips and lumbar-sacral vertebral region.

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THE SUCCESS OF CONSERVATIVE TREATMENT OF A CHILD WITH LATE DIAGNOSED CONGENITAL DISLOCATION OF THE HIP

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Among the anomalies in the development of the osteoarticular system, the most common congenital dislocation of the hip. This pathology is the most severe defect of the musculoskeletal system, which is detected in children. Despite the development of the possibilities of modern medicine, the urgency of the diagnosis and treatment of orthopedic anomalies does not change, but continues to grow, taking the leading place in a series of congenital pathologies.

On the recommendation of World Health Organization every newborn should be examined in the maternity hospital by an orthopedic surgeon. Congenital dislocation of the hip is a common pathology, 5–8 people per 1000. The result of treatment directly depends on the time of diagnosis and the beginning of treatment. If the diagnosis is made to the child in the hospital, it is almost 100% recovery in a short time. At a late diagnosis, after 6 months, the duration of treatment increases 2–3 times (an average of 1 year), worsening of long-term results and the recovery rate is about 50%. When the diagnosis is made extremely late, after 14–16 months, most of the method of choice is surgical treatment. Earlier, the pathology of itself screamed, but over the past 15 years, the clinical manifestations of congenital dislocation of the hip have become invisible and often there is not a single suspicious symptom on examination, and only a screening ultrasound can diagnose and immediately begin treatment. In our arsenal, there are many options for treating hip dysplasia: Freck's feather, Pavlik's harness, Tubinger's orthosis.

But there is a category of children who are diagnosed in the maternity hospital and put after 1 year. Therefore, ultrasound monitoring is required by children at risk: cases of congenital hip joint pathology in the family, any non-head presentation, a combination with another orthopedic pathology. Such patients subsequently enter the surgical departments for the surgical treatment of congenital hip dislocation. So it was in our case. It is known from the anamnesis that the girl was born on time, in breech presentation, with a weight of 3800 gramm and an Apgar score of 8/9. On the 4th day she was discharged home. Observed by an orthopedist on a decree. Pathology was not identified. According to the data of ultrasound of the hip joints in 3 months - the norm. The child grew and developed normally. Sitting girl started at 7 months, got up at 9 months, started walking independently at 14 months.

Parents did not like the gait and at their insistence the child in 19 months had a radiography of the hip joints. On the roentgenogram, a severe congenital dislocation of the right thigh was diagnosed. It was recommended an open reposition and the child was already hospitalized in the orthopedic department. But due to a viral illness. She was discharged to finish the cure for home. To us in the clinic the child turned at the age of 20 months. Given the clinical and radiological

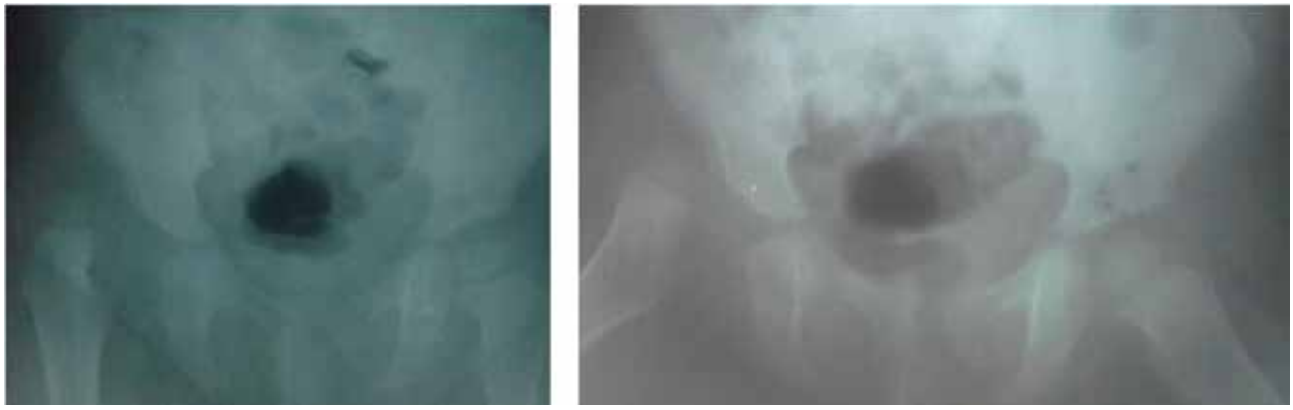

Fig. 1. *Congenital dislocation of the right hip. Late diagnosis*

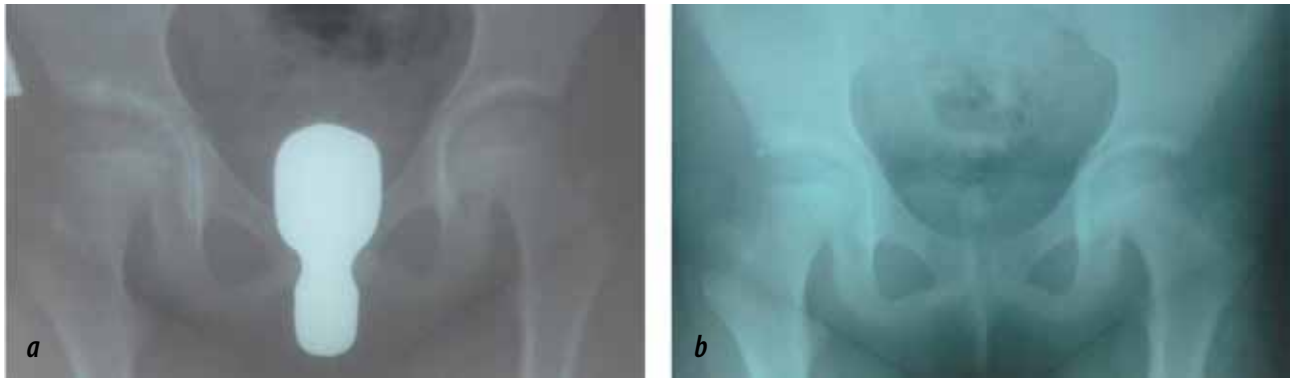

Fig. 2. *3 years after conservative treatment (a), 10 years after conservative treatment (b)*

picture, it was decided to start a stage-by-stage conservative treatment.

Stage 1 — extension of the lower extremities by the principle of over head for 10 days. The subsequent closed control under the control of the electron-optical converter turned out to be successful. The head is centered in the acetabulum, the latter practically absent.

Stage 2 — a koksit-plaster bandage was applied, in which the child stayed for 4 months. After that, the child was in a lightweight plaster bandage for 10 months.

Stage 3 — the Vilenskiy ortes was imposed for 6 months. For 3 years she received constant courses of physiotherapeutic treatment and massage of back muscles. At present, the child is 12 years old. There are no complaints. Movement in the hip joints in full (!). the child leads an active lifestyle.

Despite the extremely late diagnosis of such a severe orthopedic pathology, it is not always necessary to send a child to an operation at once. It is necessary to analyze the clinical and radiological picture, to make an attempt of closed correction of the hip dislocation. With the possibility of holding the head of the femur in the acetabulum, the child is shown a long-term conservative therapy with the aim of forming a joint, possibly not requiring subsequent surgical treatment.

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LABORATORY CRITERIA FOR ASSESSING THE SEVERITY OF CONDITION OF PATIENTS WITH PERITONITIS

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ABSTRACT — Until recently, peritonitis has been one of the severest complications in abdominal surgery.
It is known, that occurrence of any acute inflammatory process is followed by body acute phase response. Acute phase response is a complex of focal and systemic reactions mediated by various mediators — cytokines, prostaglandins, kinins, hormones. The amplitude and nature of the response depends on the process activity.

KEYWORDS — peritonitis, C-reactive protein (CRP), inflammatory proteins.

INTRODUCTION

One of the actual and yet unsolved problems of urgent abdominal surgery is the optimization of post-surgery intensive therapy methods for diffuse peritonitis. The overall mortality for this pathology even in large, well-equipped clinics is no less than 24–35%; it reaches 60–70% with the progression of toxic shock syndrome and 80–90% if multiple organ failure (MOF) is added [3,4,5], the rate of mortality is even higher with postoperative peritonitis. Herewith progressive multiple organ failure is the leading cause of death [2].

Difficulties in treatment of this severe disease depend to wide extent on processes in the immune system of patient. Massive antibacterial therapy, severe endogenous intoxication, multiple organ failure, gross metabolic shifts, use of medicines (for therapeutic purposes) with immunodepressive effect contribute to the development of evident immune alterations of secondary genesis in patient's body. Given that, immune alterations when peritonitis is in progress are very frequent and significant. Inadequate selection of material for research. In a number of cases, analysis

of material obtained from affected organ (or peritoneal exudate in case of peritonitis) may reflect the true state of immune system largely than analysis of peripheral blood, and, correspondingly provides more detailed information for disease immunodiagnostics and therapeutic decision. It is known, that occurrence of any acute inflammatory process is followed by body acute phase response. Acute phase response is a complex of focal and systemic reactions mediated by various mediators — cytokines, prostaglandins, kinins, hormones. The amplitude and nature of the response depends on the process activity [1]. It is showed that acute phase response is followed by increase of level of certain blood proteins group (proteins of acute phase (PAP), which concentration changes in response to inflammation, trauma and other pathological impact [5, 6, 7]. Advanced study of peritonitis' pathogenesis requires the search of new assessment methods of homeostasis change.

MATERIALS AND METHODS

86 children with acute diffuse peritonitis aged from 3 to 14 years, who were on treatment in surgery of Astrakhan Oblast Children's Clinical Hospital named after Silischeva, were examined. The causes of peritonitis were: acute destructive appendicitis, intestinal obstruction, perforation of bowel wall by foreign objects. The patients were divided into groups: patients with diffuse serous peritonitis, patients with diffuse serous fibrinous peritonitis, and patients with diffuse fibrinous purulent peritonitis. Course of peritonitis was assessed based on clinical symptoms and objective indexes of endointoxication. The complex of clinical research included: general blood test, common urine examination, biochemical analysis (rest nitrogen and blood urea, aminotransferase, creatinine, alkaline phosphatase, hemodiastase and urina amylase, water and electrolytic composition), determined by standard methods.

The concentration of C-reactive protein (CRP) in patients' blood serum was analyzed by method of immunodiffusion analysis (mg/l) on admission, on the day of surgery and again in 3–5 days after the surgery.

The findings of analyses were processed with the statistical analysis software Statistica 6, SPSS V 10.0.05, software "STATLAND", "EXCEL-97", "Basic Statistic" with due consideration for standard methods of variation statistics, including Student's t-test to estimate statistical significance.

RESULTS AND FINDINGS

The results of C-reactive protein immunochemical analysis are compared with the data of general clinical analysis and are presented in Table 1.

Increase of CRP concentration in blood serum and peritoneal exudate correlates with the disease severity. At that, the highest protein concentration is observed in purulent peritonitis forms.

Table 1. *Concentracion of CRP in blood serum and peritoneal exudate of patients with peritonitis*

Protein-reactant Immunodiffusion analysis (mg/l)	The results of proteins of acute phase concentration in peritonitise		
	diffuse serous peritonitis (n=42)	diffuse serous fibrinous peritonitis (n=30)	diffuse fibrinous purulent peritonitis (n=16)
SRP cerum	47,7±15,45	84,6±16,4	148,5±27,63
SRP exudate	45±17,64	78,2±24,3	97,2±22,96

CONCLUSION

Assay of proteins of acute phase for children in grave condition besides its clinical diagnostic relevance allows to determine the adequacy and effectiveness of ongoing therapy, as well as to predict possible complications without undue delay.

Modern standards of acute diffuse peritonitis treatment require effective therapy from the time of admission and division of patients pursuant to forms of progressive and retrogressive acute diffuse peritonitis.

We think that studied proteins of acute phase can serve as indicators of therapy effectiveness for patients with acute diffuse peritonitis. Increase of these indexes in 1,5–3 times may be a criterion of weakly effective therapy.

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OPERATION CORRECTION OF CHILD PLANOVALGUS DEFORMITY BY APPLYING POROUS TITANIUM NICKELIDE IMPLANTS

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INTRODUCTION

Nowadays, there are numerous operative treatment methods for axial deformities of foot and shin bone (tibia), which eliminate different pathological components [1, 3]. Such a number of methods could be explained by the ambiguous opinions of researchers on the pathogenesis of deformation. All existing surgical methods applied in treating axial deformities of foot and shin bone (tibia) could be classified as:

1. operations on tendon-ligamentous and capsular-ligamentous apparatus;
2. operations on bones and combined operations.

The first operation type on capsular-ligamentous apparatus to remove planovalgus deformity is performed on the soft tissues with further plaster bandage fixation.

The second operation type for 12+ children involves arthrodesis. Joint fusion in functional-reliable position to relieve impactable pain and recover from severe foot deformity. Such interferences remove foot deformity, but anatomic foot length is decreased as articular cartilage is resected, which, in its turn, reduces the functional treatment result. According to Jross data (1986) poor results of such interferences are about 47%. Today researchers are in constant range-finding study in up-dated treatment methods of above-mentioned pathology due to biotechnical foot function disorders as amortization, support and tension [5, 6].

Recently, the gold standard is the operation in subtalar sinus. This operative treatment includes correcting talocalcaneal joint configuration by inserting implant, shaping anatomically correct arch of foot in appropriate position and its reliable fixation in over-correction position by plaster bandage.

Colleagues from Nizhny Novgorod R&D Institute of traumatology and orthopedics, headed by M.V. Vlasov proposed subtalar implant with frustoconical body, externally screw-threaded and axially orifice connection. There are three longitudinal grooves on the body, spaced at identical intervals and dividing the body into equal sections. Grooves in the direction of screwing out have beds at the height of screw threads, while the threads of opposite side have rounded radius. This device improves the fixation reliability, excluding its migration from subtalar sinus and provides stable correction of talocalcaneal joint in appropriate position [3].

Colleagues from Turner Scientific Research Institute for Children's Orthopedics (V.V. Umnov and N.V. Dolzhenko) proposed the following implant to shape the arch of foot: autogenous bone from fibula and further fixation by twist drill needle (Kirshner wire) which prevents subtalar joint and anterointernal displaced talus, being the basic component of this deformity without significant anatomic changes [2].

Analogous operation including supplementary interference into the soft tissue component was proposed by V.A. Tupikov and his colleagues. This operation embraces not only autotransplant but also achille

plastic operation, i.e. subcutaneous recession of long peroneus to talar neck and long peroneous tendon through foremen being formed on the talar neck and tension attached by a loop. Then inserting Z-shaped shortened plasty into tibialis posterior muscle. This method provides reliable talar bone fixation in correct position, restoration of supporting foot function, reduction of surgical injury and after-operation complications [4].

A "simplier option" of above-described operation was proposed by Prof. G.P. Kotelnikov from Samar Medical University. This method included Z-shaped dissection of heel tendon, long and short peroneal muscles and externally inserting transplant into subtaral joint and dissection of talonavicular joint capsule [1]. In modern orthopedics surgical correction of planovalgus deformity is performed by means of subtalar sinus fusion through fusing infraarticular [5].

Unfortunately, the medical product market offers only foreign implants. In most cases this is Kalix2 implant, Integra Co. (France). Scientists from People's Friendship University of Russia have presented a rather complete documentation of clinical experience trials under the supervision of Prof. S.K. Tamoev. Proposed surgical treatment method involves 2 cm curved incision directly anterior and distally to lateral malleolus. Further talus bone sinus is exposed. A retractor is introduced into the subtaral sinus and reducing it towards plantar, thus removing valgus deformity and reducing the talus itself. A probe is introduced into the tarsal sinus to estimate the suitable implant size and after selected implant is installed (screwed in). The incision is closed by plastering the foot for 3–4 weeks. After the growth of a child the implant should be removed [6].

However, it should be mentioned that this applied implantation has some disadvantages. The implant is produced from polymer material, whereas its structure excludes possible ingrowth. In this case, the main problem involves its migration due to poor fixation in the subtalar sinus. In some cases, implant destruction which could be the result of the growth of a child and increasing body weight. Acknowledging these disadvantages in applying such technology and investigating more effective and universal method is challenging. Thus, the development of a more optimal method for subtaral arthroereisis is the most urgent task in today's foot orthopedics.

It should be noted that the initial disadvantage of the prototype is the fact that the implant should be removed by a second operation at the age of 16–18. Due to the high prices of such implants the medical insurance (CHI) can not cover all expenses, and only by quota. Considering the state policy related to import substitutes it is necessary to develop domestic materials and treatment methods being highly competitive with foreign ones.

MATERIALS AND METHODS

Critical analysis of literature justify the fact that this problem is becoming ever more relevant. In this case, the investigations and development of up-dated methods allege the experimental and clinical studies in surgery correction of valgus deformity preventing further progression and recurrence.

In the last years in Russian medicine new alloys such as Ni Ti have been introduced. It is possible to develop various Ni Ti implants which would enhance the surgery treatment efficiency of orthopedic pathology. The most non-conventional material in implantology could be titanium nickelide structures [3]. New technical result — decreasing surgery injury and complications due to one-time use of installed implant-correctors.

Mesoporous titanium nickelide implants with porosity of 81%, pore size 420 micron (permeablity) have been used. These physico-technical properties are quite closely related to those of spongy bone tissue, which, in its turn, optimizes the osteo-integration of the biocomposite metal-bone. When installing the implant immobility is fixed by the material surface roughness, while its geometrical shape as frustoconical body excludes the migration of the implant into the subtaral space.

To achieve new technical results in surgery correction of children paralytic valgus deformity by applying implants which involve 2 cm curved incision directly anterior and distally to lateral malleolus, further exposing talus bone sinus, removing valgus deformity and reducing the talus itself. After estimating and selecting the suitable implant size the porous composite titanium nickelide implant is inserted with the medical instrument "clamp" at an angle of 10–15° relative to frontal plane; the incision is closed by plastering the foot for 8–12 weeks.

In the R&D Institute of Medical Materials and Smart Implants conic porous composite titanium nickelide implants in experimental diameter from 10 mm to 18 mm (fig. 1).

Fig. 1. *Set of subtaral porous titanium nickelide implants*

General appearance of foot and X-ray examination of the patient before treatment are presented in figure 2 a, b.

a *b*

Fig. 2. *General appearance of foot (a) and patient X-ray examination (b) before treatment*

DISCUSSION OF RESULTS

The description of the method is following: the operation is performed under spinal anesthesia. Patient-supine position. Pneumatic tourniquet is applied on middle third hip area. Preliminarily wrapping the operating lower limb with elastic bandage, then pumping pneumatic tourniquet, so as to minimize the blood loss. The lower limb is antiseptically treated three times. First, 4 cm oblique skin incision slightly anterior and distally to lateral malleolus; layer-to-layer exposure to subtalar joint; with Luer forceps strip scar tissue and ligament-filled subtaral joint from out of sinus.

Joint surface talar bone and mid–and–frontal heel bone facet is cleaned from cartilage tissue with Volkmann small spoon, whereas cartilage tissue is extracted to pinpoint bleeding. The foot is placed in normal correction position. In subtaral joint region with a special instrument the implant size from 10 mm to 18 mm is selected. After selecting the optimal sized implant of maximum correction degree, porous titanium nickelide conical-shaped implant is single-stepped inserted into the subtaral joint space in base turned outwardly to heel at an angle of 10–15° relative to frontal plane; further, with Kocher forcep implant is additionally fixed to the joint by nail punch (figure 3 a, b).

Test trials of foot movement is performed to check if the implant is firmly fixed in the joint and excluding migration (Figure 3 a, b).

Layer-by-layer the incision is closed with vicryl and without drainage. The skin is stitched with separate vicryl. Aseptic dressing is placed on the post-operation stitch. The lower limb is put in a support under plaster, then circular plaster fiber glass bandage is put on the lower limb, from upper third tibia to toe ends at a right angle. Pneumatic tourniquet is loosened.

Check-up X-ray in frontal and lateral projections is performed in 3–5 days after the operation in plaster bandage.

Time in plaster fiber glass bandage is 8–12 weeks after operation; check-up X-ray in 6th and 8th week after operation; plaster bandage is removed if bone block has been formed around titanium nickelide implant and no sensation of pain or discomfort in projection of foot subtaral joint. After removing plaster bandage orthopedic shoes with fixed heel, high firm bootleg and insole with uplifted edges are prescribed. These shoes provide maximum relief on midfoot. These shoes should be worn for 6 months after operation. After six months check-up X-ray of foot in frontal and lateral projections. Further, check-up X-ray once in 12 months and consultations of children orthopedist.

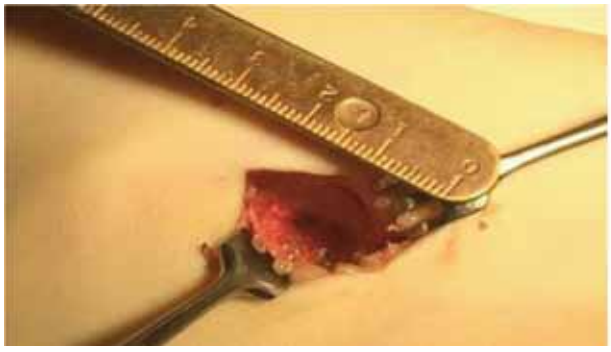
Based on Order №1027 dated 05.08.1986 of Ministry of Health Care titanium nickelide implants were permitted in clinical practice.

Conic porous composite titanium nickelide implants in experimental diameter from 10mm to 18mm developed by R&D Institute of Medical Materials and Smart Implants are applied in the above-described surgery method.

CONCLUSIONS

The proposed surgery treatment comparable to prototypes excludes supplementary operations, such as open or integumental elongation of achillo-tendon, correcting open or closed heel bone osteotomy, correcting 1 instep bone osteotomy. In the case of combined paralytic valgus and heel deformity and achillo-tendon hyperextension, operation of detruncating plasty of achillo tendon is performed parallel to arthrodesis.

This method prevents implant displacement, as bone tissue adheres to implant pores, making its structure much more harder, which, in its turn, excludes possible breakage. In this case, it is not necessary to remove the implant during the adolescent period. This is due to the fact that this implant is a supplement to the deficient bone structure and provides the maximum contact with the surrounding tissues, as well. Another important factor is the impossibility of vascular disorders (these disorders could result in the remodeling of the bone tissue and / or recurrence of the deformity).



a

b

Fig. 3. *Bed for implant (a) and installed implant (b)*

a

b

Fig.4. *General appearance of foot after operation (a), X-ray examination with implant (b)*

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MODERN METHODS OF SURGICAL TREATMENT OF H-TYPE FISTULA IN GIRLS

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The surgical treatment of girls' H-fistula is the one of main tasks of coloproctology. Different operations have been used including extirpation of fistula into rectum and PSARP. But frequent recurrence of fistula and scarry deformation of vaginalvestibule make us to search for the ways of solving the problem.

The aim of our investigation is to improve methods of surgical treatment of H-fistula.

Material and methods. Between 1994 and 2016 in the surgical department of Scientific Center of Pediatrics and Pediatric Surgery 66 (100%) children were operated. Age range was from 3 to 9 years. Diagnosis is based on the results of clinical data, X-ray, endoscopic and histological investigations.

The most informative, simple and available investigation is X-ray, performed by contrasting of distal rectum using ballon technique and was applied in 19 (28.7%) patients with H-fistula. This investigation enables to identify length and height of fistula, however all these fistulas had a low position.

In 3 (4,5%) patients rectovaginal fistula was found while in 63 (95,5%) — recto-vestibular fistula. 25 (37,8%) patients had cylinder form of fistula and 41 — conical (62,2%). In 27 (40,9%) girls fistula located on the left vaginal vestibule, in 26 (39,4%) on the right side and in 13 (19,7%) cases located centrally. Combined congenital pathology was revealed in 6 (9.1%) patients from 66 patients. Particularly sacral teratoma in 1 case, vesicoureteral reflux in 2 case, sacral vertebrae abnormality in 2 case, heart abnormality in 1 case.

In all 66 patients following types of surgery was performed:

Invaginatory extirpation of fistula was made in 8 (12, 1%) patients: 1(1,5%) girl with rectovaginal and 7(10,6%) with rectovestibular fistula; in 41 (62,2%) children with H-fistula anterior anorectoplastic was performed, 7 (10,6%) had surgical correction by fistula cutting method with forming united crevice. 10 (15,1%) had elimination of H-fistula using transanal method.

Results. 6 cases of 8 (12,1%) who had invaginatory extirpation of fistula occured reccurrence, and one of them had closed fistula with second healing, 5 children with recurrence were operated again — cutting the probe with satisfactory result.

2 cases of 41 (62,2%) girls who underwent anterior anorectoplastic had complication such as seam divergence and they were put terminal colostomy. These 2 patients had fistula recurrence again, which were operated repeatedly by fistula cutting method on the probe. 1 patient had bleeding on the seventh day and was reoperated with satisfied result. 10 (15,1%) patients operated by transanal method who were conducted layered mobilization of front wall of rectum over 1 cm from Morgan cript with fistula distraction and anatomy was restored. There were no complications.

Remote result of 59 (89,4%) patients was studied in 6–18 months after operation.

4 patients had encopresis and 6 had constipation, which was regulated by drugs.

Patients with encopresis were those who had the second surgery by fistula cutting method on probe.

To sum up, our treatment results show that using transanal method of surgical correction is treatment of choice, which tends to be more effective surgical treatment of this pathology and for recurrence of fistula is cutting on probe with forming united groove.

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SURGICAL TREATMENT OF DIFFUSE POLYPOSIS OF GASTROINTESTINAL TRACT IN CHILDREN

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Diagnosis and timely treatment of obligate precancerous diseases of the colon is a prevalent problem in modern coloproctology. Annually 800 thousand new cases of colon and rectum cancers as well as 400 thousand deaths caused by these types of cancer are registered.

Diffuse polyposis of gastrointestinal tract in children is a rare and severe pathology, which after the age of 16 develops into cancer in 100% of cases.

Material and methods. In the Scientific Center of Pediatrics and Children's Surgery (NCPCS), 17 children underwent surgery during the period from 1994 to 2016. In two (11.8%) children, hamartomatous polyps (Peutz-Jeghers syndrome) were found; in one (5.9%) child, adenomatous polyps in the colon in combination with Meckel's diverticulum were found. 14 (82.3%) patients were diagnozed with juvenile polyposis; of them, in 2 (14.3%) children, the whole stomach, small and large intestine were damaged.

All children underwent a comprehensive examination, including ultrasound examination of the abdominal cavity organs, irrigography, fibrocolonoscopy, and fibrogastroduodenoscopy.

When parents were interviewed, the hereditary nature of this disease was confirmed in 4 (23.5%) children. In the same families, 2 parents were diagnosed with colon carcinomas. Of the children admitted, 13 (76.5%) were anemic. Rectal bleeding of varying degree of severity was observed in 12 (70.6%) patients. Decreased appetite was detected in 9 (52.9%) children. Hypotrophy was seen in 11 (64.7%) patients. 3 (17.6%) children were urgently admitted with intussusception. In 2 (11,8%) patients with Peutz-Jeghers syndrome, externally visible signs of pathological melanotic hyperpigmentation of the lips and oral mucosa in the form of small brown spots were found. Before surgery, polyposis was diagnosed in 11 (64.7%) patients based on the results of a histological examination.

Results. All the children were operated in a planned manner. 2 (11.8%) children with Peutz-Jeghers syndrome underwent multiple polypectomy from small incisions of the intestine, directly in the polyp localization zone. The polyps were removed with mucous stitching. In one (5.9%) child, the polyps in the nestis area were clustered along 12 cm. This patient underwent segmental resection of the nestis.

In 1 child with adenomatous polyposis of the large intestine, total colectomy with the imposition of an ileoanal anastomosis was performed. Meckel's diverticulum was intraoperatively revealed in this child (a wedge resection of the small intestine was performed).

12 (85.7%) patients with juvenile polyposis received total colectomy with ileo-anal anastomosis (Soave procedure), one child received total colectomy with permanent ileostomy, and in one child, with overall gastrointestinal affection, segmental resection of the small and large intestines with permanent ileostomy was performed.

In the catamnesis, after 1 to 4 years, 12 (70.6%) children were examined. In 10 children (83.3%), the results were satisfactory. The children are socially adapted. In 3 (25%), fecal incontinence of I-II degree was noted. These children receive outpatient care. Of 2 patients with total lesion of the gastrointestinal tract, 1 the child is under clinical supervision. The second child died.

Thus, our results of treatment indicate that in case of diffuse polyposis of the colon, early surgical removal of the large intestine is necessary. The method of choice is total colectomy with ileoanal anastomosis. Early diagnosis and the correct choice of surgical treatment prevents the development of various complications.

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THE URGENCY OF USING TUBINGER'S ORTHOSIS IN TREATMENT OF HIP DYSPLASIA IN CHILDREN

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Currently, little enough attention is paid to one of the types of functional adaptations for conservative treatment of congenital dislocation of the hip — Tubingen Hip Flexion Splint. Tubingen Hip Flexion Splint has proved to be a highly effective orthopedic tool for treating hip dysplasia in Germany and other European countries. It consists of two femoral supports, a middle spacer and a shoulder strap.

The development of this splint was taken into account the conditions for the effectiveness of the treatment. It is very important to reproduce the position that best corresponds to the natural posture of the fetus in the womb of the mother. This position can not be created with the help of other devices for abduction of the hip, as in most cases they do not allow to reach the required angle of hip flexion and are less effective for maintaining it. Human position of the hip in the first place requires maintaining the required angle of bending, while excessive hip dilution is highly undesirable.

At the same time, the restriction of movements in the hip joints of the child should be minimal, since these movements contribute to the development of the acetabulum. Orthosis device prevents uncontrolled dilution of the hips of a child under the influence of their own weight.

Excessive diversion is one of the main causes of necrosis of the femoral head due to a violation of its blood supply, because of the infringement of the limbus between the head of the femur and the acetabulum. In addition, natural thigh movements prevent the risk of developing a "round" back. Since the bent leg position is normal for the child, it is easily achieved and tolerated. In spontaneous movements, the child also has the ability to turn on his side.

All of the above can have a basis for a set of clinical experience in the application of this orthosis for the treatment of hip dysplasia and position it as a priority method in outpatient practice.

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MORPHO-FUNCTIONAL FOCAL DYSPLASTIC CHANGES OF THE KNEE JOINT IN ADOLESCENTS

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The purpose of the study is the identification of dysplastic changes of the bone system with functional disorders of knee joint in children and adolescents.

Clinical and anamnestic, instrumental and functional methods of examination of 86 children with diseases of the knee joint were analyzed. It was established that the risk factors for the development of complications are manifestations of connective tissue dysplasia, which require a comprehensive differentiated approach to treatment.

Indications of accented trauma were absent in most of the children. At admission it was determined that all children had hypotrophy of 4 head muscle on the side of the affected knee joint, naturopathica and hypermobility of the patella, instability of the knee joint in the frontal plane. The pain was localized in the region of the internal condyle of b/fibula. Clinical signs of damage to the menisci and ligaments were missing or questionable. One-third of the adolescents had synovitis. In radiation studies of the knee incongruence of the joints of the femur and tibia, worse under load, was determined. According to the MRI degenerative changes of the menisci and cruciate ligaments were revealed.

Objectively the children had asthenic physique, decreased muscle tone of the upper and lower limbs, valgus deviation (10–15°) and internal rotation of the tibia (up to 20°), PLANO-valgus setting of feet, hypermobility of peripheral joints. Posture was broken due to the increased thoracic kyphosis and lumbar lordosis. Motion in the cervical spine was limited by the rotation in both directions (up to 20–30% of normal mobility).

On radiographs of the spine those or other pathological changes were determined. In the cervical spine: the asymmetry of the joint C1–C2, Kummerle anomaly, saddle-like deformation of the side of the Atlanta masses, kyphosis of the middle department; platyspondyly; thorax kyphosis, scoliosis, wedge-shaped deformation of bodies of D6-9, the narrowing of the intervertebral spaces, subchondral hardening; in the lumbar — spina bifida occulta in L5 and S1 rear arches, anomalies of tropism, hyperextension of the sacrum.

Thus, in a certain category of children "surgical" problems of the knee joint arise on the background of dysplastic changes. Treatment provided locally and symptomatically does not lead to recovery. An integrated approach is needed and the treatment according to biomechanical disorders caused by connective tissue dysplasia are necessary.

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RESULTS OF SURGICAL TREATMENT OF CHONDROSARCOMA AT DIFFERENT LOCALIZATIONS IN THE BONES OF THE SKELETON

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Introduction. Chondrosarcoma amounts 7–16% of the total number of malignant bone tumors. Around 60% of cases of the disease are diagnosed in middle-aged and elderly patients (40–60 years) [4]. Chondrosarcomas are divided into primary and secondary, and by the degree of malignancy are divided into the highly differentiated, moderately differentiated and poorly differentiated [1, 2]. The main method of treatment of this disease is surgical. The prognosis depends on the degree of chodrosarkoma malignancy [3].

The purpose of the work. To show the possibility of surgical treatment of chondrosarcoma at different localizations and extent of the tumor in the bones of the skeleton.

Materials and methods. The analysis of treatment results of 42 patients with various localization of chondrosarcoma was carried out. Chondrosarcoma of bone in the extremities was observed in 29 (69%) patients, the pelvis in 13 (31%). Surgical treatment in the amount of bone segment resection with arthroplasty was performed in 19 (45,2%) patients; in the amount of bone segment resection without replacing a defect - in 16 (38,1%), amputation or disarticulation of limbs in 7 (16,7%). The average age of the patients was 52,4±1,2 years. Knee arthroplasty was performed in 8 patients, hip — 5, shoulder — 4, ankle — 1, mega total femur arthroplasty — 1; pubic bone resection was performed in 5 patients, iliac — 5, ischium — 3, the proximal part of the fibula — 3. Radical operations were performed in 37 (88,1%) patients. Non-radical operations were performed in 5 (11,9%) patients with localization in the pelvis. The functional outcome of the operated limb was calculated by MSTS system (Musculo-Sceletal Tumor Staging / System /). Quality of life was measured by questionnaire EORTIC-QLQ-C30. The survival rate of patients evaluated by Kaplan–Meier method.

Results. Postoperative complications were observed in 7 (16,7%) patients, tumor recurrence in 8 (19%). After radical surgery recurrences were detected in 3 (8,1%) patients; after non-radical surgery — in 5 (100%). Distant metastases of chondrosarcoma were observed in 10 (23,8%) cases. After sweeping operations tumor metastases were found in 6 (16.2%) patients after nonradical in 4 (80%). Postoperative recovery of limb function and supporting ability was observed in 35 (83,3%) patients. Functional outcome of the limb after arthroplasty amounted 64–92%. The quality of life of patients increased with preoperative 25 points to 84 points after the surgery. Three-year overall survival of patients was — 72,2±4,1%, the five-year — 64,5±4,6%.

Conclusions. The occurrence of chondrosarcoma relapses usually depends on radical surgery. Chondrosarcoma metastases are determined by the degree of tumor cells differentiation.

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USE OF A MATERIAL BASED ON BIOACTIVE GLASS IN CASES OF BENIGN BONE TUMORS

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Introduction. Generally accepted method of treatment of benign tumors and tumor-like bone disease is surgical. Bone defects that require replacement sometimes occur in the surgical treatment of benign tumors and tumor-like bone diseases. For substitution of bone defects are used: allografts, autografts, bone cement and other various synthetic plastics [2, 3, 4]. Many different biological grafts, organic, and synthetic inorganic materials are proposed in orthopedics to replace residual bone defects. Recently are actively studied properties of the new materials based on biocomposite bioactive glass [1]. These materials have much less intense inflammatory reaction and are much better in comparison with hydroxyapatite, as they have more effective osteostimulating factor [5].

The purpose of the work. To show the advantages of osteoplastic operations using implant material based on bioactive glass by substituting post-resection bone defects in children with benign tumors and tumor diseases.

Material and methods. During the period from 2009 to 2017 in a clinical department osteoplastic operations using material based on bioactive glass in benign tumors and tumor-like bone diseases were performed in 59 children. The average age of patients was 13,3 years (range from 9 to 17 years), girls amounted 31 (52,5%), boys — 28 (47,5%). The localization of the tumor: the femur — 14 (23,7%), shoulder — 14 (23,7%), hand bones — 11 (18,6%), foot bones — 9 (15,3%), tibial — 9 (15,3 %), pelvis — 2 (3,4%). Morphologically met: enchondroma — 17 (28,8%), giant cell tumor of bone — 15 (25,4%), aneurysmal bone cyst — 13 (22%), chondroblastoma — 6 (10,2%), solitary bone cyst — 6 (10,2%), eosinophilic granuloma — 2 (3,4%). Material based on bioactive glass is a multi-phase inorganic material synthesized by chemical vapor deposition and ceramic technology. The phase composition of the material based on bioactive glass: bioactive glass — 50–65 wt.%, hydroxyapatite — 14-17 wt.%, whitlokite — 14–17 wt.%, wollaston — 9–7 wt.%. Material based on bioactive glass is osteoinductive and osteoconductive biomaterial that quickly integrates with the bone, the bone-forming ceramic complex and in some period of time is converted into bone. Surgery was performed in the following amounts: intraosseous bone tumor resection, the substitution of the bone defect by implant material based on bioactive glass in the form of granules or powder. Depending on the location and size of the bone defect a plaster splint on the limb was imposed in order to prevent bone fractures at the site of implantation.

Results and discussion. As a result of bone and plastic surgery for benign tumors and tumor diseases of hand bones, using plastic bone material based on bioactive glass, postoperative complications of surgical wounds were found in 59 patients who underwent resection of intraosseous bone tumor. Recurrences of benign tumors or tumor diseases were detected in 5 (8,5%) patients. In connection with recurrent tumors patients underwent repeated surgery: removal of tumor recurrence and bone defect replacement by material based on bioactive glass. In the dynamics of observation by X-ray control was observed adjustment and replacement by the plastic material of the newly formed bone tissue. Patients used the operated limb on average in 3–6 months.

Conclusions. The use of material based on bioactive glass as a plastic material in osteoplastic surgery has several advantages — reduces the amount and time of the operation, stimulaties reparative osteogenesis in bone that helps to restore the operated bone and limb function, and thus the quality of life of patients.

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CAUSES OF RECURRENCE OF MALIGNANT BONE TUMORS OF EXTREMITIES AND TACTICS OF THEIR TREATMENT

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Introduction. Primary bone tumors are relatively rare and account for 1–4% of the total structure of all human cancer, but the severity of the pathology is one of the most difficult in the diagnostic and treatment aspects of clinical onco-orthopaedics [1]. The main method of treatment for most malignant bone tumors is surgical treatment. Wide excision of a malignant tumor with the surrounding tissues reduces the risk of recurrence of a tumor to a minimum [2]. Neurovascular bundle involvement in the tumor process makes it impossible to remove the tumor without amputation of the affected limb. Patient survival after amputation remains high in case of adequate courses of chemotherapy [3]. Quality of life of these patients significantly improved after the residual limb prosthetics.

The purpose of the work. Determining the causes of relapse and treatment failures of primary malignant bone tumors of extremities and tactics of their treatment.

Material and methods. In clinical departments for the period from 2009 to 2017 a comprehensive treatment was conducted for 117 patients with malignant bone tumors of extremities. The main type of treatment is conserving surgery followed by chemotherapy and (or) radiotherapy. The degree of aggressiveness of the tumor determines the amount of tissue removed and borders of neoplasm resection. According to the morphological structure were met: giant cell tumor of bone — 45 (38,5%) patients, osteosarcoma — 37 (31,6%), chondrosarcoma — 17 (14,5%), fibrosarcoma of bone — 6 (5,1%), malignant giant cell tumor of bone — 5 (4,3%), malignant fibrous histiocytoma of bone — 4 (3,4%), Ewing's sarcoma — 3 (2,6%). Advanced cases of malignant tumors in the presence of distant metastases or terminal stages of the tumor process determined the choice in favor of symptomatic treatment or a mutilation.

Results and discussion. The most frequent complications of organ surgical treatment of malignant tumors were recurrence or continuation of growth of the tumor after its removal. Recurrences were observed in 17 (14,3%) patients, mainly during the first year, in three patients — after the first year. The study of the causes of recurrence has shown that in most cases they were caused not only by non-radical removal of the neoplasm (compliance with the principles of zoning and circularity), but also the aggressiveness of the tumor in each particular case. Tumor recurrences were observed usually in soft tissue surrounding the prosthesis, resulting in a further rise to distant metastases. This observation suggests that the recurrence behave more aggressively, suggesting expansion of resection for reoperation. Out of 17 patients with revealed recurrence of the tumor, 10 patients had an amputation or disarticulation of limbs. All patients underwent prosthetic limb fitting. Supportability of the residual limb recovered after an average period of 7 months.

Conclusions. Causes of recurrence of malignant tumors, the frequency of which was 14,3%, were the errors of diagnosis, incorrect assessment of the degree of aggressiveness of the tumor, mistakes and errors in surgical technique.

The level of amputation of extremities with recurrent malignant bone tumors should be elected strictly individually, taking into account the location, extent and degree of malignancy of the tumor process.

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OPTIMIZATION OF SURGICAL TREATMENT OF BURNS

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The effect of high temperature leads to local damage to the skin, as a consequence, to the disruption of the protective functions of the integumentary tissues and intoxication of the body with the products of disintegration in the lesion, followed by a disturbance of hemodynamics, microcirculation, leading to shock and development of a complex of pathological processes throughout the body and skin itself in the region damages [1, 6, 13]. Modern infusion therapy and other methods of resuscitation in most cases can cope with burn shock and restore disturbed homeostasis [8]. Most of the fatal outcomes in burned people are now observed in the subsequent stages of burn disease and is associated with progressive intoxication, burnout, development of purulent-septic complications leading to multiple organ failure syndrome and death of victims [5, 9]. With significant success achieved in reconstructive and plastic surgery, in the development of new methods of surgical interventions, many questions of treatment and rehabilitation of patients who have suffered a thermal trauma remain unresolved. Currently, it is generally accepted that early surgical necracetomy with one-stage or delayed autodermoplasty is the treatment of burned pathogenetically grounded [4, 11]. However, the possibility of using this method is limited for burns occupying a large body surface [2, 10, 14]. Insufficient area of the donor sites is a factor that detracts from the time of autodermoplasty [12]. In addition, the explantation sites themselves are a factor of significant pain on the patient, increase the area of wounds that need healing [3]. The purpose of our study is to improve the methods of active surgical treatment of severely burned, determine the optimal timing of autologous transplantation, and shorten the time spent in hospital.The work is based on the study of 62 patients aged 18 to 60 years with thermal burns, who were treated in the Primorsky burn department of the Far Eastern Federal District Medical Center of FMBA of Russia in the period from 2007 to 2015. Inclusion criteria were the presence of IIIA–IIIB burns with an area of 10 to 20% of the body surface, the Frank index of 30–60 units. Exclusion criteria were a large area of surface burns of I and II degree, as well as deep IV degrees. Histological examination of biopsy specimens on the first and second days after the burn injury in the pathological foci recorded areas of hemorrhages and there was a slight increase in the number of blood vessels in the loose fibrous connective tissue that was subject to the epidermis or to the wound surface. In the region bordering the zone of damage, low proliferative activity of cambial elements was recorded. In the spiny layer, as well as in the walls of the hair follicles and in the sebaceous glands, the activity of the Ki67 gene was absent. The endothelium of the blood vessels also contained a small amount of proliferating cells. According to our clinical, morphological and histochemical studies of the processes occurring in burn wounds, the optimal time for complete covering of burn wounds is 7–8 days after injury. In the burn wound after autodermoplasty, performed in late terms, there is a violation of reparative processes associated with pathological angiogenesis, an aggressive reaction of immunocompetent cells leading to non-infectious destruction of the graft, to its lysis. Diagnostic criteria for graft lysis can be CD8+ cells and macrophages and Langerhans cells.

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SURGICAL CORRECTION OF FUNNEL CHEST DEFORMITY IN CHILDREN WITH USE OF IMPLANTS FROM NITINOL

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Introduction. Congenital deformations of a thorax represent the malformations connected with change of its form. Most often funnel chest deformity (pectus excavatum (PE)) meets [1].Except cosmetic defectthis malformation is followed also by functional violations from cardiovascular and bronchopulmonary systems. According to authors of Russia PEmeets at children from 0,06 to 2,3%, and according to foreign authors from 0,2 to 1,3% [3].

Surgical treatment of PEat children is one of the most serious and actual problems of thoracic surgery. Now there is a set of methods of a thoracoplasty [2]. Improvement and widespread introduction of low-invasive and hi-tech methods in surgical treatment of funnelchest deformity is a step forward in this direction [3, 4]. However,questions of optimum tactics of treatment of patients concerning the choice of a way of the thoracoplasty and ways of fixing of a sterno-costal complex are actual and unresolved nowadays.

Surgical correction of deformations of a thorax has to be timely and full. It promotes improvement of function of cardiorespiratory system and carrying out early rehabilitation of patients. For this purpose we have used an author's method of surgical treatment of funnel chest deformity in the conditions of the growing organism with use of smooth biocompatible composite materials from a nitinol, which have biological inertness, isoelasticity and effect of shape memory.

The purpose of this study was to create a device which allows conducting a pectoral plate without risk of damage to internal organs in difficult anatomical

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conditions. The task of the proposed method was to facilitate the insertion of the plate in difficult anatomical conditions by using a guide pinconnected to a plate by cord. In the clinic of the medical university in Tomsk, 43 children with PE were operated by an authoritative method.

Material and methods. The device consists of a guide pin made of stainless steel with a length of 350 mm and a thickness of 3 mm with a handle of 100 mm having an oval-shaped bend 15°. At the top of the conductor there is a hole 3 mm in size through which a kevlar cord 5 mm thick and 10 mm long is fastened, the other end of the cord is fastened to the hole in the implant plate with a width of 15 mm 2 mm thick, 30 cm long, pre-adjusted based on the anatomical deformation and the degree of necessary correction.When using the device retrosternal carrying out is made in one stage, at the expense of very short (1 cm) kevlar cord bridging the conductor and a plate. Thanks to addition of efforts — pulling (for a guide pin) and forward (on a plate) carrying out a plate in difficult anatomic conditions of retrosternal space is facilitated. It warns an internal injury and tissues that it reduces risk intra- and postoperative complications.

Appearance of a thorax of the patient with PE before operation and in 3 years after treatment with use of a plate from a smooth nitinol with shape memory is presented in the Fig. 1.

Results and discussion. In the long-term postoperative period, we received complications in the form of a rupture of a smooth plate of nitinol lavsan ribbon fixing to the rib in 2 children (0.8%). This type of complication on outcome of treatment of patients was not affected. And in one patient (0.4%) during progressive growth, the existing scoliotic deformity increased, which led to secondary deformation of the chest above the established plate. The patient was operatedagain, she was given a second plate.

Fig. 1. *Appearance of a thorax of the patient with PE, before operation (a) and in 3 years after treatment with use of a plate from a smooth nitinol with shape memory (b)*

The rupture of the lavsan tape is related to the failure to follow the prescribed regime (the child was engaged in wrestling).

Conclusions. Using the author's method makes it easier to load the plate in difficult anatomical conditions, reduce the traumatism of the intervention and shorten the duration of the operation, reduce the risk of damage to the vital organs of the chest, improve the aesthetic outcome of the operation, and simplify the operation technically.

The use in the clinic of the author's method of surgical correction of patients with PE made it possible to obtain good results in 95.4% of cases and satisfactory results in 4.6%. The absence of unsatisfactory results gives grounds to recommend and use the tactics developed by us for the surgical treatment of patients with chest deformities using smooth plates of nitinol in practical activities.

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ALGORITHM FOR FORECASTING THE SHAPE AND SIZE OF DENTAL ARCHES FRONT PART IN CASE OF THEIR DEFORMATIONS AND ANOMALIES

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ABSTRACT — A study was conducted involving 96 people of both sexes with physiological occlusion and with no congenital maxillofacial pathology. As a result, an algorithm was proposed for forecasting the shape and dimensions of the dental arches, which is based on measuring relatively stable parameters, namely, the dimensions of the anterior teeth and the basic features in the maxillofacial area. The algorithm is based on mathematical calculations of the circle geometry and the dependence of the length of the arch, chord and height. The circle diameter was calculated as the ratio of the dental arch width between the canines to the sine of the central angle shaped by the radii of the circle limiting the chord. The size of the front-canine diagonal is comparable to the size of the front teeth in a certain ratio.

KEYWORDS — facial measurement methods, odontometry, dental arches study methods, gnathic type of dental arches, normodontia, macrodontia, microdontia.

INTRODUCTION

The progressive level of fundamental and applied research concerning the issues of morphogenesis, generic and individual variability of morphological structures in the maxillofacial area leads to significant successes in the contemporary modern clinical dentistry. However, despite the scale and the depth of the national and foreign research carried out

in the area, most aspects of this important issue remain unclear [4, 7, 11, 19, 24].

Gaining the optimal morphological, functional and aesthetic balance in the maxillofacial area is a priority for any patient undergoing orthodontic treatment. Such a balance between morphology, function and aesthetics will make it much easier to achieve the most acceptable outcomes of treatment in each clinical situation [3, 14, 22, 25, 29, 35].

The announced results of anatomical and topographic studies create grounds for stating that one of the most important ways to evaluate the self-regulation of the dentoalveolar system involves the morphometric parameters establishing the consistency between the tooth sizes and the dentoalveolar arches parameters, which is due to the individual variability of maxillofacial features. Therefore, the identification and individualization of topographic anatomical maxillofacial features, performed through biometric research methods prior to orthodontic treatment, appear most relevant [10, 28, 33].

The algorithms employed to forecast the shape and size of dental arches have a long history and have already been described by domestic and foreign experts [2, 32].

The authors prove here that the dental arches frontal parts, which differ in the sagittal and transversal planes, often reveal anomalies and deformations whose etiology implies premature removal of milk teeth [1, 13, 26].

The variability of the main linear parameters is due to both the gnathic (dolicho-, meso- and brachygnathic), and the dental types of the face and dental arches [6, 9].

There has been a relationship shown between the size of different sections in dental arches [5, 16].

Until now, the measurement of dental arches has been mostly performed through the Pont (Linder-Hart) methods, which have become subject to criticism from specialists due to the different values of the proposed indices when measuring the same parameters. The anterior part is limited to the first premolars, which is not always used by clinical experts. In most cases, special attention is paid to the canines, seen as the key teeth, and the inter-canine distance [8, 15, 30, 34].

There has been the dependence shown between the inter-canine distance and the teeth size, for all gnathic types of dentoalveolar arches [17, 20].

Special emphasis has been put on the inter-canine distance, as well as the correlation shown with the external nose dimensions. Indices have been proposed for determining the inter-canine distance. However, the ***al*** point (located on the wings of the nose) has been recommended as the main points for measuring the external nose [12, 21].

The forecast for the shape of dental arches, depending on the size of the anterior teeth, relies on the Hawley-Gerber-Herbst arch. However, there have been some faults of this technique pointed, which are associated, first of all, with the length of the chord being shorter than the segment arch length, and the sum of the dimensions of the three front teeth always being smaller than the circle radius [18, 27, 32].

Attempts to link the construction of the arch with interdependent parameters, namely – the depth and the width, can take place only with physiological occlusion, and even then they depend on the specific features of the dental arches [23, 31].

Attention is to be paid to mathematical modeling of dental arches while taking into account the logic of the circle geometry; however, the proposed pattern is based on the measurement of the inter-canine distance, which can vary in case of abnormal canine location. At the same time, respective literature lacks information on forecasting the shape and dimensions of the dental arches relying on measuring relatively stable parameters.

Aim of study:
development of an algorithm for forecasting the shape and size of dental arches in view of the teeth size and the major maxillofacial parameters.

MATERIALS AND METHODS

The comparison group included 96 people of both sexes with a full set of permanent teeth, physiological occlusion and with no maxillofacial congenital pathology. The development of a forecast algorithm for the shape and size of the dental arches took, at the first stage of the study, a comparative analysis of the main linear parameters of the face and dental arches among the comparison group patients.

To do this, measurements were performed to check the distance between the ***ac–ac*** points (***alarcurvature***). The ***ac*** point is the commonly accepted point indicated in the "Biometric Identification" standards (GOST R ISO / IEC 19794-5-2006), and is located on the bend of the nose wing or as the most outward prominent point on the nose wing bend (Fig. 1).

Jaws cast models were used to carry out odontometry in the medial-distal plane as well as to measure dental arches in the sagittal, transversal and diagonal planes.

The width of the dental arch anterior section was measured between the points located on the canine cusps. The depth of the anterior part was taken as the distance from the interincisal point (between the medial incisors on the vestibular side) up to the conditional line connecting the points located on the canines. The front-canine diagonal corresponded to the distance from the inter-incisal point to the canines (Fig. 2).

Fig. 1. ***ac*** *point location on the face*

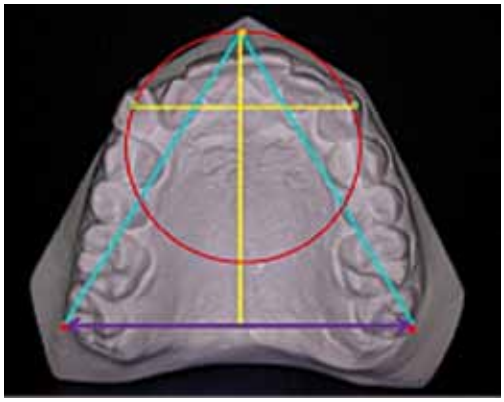

Fig. 2. *Abnormal position of canines on the model with the target location of the key teeth and reference lines to measure the dental arch parameters*

The actual values were compared to the estimate indicators.

The dependence of the length of the arch, chord and height was determined based on Huygens and calculated following the formula we used in our studies

$$64H^2 = 9L^2 + 6LX - 15X^2$$

H — the height of the segment; *L* — the arch length; X — the chord length.

The statistical processing was performed directly from the common data matrix of ECXEL 7.0 (Microsoft, USA) also involving certain features offered by the STATGRAPH 5.1 (Microsoft, USA) software, ARCADA (Dialog-MGU, Russia), and implied detecting the median values, its mean root square deviation, and the non-sampling error. Further on, following the patterns commonly employed for medical and biological studies (sample numbers; type of distribution; non-parametric criteria; reliability of the difference of 95%, etc.) the significance of the sampling difference was evaluated subject to the Student's criterion (t) and the respective significance index (p).

RESULTS AND DISCUSSION

Given the wide range of the linear values in humans, we carried out a comparative analysis of the calculated indices with linear dimensions of the dentoalveolar arches, taking into view the type of gnathic part of the face (dolicho-, brachy- and mesognathy) and tooth size features (micro-, macro- and normodontia) (Fig. 3–5).

A comparative analysis of the calculated and actual values, the discrepancies were found to be unreliable and due to insignificant measurement errors, as well as features of the material used for the jaw cast models, which allowed us developing an algorithm to forecast the shape and dimensions of the dental arches.

ALGORITHM FOR FORECASTING THE SHAPE AND SIZE OF DENTAL ARCHES IN VIEW OF THE TEETH SIZE AND THE BASIC MAXILLOFACIAL PARAMETERS

First, the mesial-distal (M–D) dimensions of the anterior teeth were measured as well as the length determined for the dental arch's anterior part, limited with the canine cusps (Fig. 6).

When determining the length of the anterior part of the dental arch, in view of the fact that the arch is bounded with the medial part of the canines, we recommend the length of the anterior part (*L*) be calculated as the sum of the medial-distal dimensions of the four incisors to be further added to the sum of the canine sizes multiplied by 0.75, following the formula below:

$$L = M\text{–}D_{\substack{\text{medial}\\\text{incisors}}} + M\text{–}D_{\substack{\text{lateral}\\\text{incisors}}} + (0.75 \cdot M\text{–}D_{\text{canines}})$$

Second, we determine the inter-canine distance. In case of anomalies, the canines often have abnormal position, due to which we recommend that the dental arch width between the canine cusps be estimated by the size of the external nose.

The dental arch width between canines ($W_{3\text{-}3}$) corresponds to the nose width between the ***ac–ac*** points.

In case of abnormal dental arch shapes, measuring the mesial-distal dimensions does not present any issue. However, it is hard to measure the front-canine diagonal and the depth of the dental arch's anterior part.

Fig. 3. Pictures of the oral cavity of the patient with permanent teeth microdonthism in the anterior (a), lateral right (b), and lateral (in) projections

Fig. 4. Pictures of the oral cavity of the patient with permanent teeth macrodonthism in the anterior (a), lateral right (b), and lateral (in) projections

Fig. 5. Pictures of the oral cavity of the patient with normodontism of permanent teeth in the anterior (a), lateral right (b), and lateral (c)

Fig. 6. Photo of a plaster model with a designated length of the anterior part of the dental arch

Given that the front teeth are located arch-wise, while the front-canine diagonal is a straight line, determining its size could be performed using the formula, which Huygens once noticed and pointed at the dependence of the length of the arch, chord and height. Therefore, the depth of the dental arch's anterior segment was calculated from formula:

$$D_{1-3} = \sqrt{[(9 \cdot L^2) + (6 \cdot L \cdot W_{3-3}/2) - (15 \cdot W_{3-3}/2)]}/64$$

The front-canine diagonal can be calculated as the sum of the product of the arch half-length by 0.75, and the half-width of the dental arch's anterior part by 0.25, following the formula:

$$\text{The front-canine diagonal} = (0.75 \cdot L/2) + (0.25 \cdot W_{3-3}/2)$$

Of particular interest is identifying the diameter (radius) of the circle on which the front teeth are to be located. In this case, the value of the central angle (α) shaped by the circle radii that bound the chord corresponds to twice the arctangent of the ratio of the doubled depth of the dental arch's anterior part to the width of the arch between the canines, and is subject to the formula:

$$\alpha = 2 \cdot \text{arctg}\, 2\, D_{1-3}/W_{3-3}$$

The circle diameter was defined as the ratio of the dental arch's width between the canines to the central angle sine:

$$\text{The circle diameter} = W_{3-3}/\sin\alpha$$

On the resulting circle, from its upper point on, we measure segments equal to the front-canine diagonal. The calculations based on these formulae may seem too complicated at first glance.

All the calculations can be downloaded in Excel while the clinical expert will only have to measure the medial-distal dimensions of the three front teeth and the nose width between the ***ac–ac*** points.

CONCLUSIONS

1. In view of the results of morphological, clinical studies and mathematical modeling, an algorithm for forecasting the shape and dimensions of dental arches has been proposed, based on measuring the relatively stable parameters, namely, the anterior teeth dimensions, and the basic parameters in the maxillofacial area.

2. The algorithm is based on mathematical calculations of the circle geometry and the dependence of the length of the arch, chord and height.

3. The circle diameter was defined as the ratio of the dental arch's width between the canines to the sine of the central angle formed by the circle radii limiting the chord.

4. The size of the front-canine diagonal is comparable with the size of the anterior teeth in a certain ratio.

5. The developed algorithm (a set of biometric measurements and mathematical calculations) is a highly informative, diagnostically significant sequence of actions that can be employed to describe physiological occlusion, make forecasts concerning the shape and size of dental arches when treating patients with dentoalveolar anomalies, as well as to select the tactics and the extent of orthodontic treatment.

6. In clinical orthodontics, the introduction of a forecast algorithm based on the measuring the relatively stable parameters will reveal the deviations in the teeth location as well as in the shape and size of the upper dental arch in the transversal and sagittal planes, reducing the time spent in the early diagnostics phase and increasing the effectiveness of monitoring the outcomes of orthodontic correction.

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SETTING REFERENCE POINTS FOR KEY TEETH LOCATION IN CASES OF ABNORMAL DENTAL ARCH SHAPE

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ABSTRACT — The results of anthropometric, clinical studies and mathematical simulation were used to develop an algorithm for examining patients with anomalies in the shape and size of dental arches, which allows determining the position of the central (inter-canine) point. The algorithm is based on the measurement of the dental arch width between the second molars and the front-distal diagonal value, which is defined as the ratio of the half sum of 14 teeth to 1.04 coefficients. It has been proven that the canine teeth location is determined from the size of the front-canine diagonal calculated as the ratio of the dental arch diagonal to the ratio of the dental arch length and the sum of the width of the 6 anterior teeth crowns, employing the correction factor of 0.1.

KEYWORDS — anomalies of shape and size of dental arch, facial measurement methods, teeth size, key teeth.

INTRODUCTION

The integrity of the human body, as well as the interdependence of its organs and systems' form and functions, can be definitely seen when studying the interrelation (interdependence) of local and general somatic disorders arising in case of dentoalveolar anomalies [4, 7, 11, 19, 26, 29].

Russian and foreign experts have proven that dentoalveolar anomalies manifest themselves through abnormal development of teeth and jaws. The symptoms in such cases

include abnormal occlusion, which must be differentiated from various types falling within the normal range, and which do not involve functional and aesthetic disorders. There is no definite standard norm for the jaw system structure, but on the contrary, there are individual features of the shape, size and location of the teeth and jaws that fit within the limits and concept of the norm as long as they provide for an aesthetic optimum and proper function of the dental apparatus [2, 17, 24].

Anomalies of the occlusion whose distinctive features include incorrect position of the teeth, absence of multiple contacts between the dentition, changed shape of the alveolar process, disturbed size of the jaw bones and their spatial arrangement in the skull, are aggravating factors adding to the development of functional disorders pertaining not to maxillofacial area alone yet also to the macroorganism as a whole [6, 14, 25].

Planning the treatment of patients with dentoalveolar anomalies involving a thorough clinical and paraclinical examination, an individual approach in view of the respective set of anthropometric and X-ray cephalometric parameters, with deep knowledge of the terminology and contemporary classification of dentoalveolar anomalies, and specific features of dentoalveolar development, would allow shaping a well-balanced, functional and aesthetic occlusion [1, 3, 23, 35].

The anomalies of dental arch sizes and shapes are diverse and respective literature contains various classifications for them [5, 16, 20].

There are many research methods that allow not only detecting abnormalities and deformations, yet also identifying the treatment methods in orthodontic clinics [12, 30].

Note to be made that human dentoalveolar arches present a wide variety of shapes and sizes even within physiological occlusion, proof to this fact being numerous studies published in Russian and other languages [8, 18, 21, 33].

There are methods of estimation as well as the basic sizes shown for different varieties of the dental arch shape. Apart from linear dimensions, angular parameters are presented – namely the torque size and angulations, which is of particular importance when selecting braces [9, 27].

Special attention is paid by clinicians to the location of the central (or inter-incisal) point which changes its position in case of the dental arch asymmetry, protrusion or retraction of the incisors. The spot located between the medial incisors is used by clinicians to identify the depth of the dentoalveolar arches [13, 22, 34].

Identification of the depth of the dental arch anterior segment is an essential attribute when diagnosing occlusion disturbances [10, 31].

Evaluation of the transversal and sagittal dimensions is performed employing the Pont (Linder-Hart) methods, while clinical experts claim these methods to be faulty [15].

Special attention is to be paid to studies focusing on evaluation of the dental arches dimensions based on the relatively stable cranio-facial parameters [28, 32].

Nevertheless, while studying the available research outcomes, we failed to find data regarding how to determine the position of the central point and key teeth (namely canine teeth) in people with abnormal shape and size of the dental arches, which might guide the choice of methods for orthodontic treatment.

Aim of study

identification of the position for the central point and canines in case of abnormal shape and size of the dental arches.

MATERIALS AND METHODS

The study involved 57 patients with physiological occlusion of permanent teeth and 52 people with anomalies in the shape and size of dental arches.

The method for forecasting the references concerning the location of the key teeth at abnormal shape of the dental arches is based on examining patients with physiological occlusion.

The most stable parameter of the upper arch is the width between the second molars and the permanent teeth dimensions.

Teeth were measured in the mesial-distal plane at the widest point between the proximal surfaces (the tooth crowns width). The dental arch width was determined between the points located on the vestibular distal tubercles near the crowns' occlusal contour (Fig. 1).

The front-distal and canine diagonals were determined from the central point located between the medial incisors near the cutting edge, to the points located on the molars and canines, respectively (Fig. 2).

The depth of the dental arch was determined from the central intercellular point to the line connecting the antimeres, the canines and molars in particular (Fig. 3).

The statistical processing was performed directly from the common data matrix of ECXEL 7.0 (Microsoft, USA) also involving certain features offered by the STATGRAPH 5.1 (Microsoft, USA) software, ARCADA (Dialog-MGU, Russia), and implied detecting the median values, its mean root square deviation, and the non-sampling error. Further on, following the patterns commonly employed for medical and biological studies (sample numbers; type of distribution; non-parametric criteria; reliability of the difference of 95%, etc.) the significance of the sampling difference was evaluated subject to the Student's criterion (t) and the respective significance index (p).

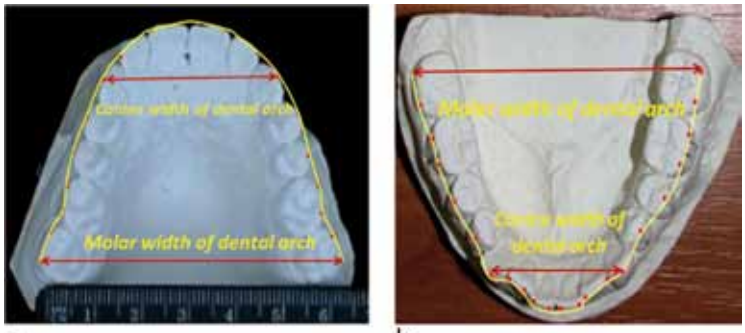

Fig. 1. *Photographs of plaster models of the upper (a) and lower (b) jaws with plotted reference lines for measuring the width of the dental arch*

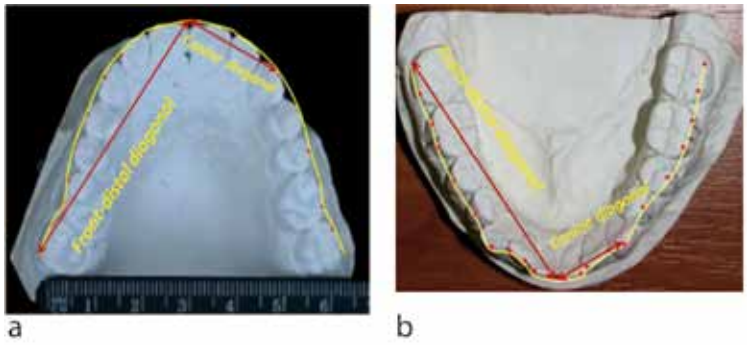

Fig. 2. *Photographs of gypsum models of the upper (a) and lower (b) jaws with marked reference lines for measuring the frontal-distal and canine diagonal of the dental arch*

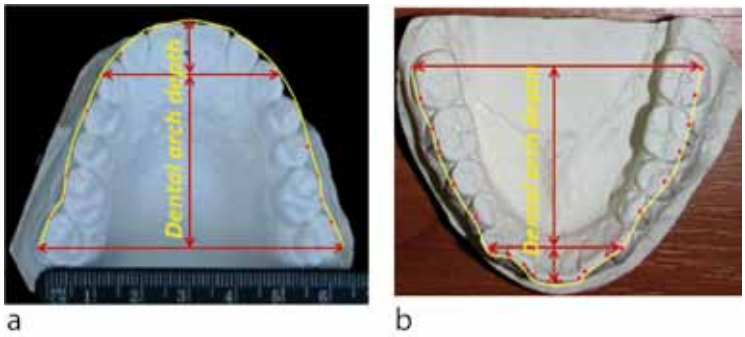

Fig. 2. *Photographs of plaster models of the upper (a) and lower (b) jaws with plotted reference lines for measuring the depth of the dental arch*

RESULTS AND DISCUSSION

The study carried out among people with physiological occlusion has shown that the sum of the upper jaw 14 teeth (the length of the upper dental arch) averaged 114.66±1.98 mm, which fell within normodontia. At the same time, the 6 anterior teeth accounted for 47.04±1.02 mm. The ratio of the dimensions of all teeth to the anterior teeth was 2.437±0.098 mm. The front-distal diagonal (FDD) was 55.125±0.39 mm on each side, which was 1.04 of the dimensions of the teeth making up the dental arch. The obtained value can be used as a factor in determining the dental arch diagonal through the teeth size.

The patients under examination had a front-canine diagonal (FCD) of 21.72±0.34 mm in the average. In this regard, the ratio of FDD to PCD for the group as a whole was 2.538±0.026, which was 0.1 mm above the ratio of all the teeth to the front teeth. This means that the obtained data can be used to identify the size of the front-canine diagonal in patients with abnormal dental arches. In this case, the formula below is recommended:

$$FCD = FDD / (\Sigma_{14\ teeth}/\Sigma_{6\ teeth} + 0.1)$$

The dental arch width between the molars was 59.7±1.45 mm, while at the canines it was 37.31±0.98 mm. The ratio between the measured dimensions in the transverse plane was 1.6, which can also be used as a reference to determine the forecasted width of the dental arch between the canines based on the size of the arch width at the molars in case of abnormal dimensions of the dental arches and abnormal arrangement of the canines or their retention.

The ratio of the dental arch length to its width was 0.96±0.03, which signified mesognathic dental arches in the majority of the patients examined.

The dental arch depth at the anterior part was 11.09 mm and corresponded to the calculations for the width of the anterior and front-canine diagonals, like a right-angled triangle leg.

The obtained data laid the basis for the algorithm employed to identify the position of the key teeth and the dental arch size evaluated in patients with abnormal occlusion.

The algorithm is based on identifying the central spot, which corresponds to the location of the inter-incisal point located in front or backwards, depending on the retrusive or protrusive position of the incisors in anomalies. To do this, a horizontal transverse line was drawn on translucent paper (tracing paper), which corresponded to the dental

arch width between the second molars. A perpendicular was built from the center of this line. Then, from the points bounding the first line, segments were cut equal to the FDD to the perpendicular, while the resulting intersection point corresponded to the location of the inter-incisal (central) spot (Fig. 4).

Note to be made that the FDD size was determined through the sum of the mesial-distal diameters of the teeth. The formula we recommend is here below:

$$FDD = \Sigma_{14\ teeth}/2/1.04$$

Second, the forecasted width of the dental arch between the canines was determined. To do this, the value of a relatively stable parameter, namely the dental arch width between the second molars, was divided by the index of 1.6.

Third, the size of the front-canine diagonal was calculated. When determining the potential size of the front-canine diagonal in patients with dental arch anomalies, the calculation followed the formula below:

$$FCD = FDD / (\Sigma_{14\ teeth}/\Sigma_{6\ teeth} + 0.3)$$

The forecasted depth of the dental arch was calculated as a right-angled triangle leg, where the hypotenuse was the front-canine diagonal, the second leg being half the width of the dental arch between the second molars:

$$\text{The depth of the anterior part} = \sqrt{FCD^2 - (\text{half inter–canine width})^2}$$

The marks on the tracing paper were applied to the cast model of the upper jaw to determine the position of the key teeth and to develop further plan of orthodontic treatment (Fig. 5).

The radius of the circle on which the six front teeth are to be located, was carried out through the generally accepted in geometry method employed to determine the diameter of the circle along the length and height of the sector bounded by the chord.

Besides, the circle diameter (D) was calculated by the ratio of the arch length (L) to the central angle (α):

$$D = \frac{L}{\alpha}$$

The central angle was shaped by the circle radii bounding the chord, and was calculated subject to the formula:

$$\alpha = 2 \cdot \text{arctg}\ \frac{2H}{X}$$

where H is the segment height and X is the chord length.

The length of the arch bounded by the chord was calculated as the product of the ratio of the chord length to the central angle ratio to its sine:

$$L = X \cdot \frac{\alpha}{\sin \alpha}$$

In calculation of the circle diameter when constructing the dental arch, the length of the chord (X) corresponded to the inter-incisal distance. The height of the segment (H) determined the depth of the dental arch anterior section and was calculated as a leg to a right-angled triangle shaped by the front-canine (canine) diagonal and half the width of the dental arch between the canines.

Given the above, identifying the basic references for the location of the key teeth, it is sufficient to measure the mesial-distal diameters of the 14 teeth that make up the dentition, and the width of the dental arch between the second molars. The appropriate ratios are used to identify the location of the inter-incisal (central) point and the canines' position.

CONCLUSIONS

1. In view of the outcomes of morphological, clinical studies, and mathematical modeling, an algorithm for examining patients with anomalies in the shape and size of dental arches has been developed, which allows identifying the position of the central (inter-incisal) point.

2. The algorithm is based on measurements of the dental arch width between the second molars and the front-distal diagonal, which is defined as the ratio of the half sum of 14 teeth to the ratio of 1.04.

3. It has been proven that the location of the canines is determined based on the size of the front-canine diagonal calculated as the ratio of the dental arch diagonal to the ratio of the dental arch length to the sum of the crowns width of the 6 anterior teeth, with a correction factor of 0.1 used.

4. The introduction of the algorithm (a sequence of morphometric measurements and mathematical calculations) would allow, with a high degree of certainty, detecting the position of the central point and the key teeth. Employing such reference points when working with patients revealing abnormal dental arch shape or size, might lead to a better reasoned choice of tactics and the manipulations to be performed, which would allow shortening the time spent on diagnostics and enhance the effectiveness of orthodontic treatment.

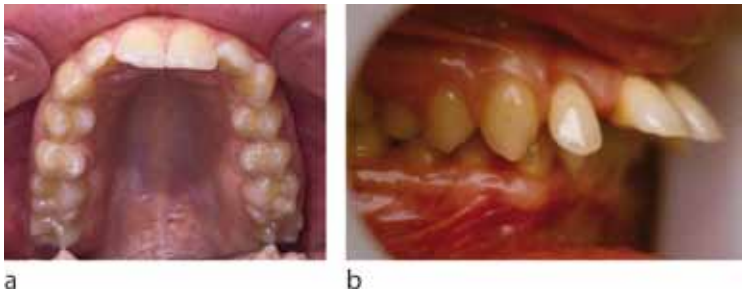

Fig. 4. Changed position of the central point at retrusion (a), protrusion (b) incisors

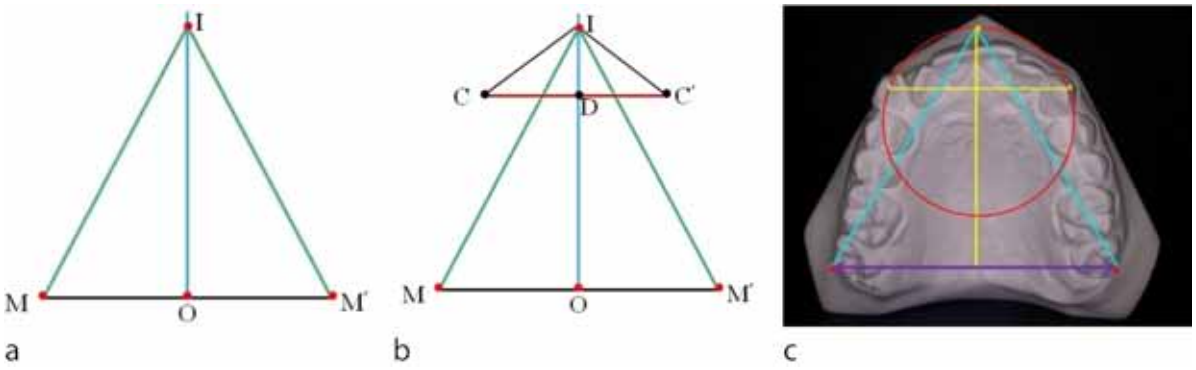

Fig. 5. Method for identifying the position of the central point (I) — a, the depth of the anterior part (ID), the positions of the canines along the FCD (IC and IC') — b and the evaluation on the upper jaw cast model (c)

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CHEMICAL COMPOSITION OF PEPTIDES OF NIOSOMAL GEL "REGENERIN"

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Placenta extract has a complex molecular composition, which leads to diverse clinical effects. The objective of the research was to study the chemical composition of the drug "Regenerin" on the basis of the peptides of the placenta of animal origin by liquid chromatography and time-flight mass spectrometry.

It is shown that mass spectra obtained include signals of different intensity in the range 2000–10500 Da. This releases a number of characteristic features. The peptides of molecular weight 1000–10000 Da represent cytomedines that play an important role in maintaining the structural homeostasis of cell populations. These substances have the ability to regulate the functional activity of the cell populations, which explains the regenerative ability of the drug in treating chemical burns.

Thus, the regenerative effect of the drug "Regenerin" based on the impact on the signaling mechanisms of intercellular interaction. We can conclude that the regeneration process the "inside", which allows its use for immune regulation, wound healing, neurotrophic therapy, hepatoprotection and in the treatment of chemical burns of the cornea [1, 2, 3].

The use of placenta extract of animal origin, standardised according to indicators the chemical composition (peptides, amino acids, trace elements, vitamins, etc.), allows to achieve high efficiency in the regulation of regeneration processes of the cornea drug "Regenerin".

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THE TREATMENT OF CONGENITALLY MISSING MAXILLARY LATERAL INCISORS: AN INTERDISCIPLINARY APPROACH

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The aim of our work — to determine the indications and contraindications for the treatment of edentulous maxilla lateral incisors, according to clinical guidelines for the treatment of this disease with the use of dental implants.

Materials and methods. The basis of this study presents the clinical results of treatment of patients with edentulous maxilla lateral incisors, who were treated at the "North Caucasian Medical Education Center" from 2009 to 2014. We observed 12 patients. All patients were women aged 18 to 32 years old.

Recommendations:

1. Implant treatment of this pathology is recommended after 18 years of age, when the growth of the facial skeleton is finished. If orthodontic treatment is performed at a younger age, this group of patients needs to use removable prosthesis until the facial skeleton is completely formed. Such prosthesis should be adjusted every six months.

2. When the space between the central incisors and canines is expanded enough using orthodontic treatment, implant treatment should not be started earlier than 6 months after orthodontic treatment is finished.

3. The minimum distance between the central incisors and canines should be 5.5 mm.

4. Preference should be given to CAD / CAM technologies when manufacturing implant fixed prosthetic constructions in such clinical cases.

Conclusion: An interdisciplinary approach must be applied for planning of the treatment of patients with edentulous maxilla lateral incisors. Installation of single implants in such situations is a predictable treatment, while remaining the method of choice for clinicians.

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THE EFFECTIVENESS OF THE COMPREHENSIVE PROGRAM OF PREVENTION OF CARIES TEETH IN CHILDREN WITH RESPIRATORY DISEASES

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The human body is a complex biological structure all the organs, systems and processes which are closely linked. It is known that lesions of the nasopharynx and respiratory tract leads to the violation of nasal breathing, which in turn is one of the reasons for the formation of anomalies of dentoalveolar system. In addition, in the pathology of the respiratory system it affects the mucous membranes of the oral cavity, breaks down its trophic and metabolic processes that subsequently lead to exhaustion, degeneration and necrosis.

In turn, the poor state of the oral cavity, the presence of teeth with caries create favorable conditions for the formation of pathogenic microflora, reduced local immunity, which leads to diseases of the digestive tract, the respiratory system.

Chronic foci of infection in the mouth can trigger and exacerbate a number of diseases of the bronchopulmonary apparatus.

According to who, every year diseases of the respiratory system sick every third inhabitant of the planet. One of the most important challenges in Pediatrics is a disease of the respiratory system. Modern medicine has made great strides in the diagnosis and treatment of diseases of the respiratory system. However, the share of respiratory diseases account for different data from 66,5% to 72.3% of the total number of diseases [1, p 15–22]. According to local researchers, the overall incidence of the Russian population with respiratory diseases in children under 14 years between 1993 and 1998 increased from 770,3 to 811,8 on 100 thousand population of corresponding age.

The clinical picture of inflammation in periodontal tissues is characterized by hyperemia, edema, bleeding disorders. At the cellular level, the inflammatory process is manifested by appearance of cellular infiltrates and the release of cytokines, leading factors of inflammation, combined with the factors of the compliment.

Thus, there are a number of studies that allow to reveal the close relationship of diseases of the oral cavity with some respiratory diseases. It is therefore necessary to develop measures of prevention of diseases of the oral cavity in terms of a somatic disease.

One of the most common diseases are bronchitis, to their share, according to several authors account for between 50–90% of children.

In children suffering from chronic bronchitis, noted the pallor and pasty mucous membrane of the lips and cheeks that occurs due to constant oxygen starvation. They are often diagnosed chronic catarrhal cheilitis with severe sloughing of the epithelium, angularly cheilitis, the skin in the corners of the mouth maseribane, there are minor cracks and a whitish-yellow crust, the cracks on the red border of the lips [4,p 112].

Currently, doctors practice the use of bronchodilators as well as inhaled glucocorticoid drugs for acute and recurrent bronchitis. During the inspection of the oral cavity in 18.7% of children reveal petechiae in the field of hard and soft palate, which merge to form hemorrhagic spots. In 23% of cases viewlet oral thrush. From the red border of the lips changes in the form of the dry form of exfoliative cheilitis and angulares 11.3% and 3.1% respectively, in 9% of cases observed cracked lips corners of the mouth. Dryness of the lips occurs in 53% of children.

Therefore, children suffering from respiratory diseases that require a more careful readjustment of the oral cavity and the prevention of dental diseases.

Objective: to study the effectiveness of complex program of dental diseases prevention for children and adolescents with chronic bronchitis (ICD 10 code:J41.8).

Materials and methods: In a voluntary clinical research study agreed to take part in 106 children and adolescents aged 6–15 years from Vladivostok. Was conducted a dental examination of the patient: inspection, palpation, percussion, probing, staining "color-test".

The intensity of caries was determined by the index KP, KPU KP, KPU. The prevalence of dental caries was determined by the percentage of persons with caries teeth of patients. Using the gingivitis index GI (Loe H., Sileness J.,1963) determined the periodontal status. The level of hygiene was examined using a simplified index OHI-S (Green J. S., J. K. Vermillion,1964).

After the dental examination and determine the level of oral health, all patients underwent professional oral hygiene. All patients were prescribed a course of preventive medical measures, which included: appliques within 3 minutes of the drug "Gluftored" (doctrate, with an interval of 5 days), the appointment of the drug "Imudon" 6T/day course of 10 days.

The results of the study. From the results of the study shows that at carrying out of preventive programs with the use of drugs ", Gluftored", "Imudon" was a decrease in the intensity of caries, decreased indices of hygiene and gingivitis, and hence, improved oral health in general.

The rate study	Before the study	After the study
The prevalence of dental caries	78,5%	78,5%
The intensity of caries	7,0	6,4
The index of hygiene	2,87±0,08 (p<0,001)	1,76±0,03(p<0,001)
A gingivitis index	0,48±0,04(p<0,001)	0,21±0,02(p<0,001)

Discussion of the results of the study. Analyzing the data in the literature about the poor dental status of children and adolescents with chronic bronchitis, given our clinical observations and studies and taking into account possible negative (exacerbation of the underlying disease) the effect of therapeutic drugs used in dentistry, we believe that the most important place in the practice of a dentist is to prevent dental diseases

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RESTORATIVE TREATMENT OF PARODONTAL PATHOLOGY WITH THE USE OF NATURAL MINERALS

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When treating periodontal diseases, one prefers to use dosage forms that do not have side effects. These drugs include a drug based on bischofite and glycerol solvate of titanium "Tizol", it stimulates the regeneration of tissues, has anti-inflammatory, immunostimulating, antibacterial and anesthetic effect.

"Tizol"" is a preparation based on the aqua complex of titanium glycerol solvate (manufacturer – pharmaceutical company "Society for Laboratory Research of Medical Preparations" (LLC "Olimp", Yekaterinburg). "Tizol"" is approved for medical use as an anti-inflammatory, antiedematic, antiallergic, antimicrobial, analgesic and radioprotective agent.

According to preclinical and clinical studies, the effectiveness of using bischofite in dentistry has been proven, in particular, for the treatment of patients with inflammatory periodontal diseases. Thus, the use of bischofite in a concentration of up to 10%, can reduce the degree of inflammation, increase the level of microcirculation and metabolism of the mucosa of the prosthetic bed and the level of local immunity of the oral cavity, contributes to reducing the frequency of recurrence of the disease.

It has been established that the use of 10% bischofite gel "Polycatan" on the basis of bischofite combined with conventional therapy increased the

clinical effectiveness of the treatment, reducing the time of disappearance of the main symptoms of the disease by 2 times, compared with the control group of patients (without the use of the drug "Polycatan"), in patients with chronic catarrhal gingivitis and chronic generalized periodontitis of moderate severity; by 1,7 times, in comparison with the control group, in patients with chronic generalized periodontitis of moderate severity. Six months after the therapy, remission was achieved in 100% of cases in patients with chronic catarrhal gingivitis, in 94.12% of cases in patients with chronic generalized periodontitis of mild severity, in 91.3% of cases in patients with chronic generalized periodontitis of moderate severity. The use of the preparation "Bischofite and Tizol® gel" on the 1st, 7th, 30th day of the observations contributed to the activation of the regenerative process of periodontal tissues.

Thus, the use of natural minerals containing magnesium (bischofite) both in native form and in combination with modern penetrators allows efficient use of bischofite in dental practice for the treatment of periodontal pathology.

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INTERMAXILLARY CORRESPONDENCE COEFFICIENT IN PEOPLE WITH PHYSIOLOGICAL OCCLUSION AND VARIOUS FACE TYPES

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Features of the structure of the dental arches and the relationship between their main parameters have been of interest to morphologists and dentists for many decades. Numerous methods of investigation have been proposed and the main parameters of dental arches have been determined taking into account sexual and racial features. Interrelations of sagittal and transversal sizes of dental arches are shown. At the present time odontometric data are analyzed in sufficient detail and linear parameters of the lower dental arches are shown in people with dolichognathic, brachygnathic and mesognathic forms of dental arches with their normo-, macro- and microdontism. However, there is insufficient information in the literature on the relationship between the main parameters of the dental arches of both jaws in people with different types of face, the intermaxillary compliance coefficients are not indicated, that was the purpose of this study.

Morphological and clinical examination of 65 people, aged 18–25, with physiological occlusion and macrodontism of permanent teeth was carried out. The main indicator of the dental arches belonging to the gnathic type was the dental index of dental arches, calculated as the ratio of 7 teeth of each half of the dentition in the width of the dental arch between the second molars. With the mesognathic type of dental arches, the value of the index was 0.94 ± 0.03. The index value of less than 0.9 corresponded to brachygnathia, and more than 0.97 – to dolichognathia. Macro-dental type included dental arches, the length of which exceeded 118 mm. Transversal dimensions were determined between the points located on the vestibular distal tubercles of the second permanent molars. In the region of canine teeth, the distance between their tearing tubercles was measured. The diagonal of the arch was measured from the interincisal point to the second molars. The depth of the arch was measured from the interincisal point to the line connecting the vestibular distal odontomers of the second molars. The ratio of transversal, sagittal and diagonal sizes of dental arches was determined and the relationship of dental parameters was evaluated.

The results of the studies showed the interrelation of the sizes of macrodontal dental arches of the upper and lower jaw. Dimensions of the teeth are large, and the sum of the width of the crowns of 14 teeth in people with macrodontal mesognathic types of dental arches was: on the upper jaw – 120.91 ± 2.92 mm, on the lower jaw – 112.42 ± 2.79 mm. The length of macrodontal brachygnathic dental arches was: on the upper jaw – 122.81 ± 2.98 mm, and on the lower jaw – 114.69 ± 2.89 mm. Dolichognathic macrodontal types of dental arches, according to odontometry, also did not differ significantly from other gnathic forms of dental arches. The sum of mesial-distal dimensions of 14 teeth was: on the upper jaw – 121.01 ± 2.93 mm, on the lower jaw – 114.1 ± 2.87 mm.

Dimensions of dental arches in the transverse direction had features depending on their gnathic type. In people with mesognathic macrodontal types of dental arches, the width of the anterior part of the dental arch of the upper jaw was 37.78 ± 1.21 mm, the inter-canine distance on the lower jaw was 28.15 ± 1.17 mm. The ratio of these dimensions of the upper jaw to the lower one was 1.34 ± 0.03. The width of the arch between the second molars of the upper and lower jaws was 64.78 ± 1.84 mm and 58.89 ± 1.92 mm, respectively. The ratio factor was 1.1 ± 0.01. The depth of the dental arch of the upper jaw is greater than the lower one and makes 46.95 ± 1.54 mm and 44.14 ± 1.22 mm, respectively. Frontal canine diagonal on the upper jaw is 21.47 ± 0.44 mm, at the lower jaw – 16.44 ± 0.51 mm. The front-molar diagonal was: on the upper jaw – 57.03 ± 0.63 mm, on the lower jaw – 53.04 ± 1.02 mm. Brachygnathic macrodontal types of dental arches differed from mesognathic dimensions in the transversal and sagittal directions. The width of the dental arches is larger in the region of the molars and was: 71.31 ± 2.03 mm on the upper jaw, 64.82 ± 2.24 mm on the lower jaw. For dolichognathic forms, a decrease (in comparison with other types of dental arches) of transverse dimensions is typical, and were 60.87 ± 2.38 mm and 55.34 ± 1.97 mm for the upper and lower jaws, respectively.

Conclusion. As a result of morphometric studies of linear parameters and dental indicators of macrodontal dental arches, intermaxillary relationships of sizes were established. For all gnathic types of macrodontal dental arches, the ratio of the sum of the width of the crowns of the 14 teeth of the upper jaw to those of the lower jaw is, on average, 1,065 ± 0,005. The ratio of the half sum of the width of the crowns of 14 teeth to the size of the front-distal diagonal is 1.065 ± 0.005 on both jaws. The ratio of the width of the dental arch of the upper and lower jaw is 1.1 ± 0.01, regardless of the type of dental arches. The obtained information can be used in anatomy to determine the correspondence of the main dimensions of the dental arches of the upper and lower jaws, for physiological occlusion characteristics. In addition, the obtained information on the relationship between the dimensions of dental arches can be useful in clinical dentistry for predicting the shape and size of dental arches in the treatment of patients with dentoalveolar anomalies.

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CORRELATION OF THE DEPTH OF THE FRONTAL PART OF THE DENTAL ARCH WITH ODONTOMETRIC PARAMETERS AND INTERCANINE VALUES

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The effect of tooth size on the depth of the dental arch in the anterior, posterior regions, as well as at different age periods was shown in the studies of domestic and foreign experts. The works of Korkhaus show that the depth of the anterior part of the dental arch is determined by the size of the teeth. The results of the study are presented in the form of a table showing the sum of the width of the crowns of the four upper incisors and the depth of the dental arch to the level of the horizontal line connecting the Pont points

on the premolars. Clear interdependent parameters are presented and correction factors are noted. However, other dimensions of dental arches characterizing their gnathic and dental types are not given in this study. In addition, the depth was determined to the level of premolars. In the clinic of orthodontics, the estimation of the anterior part of the dental arch, limited by permanent canines, is most important. At present, the classification of dental arches is proposed and their main parameters are given, both in physiological and pathological occlusion. The effect of the inclination of the anterior teeth in the vestibular lingual direction (torque) on the sagittal dimensions of the dental arches was noted. Dependence of the depth and width of the dental arches, including the anterior part, limited by the canines on the type of dental arches (meso-, dolicho-, and brachygnathic) was noted. At the same time, the difficulty of accurately determining the depth of the dental arch due to its small size was noted. But we did not find information on the relationship between the depth of the anterior part of the dental arch and the intercanine distance, taking into account the size of the anterior teeth.

The purpose of the study: to determine the proportional relationship between the depth and width of the anterior part of the dental arch, limited by the canine teeth, taking into account the size of the anterior teeth.

The study was conducted on gypsum models obtained from 85 patients of the first period of adulthood with physiological occlusion. Patients were divided into three groups: with normodont, macrodont and microdont type of dental arches. The width of the dental arch was determined between the points located on the tearing tubercles of the canine teeth. Considering the complexities and errors in measuring the true depth of the dental arch on the gypsum model, we used the technique of determining this parameter as the leg of a right-angled triangle whose hypotenuse was a canine diagonal. The second leg was a half-width of the dental arch. The determination of the canine diagonal was not difficult with a relatively correct arrangement of anterior teeth. The diagonal was measured between the incisal and canine points. With anomalies in the position of the anterior teeth, the size of the canine diagonal was calculated from the sum of the width of the crowns of the three teeth (incisors and canines of one side of the arch), taking into account the correction factor. Gnathic type of dental arch was estimated by dental index as the ratio of the sum of the width of the crowns of 14 teeth to the width of the dental arch between the second molars. With an index value of 0.9 to 0.97, dental arches were related to the mesognathic type. The sum of 14 teeth from 112 mm to 118 mm was regarded by us as normodontism. The increase in the indicator was characteristic for the macrodontic type, and the decrease was characteristic for the microdontic type of dental arches.

The results of the studies showed that, in people with orthognathic bite and mesognathic type of dental arches, the width between the points located on the tearing tubercles of the canines with normodontism was, on average, 36.55 ± 0.82 mm. A similar parameter for the macrodontic dental system is 38.78 ± 0.91 mm, and for microdontic – 34.13 ± 0.75 mm. Thus, the dimensions of the teeth affect the width of the anterior part of the dental arch with the same type of gnathic form.

The size of the incisive-canine diagonal in the mesognathic normodontic type of the upper dental arches was 21.33 ± 0.34 mm. With macro- and microdontism, the indices were 23.67 ± 0.42 mm and 19.24 ± 0.39 mm, respectively. The dimensions of the anterior part of the dental arch in the sagittal direction (the depth to the level of the canines) in the normodontic type were 11.09 ± 0.12 mm, for macrodontism – 13.57 ± 0.14 mm, and with microdontism this parameter was 8, 92 ± 0,11 mm. The ratio of the frontal canine diagonal to the depth of the anterior part of the dental arch with normodontism is 1.93 ± 0.23, with macro- and microdontism the indicated index was 1.75 ± 0.24 and 2.16 ± 0.24, respectively.

Conclusions.

1. The depth and width of the mesognathic-type dental arches is determined by the size of the teeth.

2. The determining factor is the diagonal size of the anterior part of the dental arch.

3. Canine diagonal depends on the size of the front teeth.

4. The depth of the dental arch is directly dependent on the transversal and diagonal linear parameters.

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METHODS FOR PRESERVING THE PULP OF HUMAN TEETH

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Introduction. There are many circumstances in which the state of the pulp of the root canal due to real or potential risk, pain, infection, inflammation or functional disorders is subject to acute, irreversible pulpitis with transition to chronic pulpitis in the conditions of development of necrosis and its consequences [1, 9]. There are other circumstances in which pulp injuries are not always irreversible: initial pulpitis, iatrogenic pulp fracture, trauma, dystrophic disorders [7, 12]. A high success rate with endodontic therapy testifies to the elimination of the disorder and the absence of a tendency to necrosis. However, in most cases, inevitable pulpectomy occurs, which often leads to the loss of the entire dental organ [3, 8, 11]. Even successful endodontic treatment greatly weakens the whole structure of the tooth and often dictates further prosthetics, with subsequent increase in tissue loss [2, 10]. In order to preserve the mass of root tissues and tooth crowns with the possibilities of regeneration, it is necessary to direct the search for methods of conservative treatment to preserve the vitality of the teeth, which improve the prognosis of tooth preservation. It is necessary to develop a strategy for treating pulpitis in different types of situations, based on a thorough analysis of emerging risks.

Aim. Conduct an analysis of treatment methods while maintaining the viability of the pulp.

Material and methods. The analysis of own and accessible literary data.

Results. An analysis of the current state of the issue of preserving the viability of human pulp pulp showed that at the present stage the methods of treatment are actively developed by many scientists who successfully solve the problems of dentistry [6, 7]. The development of pulp therapy methods is a vital issue for many patients, since pulp disease of the tooth is the main cause that negatively affects the condition of the oral cavity [4]. Extirpation of pulp is currently the main method of dental treatment. Along with the development of minimal invasive cosmetic dentistry, with the use of various technologies for processing materials and pathogenetically substantiated preservation of healthy dental tissue with the growth of tooth crowns, the urgency of problems that require immediate resolution in the dental clinic is growing. The experience and knowledge on methods of endodontic treatment require generalization. Solving the problems of tooth pulp regeneration with the help of modern diagnostic and treatment technologies is possible on the basis of cellular technologies [5].

Discussion. Tissue repair of human tooth pulp is possible only if there is a deep knowledge of the sources of development and mechanisms of regulation of migration and adhesion of stem pulp cells, the composition of cellular ensembles that cause secretion signal molecules of a certain direction in differentiation of odontoblasts.

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CONSERVATIVE TREATMENT OF THE GONARTHROSIS (ARTHROSIS OF THE KNEE) WITH THE PRESENCE OF BAKER'S CYST

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Baker cysts usually occur in almost any form of pathology of the knee joint. More often — with arthritis, for example, rheumatoid arthritis, or damage to the cartilage, especially the medial meniscus. Baker's cysts arise between the sinews of the medial head of the gastrocnemius muscle and the semiembranous muscles. They are located behind the medial femoral condyle. Most Baker cysts support this direct communication with the synovial cavity of the knee. With the aim of conservative treatment of patients with post-traumatic gonarthrosis and the presence of Baker's cyst, we apply complex conservative treatment with sonographic control of the results of treatment (in some cases, with an intermediate control). Gonarthrosis is the leader in the incidence of the disease among articular arthrosis. There are different ways to treat gonarthrosis. We managed to develop a new modification of the method of treatment of gonarthrosis. In carrying out this method, a subcutaneous administration of the ozone-oxygen mixture and subsequent electrical stimulation of the site of introduction of the ozone-oxygen mixture with an electric current of 50 Hz, a current of up to 7–10 mA, an impulse duration of 0.3 ms and a drug interstitial electrophoresis of the drug Caripain, duration of the procedure 12–15 minutes daily, for a course of treatment of 12–15 procedures. The application of this method leads to a reduction and arrest of pain syndrome in patients with knee osteoarthritis, a decrease in the inflammatory reaction of the knee structures, restoration of the knee joint function. 397 patients were treated. The stable clinical effect of this method, obtained in the treatment of patients with osteoarthritis of the knee joint, makes it possible to recommend this method for a wide clinical application.

To assess the presence and severity of pathology at the knee joint level, a comprehensive diagnostic approach, including X-ray and ultrasound, is actively used in the sanatorium. In a number of cases, to clarify the nature of the pathological process, patients were referred for study to medical and preventive medical institutions in Barnaul for CT or magnetic resonance imaging of the knee joint. To control the results of treatment, the method of ultrasound diagnostics of the pathology of the knee joint

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After the completion of the course of treatment, patients noted that the pains significantly decreased or completely passed. In the ultrasound examination of the knee joints, a subculture bag of the gastrocnemius muscle (Baker's cyst) was determined. Typical sonographic signs: the presence of an anechoic neck (canal) of the podsuchozhal bag (between the medial head of the gastrocnemius muscle and the tendon of the semimembranous muscle), an anechogenic bag. Localization: the medial edge of the popliteal fossa (more often), the middle part of the popliteal fossa. In 39 patients (23.8%) Baker's bilateral cyst was determined, in 125 patients — one-sided, in 78 patients (62,4%) — left-sided, in 47 patients (37,6%) — right-sided. Cyst volume from 0.7 ml to 21.3 ml. Aspiration of cysts was not performed. As a result of complex conservative treatment, when performing a control study, a decrease in the volume of cysts was noted in 143 patients (87.2%). In 21 patients, the volume of cysts did not change objectively. Our control studies were performed 7–16 days after the start of therapy. In a number of cases (29 patients — 17.6%), as a result of the control studies, the disappearance of cysts was noted. The initial volume of cysts in these cases was from 0.7 to 5.1 mL.

Thus, conservative complex treatment with the use of interstitial electrostimulation and subcutaneous administration of the ozone-oxygen mixture can successfully be used to treat posttraumatic gonarthrosis with the presence of Baker's cyst. The method of ultrasound diagnosis can objectively assess the presence of a cyst, accurately determine the amount of content, provide the possibility of establishing a dynamic control of the results of treatment.

THE EFFECT OF POLY(ADP-RIBOSE) POLYMERASE INHIBITOR 4-HYDROXYQUINAZOLINE ON OOGENESIS AND CELL DEATH PATHWAYS UNDER EXPERIMENTAL IMMUNE COMPLEX-MEDIATED INJURY IN MICE

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Introduction. Recently, the nuclear enzyme poly (ADP-ribose) polymerase-1 (PARP-1) has been actively studied. In the face of moderate genotoxic stress, PARP-1 promotes DNA repair and maintains genome stability [1, 2, 3]. With excessive activation, the pathogenetic role of PARP-1 (involvement in the pathogenesis of a number of diseases, including autoimmune ones) is manifested [4, 5]. It is known that in the pathogenesis of many reproductive system organ diseases, including the ovaries, immuno-inflammatory processes play an essential role. However, the role of PARP-1 in inflammatory diseases of the female reproductive system has not been practically studied. At the same time it was shown the important physiological role of the enzyme in the reproductive function, including in gametogenesis [6, 7, 8]. PARP-1 is expressed in oocytes and follicular cells [7, 8]. Studies in experimental models of several diseases, including autoimmune (ones), showed a pronounced protective effect of PARP inhibitors [4, 9, 10, 11]. These data served as the basis for the pharmacological PARP inhibition in various inflammatory diseases. In this study, we used a murine model of immune complex-mediated pathology induced by immunization with bovine serum albumin (BSA) to investigate the effect of PARP-1 inhibitor 4-hydroxyquinazoline (4-HQ) on oogenesis and cell death pathways.

Material and Methods. The experiments were carried out on mature female mice (18–20 g, inbred strain CBA). The mice (n=17) were immunized with BSA intravenously 6 times every 7 days according to the scheme: 1) 150; 2) 175; 3) 200; 4) 225; 5) 250 and 6) 275 mg of BSA per kg of body weight. Seven days after the last injection, the mice were euthanized under ether anesthesia and their ovaries were sampled. The control mice received equivalent volumes of normal saline. The nine mice immunized with BSA were injected with 4-HQ («Sigma», USA) intraperitoneally (100 mg/kg of body weight) twice each week.

Results. We have found that administration of BSA resulted in immune cells activation, elevated level of immune complexes in serum and their enhanced deposition in the liver, spleen, aorta and kidney as well as resulted in vascular and parenchymal damage of these organs. Immunization increased the number of necrotic lymph node cells (by 4.5 times) and necrotic thymocytes (by 3.5 times). The percentage of apoptotic immune cells did not change significantly. PARP inhibition exerted a strong cytoprotective effect: viability of thymus and lymph node cells was increased mainly due to reduced level of necrosis. As shown by comet assay, DNA damage index of immune cells was increased 4,0 times in mice with immune complex-mediated pathology, $P<0.001$. The percentage of thymic cells with strong DNA damage was increased to 77% under immunization (compared to 1.5% in control mice) and the percentage of such cells from lymph nodes was increased to 80% (compared to 0% in control), in both cases $P<0.001$. Genotoxic stress was reduced by treatment of immunized mice with 4-HQ: the percentage of lymphocytes with strong DNA damage was significantly decreased. Immunization caused ovary dysfunction in female mice. The administration of BSA induced a significant reduction in granulosa

cell viability mainly due to enhanced necrotic cell death that was accompanied by impairment of the meiotic maturation of oocytes: the number of oocytes at metaphase I and metaphase II decreased significantly compared to that of control mice (corresponding data are 72.59±3.4% and 32.91±3.6% vs. 88.64±2.7% and 48.39±3.0% in control group; P<0.05). The treatment of the immunized mice with 4-HQ improved granulosa cell viability: diminished necrosis, while the percentage of apoptotic cells remained unchanged. Inhibition of PARP also improved the meiotic maturation of oocytes at metaphase I (86.44±2.5%; P<0.05) and II (45.11±3.9%; P<0.05) in comparison to immunized mice.

Conclusion. Therefore we demonstrate that PARP-1 activation may be involved in the pathogenesis of the experimental immune system failure. PARP inhibition exerted the protective effect that may be mediated, at least partially, through the attenuation of necrosis. Thus our results give evidence that inhibition of this enzyme may constitute a perspective target in immune complex diseases prevention and therapy.

Keywords: immune-complex injury, immune cells, oocytes, follicular cells, PARP inhibition, mice.

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BIOCHEMISTRY OF THE VITREOUS BY THE HUMAN EYE IN NORMAL AND PATHOLOGICAL CONDITIONS

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The paradigm of the vitreum morphology of the human eye, thanks to clinical and fundamental research on the rehabilitation and replacement of transparent eyes, dictates a deeper analysis of the available concepts of sources of development, structure, and the interaction of cellular diffrons in the transparent eyes, given the limited availability of biomaterials [1]. Therefore vitreoretinal surgery based on modern conceptions of the structure of the eye is a complex task in connection with the special histophysiology and anatomical relationships of the retina and vitreous body (CT) [2]. Some authors consider disturbances in the system of vitreoretinal interrelations, as a result of the phenotypic heterogeneity of the KIF11 gene, a representative of the kinesin family 11 associated with retinopathy. Maggio E, Polito A, Guerriero M, Prigione G, Parolini B, Pertile G. (2017) indicate the important role of St in the development of age-related macular degeneration (AMD). Reva G.V. with et al. found that with glaucoma CT is undergoing changes associated with destruction, degeneration and fragmentation of its fibrillar core: with open-angle glaucoma, hypohydration of the stroma of the anterior part of the CT occurs, and in the closed-angle gland, hyperhydration occurs. Reducing the level of collagen, the destruction of the collagen core, the loss of its property to retain water leads to hyperhydration of the whole CT, increasing the load on the drainage system of the eye. The basis of the macromolecular CT skeleton, which performs the skeletal and form-building function, is a three-dimensional network of type II collagen, proteoglycans and hyaluronic acid, which forms an entangled spongy molecular polyanion network filling the space between randomly oriented collagen fibrils and having a stabilizing effect on them, preventing contact of fibrils. Despite the abundance of works devoted to the study of the eye, the vitreous humor still remains the least studied structure: there is no complete picture of the processes of transformation of its matrix in norm and in pathology. Abdo M, Haddad S, Emam M. (2017) provides comprehensive data on the development of the organ of sight in rabbits, while similar studies on human material are clearly insufficient. In the prenatal development of the human eye, carotenoids are found: in the vitreous body – lutein and its oxidized forms; in the lens – oxidized forms of lutein. The albumin content in the eye of the human fetal eye has a maximum value significantly higher than the level of albumin in the adult body's CT, at 17–22 weeks and decreases by the 28th week, reaching a level characteristic of the adult eye. Alpha-fetoprotein (AFP) in the vitreous eye of human fetuses is found simultaneously with albumin at the same stages of development. In the eyes of human fetuses (15–28 weeks of pregnancy), the presence of lutein is detected, which is not detected in the eye of an adult person, but disappears after the 28th week of the fetal period. The content of carotenoids decreases by the 28th week, and in 30-week-old human fetuses, carotenoids are not detected. The increased content of these proteins in the CT only in the prenatal period, coinciding with the period of intensive growth of the eye, suggests that this rise should be associated with morphogenetic processes.

VASCULOGENESIS IN THE ORGANS OF THE HUMAN EMBRYON

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Introduction. Sources of development and the laying of organs of the human embryo are of great importance for the full development of the fetus [8,11]. At the present stage, there are very limited and contradictory data on the morphology and vasculogenesis in various organs of the human embryo [1, 5 ,10]. At the present stage, it is not known how epigenetic mechanisms can control the regulation of angiogenesis in embryo development.Increasing evidence suggests that multipotent stem cells are harbored within a vascular niche inside various organs. Although a precise phenotype of resident vascular stem cells (VSCs) that can function as multipotent stem cells remains unclear, accumulating evidence shows that multipotent VSCs are likely vascular pericytes (PCs) that localize within blood vessels. These PCs are multipotent, possessing the ability to differentiate into various cell types, including vascular lineage cells [11].

Absence of exhaustive data on the sources of vasculogenesis in the structure of the embryo and the dynamics of the development of vascular organ pools has determined the direction of our scientific research [7, 9].

Aim. To study the features of the development of blood vessels in systems of visceral organs and skin of the human embryo.

Material and methods. The study used material of 48 human embryos at the age of 3 to 8 weeks of prenatal ontogenesis.

Results. It is established that in the period from the 3rd to the 4th week in the body of the embryo there is an uneven laying of the blood vessels. In the ectomesenchyme surrounding the cerebral bladder of the cephalic end of the embryo, large capillaries appear, filled with megaloblasts. The mesenchyme appears later in the trunk region, capillaries and blood islands in it are absent in this period. In the tissues of the heart, lungs, liver, walls of brain blisters and neural tube there are no blood. The liver of the human embryo is represented by a network of trabeculae from hepatocytes, the cells of the network are filled with megaloblasts. These morphological findings differ from those of other authors describing vasculogenesis in the liver of mouse embryos. Our data are in accordance with the data of other authors that in some organs of a developing human the endothelium is a derivative of the cells of the developing organ that come into contact with megaloblasts and receive the corresponding direction of differentiation as a result of intercellular interactions [3 , 4].

We noted that already in the embryonic period in the parenchyma of the liver, in contact with megaloblasts, and in the ectomesenchyme surrounding the cerebral bubbles, cells bearing receptors to markers CD68 and CD163 [2]. We assume that vasculogenesis in the liver of a human embryo develops similarly to this process described in the spleen and liver in the example of rats Goldman O, Han S, Hamou W, Jodon de Villeroche V, Uzan G, Lickert H, Gouon-Evans V. (2015) [6].

Discussion. Our data do not fit into the classical concept of vasculogenesis in the tissues of a human embryo. The obtained results testify to the necessity of continuing the scientific search on this issue. Many factors necessary for physiological angiogenesis and the complexity of regulating space-time interactions in the development of vasculogenesis of the embryo dictate the direction of efforts to address these issues.

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THE MAIN FEATURES OF HISTOMORPHOLOGICAL CHANGES 24 HOURS AFTER CLOZAPINE AND CLOZAPINE-ETHANOL POISONING

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Introduction. Clozapine (atypical antipsychotic drug) and its metabolites are capable of accumulating in body tissues including the lungs [1, 2]. Several studies have shown pathological changes of the pulmonary tissue in case of clozapine poisonings [3, 4]. Morphological changes in the lungs were studied presumably at late stages of the pathological process. At the same time, the effects of ethanol in combination with clozapine on this process remain unclear.

The aim of the study. The aim of the study is to reveal morphological changes in the lungs in acute clozapine and combined clozapine — ethanol poisoning 24 hours after the intoxication.

Materials and methods. We performed a comparative study of histological sections of the lungs of outbreed male rats weighing 290–350 g. Group 1 included 5 rats treated with clozapine oral dose (150 mg/kg) and decapitated 24 hours after the intoxication, group 2 included 5 rats treated with clozapine (150 ml/kg) and ethanol (5 ml/kg) and decapitated 24 hours after drug administration. Control group included intact rats (5). Fisher's ratio test was used to estimate the reliability of the difference between the groups. The presence of the sign was considered to be reliable if the sign didn't appear in one group and appeared in 4 or 5 cases in the other group. Morphometric analysis was also performed (ten fields of vision for each tissue section). Estimated parameters were as follows: the share of the area of alveoli, the share of the area of intraalveolar septi, the share of the area of vessels, the share of the area of WBC, the share of the area of WBC in intraalveolar septi, the share of the area of distelectasis, the share of the area of edema.

Results. No pathological changes were observed in the control group. The signs detected in the study group 1 (clozapine, 24 hours) were as follows: an increase in WBC number, distelectasis, thickening of intraalveolarsepti due to edema, infiltration of intraalveolar septi by WBC.

The signs detected in group 2 (clozapine, ethanol, 24 hours) were as follows: hemorrhage into alveolar septi and alveoli, infiltration of intraalveolar septi by leucocytes, perivascular hemorrhage, thickening of the intraalveolar septi due to edema, an increase in WBC number, atelectasis, distelectasis.

The area of alveoli was significantly lower in both study groups compared with the control group. The area of intraalveolar septi, the area of edema, of the area of WBC and of the area of WBC in intraalveolar septi were significantly higher in both study groups in comparison with controls. The area of distelectasis, the area of WBC, the area of WBC in intraalveolar septi were significantly lower in group 2 (clozapine and ethanol, 24 hours) compared with group 1 (clozapine, 24 hours) .

Conclusion. All these pathological changes can be used to diagnose clozapine and clozapine-ethanol poisonings and the cause of death.

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HYDRO-ACOUSTIC WAVES IN REHABILITATION OF LIMB FROSTBITING

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The deep development of Arctic Regions, where air temperatures reach 30–50° C below zero in winter time, increases the risk of *cold trauma* (CT) — total hypothermia of the entire body and frostbite of limbs in the personnel of exploration companies (geologists, geophysicists) and employees of industrial or oil and gas extracting enterprises. Non-native population, civil and military seamen, border guards, working on a rotational basis or residing permanently in cities beyond the Arctic Circle, are also in a great danger.

Currently, there are no adequate methods of CT treatment. Conservative and surgical treatment and physical methods (low frequency, ultrasound, hyperfrequency radiation treatment) give a high percentage of disability. [1, 2, 3].

We proposed a new method of CT treatment and rehabilitation. It is a method of low-frequency hydroacoustic impact on human limbs, based on a unique sound wave generator. [4, 5].

Hydroacoustic (HA) waves are generated in the audio range from 50 to 700 Hz and pass through the entire volume of patient's limbs with negligible reflection, causing micro vibrations at molecular level and initiating the variable HA overpressure from 500 to 10000 Pa on the skin, subcutaneous fatty tissue, tendons, muscles, periosteum, capillaries, lymphatic vessels and nerve endings.

The use of this method in the first day of CT, improves microcirculation, restores hemorheological processes, reduces blood viscosity and the possibility of hypercoagulable syndrome, preventing thrombosis, stimulates tissue and vascular regeneration processes, improves lymph flow, metabolism and gas exchange of tissues.

Previously, the method was tested for athletes' and dancers' muscle overstrain [6].

The given method has autonomy, requires minimal additional equipment and supply, it can be used in any conditions or in the companies in the Arctic Regions.

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POSSIBILITIES OF CORRECTION OF INTRAOCULAR PRESSURE WITH A HELP OF ANTIHYPERTENSIVE DRUG IN COMBINATION WITH A NEUROPROTECTANT FOUND IN PATIENTS WITH DIAGNOSED GLAUCOMA OF PSEUDONORMAL PRESSURE FOR THE FIRST TIME

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Glaucoma is one of the most common eye diseases that leads to serious and irreversible changes in the organ of vision, up to blindness. According to WHO, there are more than 60 million people suffering from glaucoma in the world. It is projected that the number will increase 10 million in the next 10 years. According to various reports, there are more than 1.5 million patients with glaucoma in Russia.

The purpose of our study was to assess the efficiency of complex therapy in patients with first found glaucoma of pseudonormal pressure. With the help of anti-hypertensive drug Prolatan in combination with neuroprotectant Mexidol on the course of the disease and on the quality of life.

Materials and methods: There were 25 examined female patients, age 47,2±2.3 with a diagnosed glaucoma of pseudonormal pressure in the initial stage. Diagnosis was carried out according to accepted standards. Objective evaluation criteria included the dynamics of visual acuity, the level of intraocular pressure (IOP), the data of perimetry, (HRT) and a survey of the quality of life (SF-36). The IOP level did not exceed 21 millimeter of mercury. All patients had frequent headaches and low blood pressure.

All patients were prescribed: instillation drug Prolatan, 1 time a day at night for 6 months, the drug Mexidol (inside), 1 pill 3 times a day for 1 month (two courses of medication).

There was observed positive dynamics thanks to the therapy. The level of IOP was reduced by 30% from baseline. The results of tomography of the optic nerve showed an increase of area and volume of a disc rim band, which indicates stabilization of the glaucomatous process. According to perimetry, contraction of visual fields, enlargement of blind spots, increase relative and absolute scotoes was not determined. On the background of the therapy, all patients didn't have headaches, had visual acuity and the quality of life was improved.

In conclusion, integrated therapy is an efficient basic method to treat glaucoma of pseudonormal pressure.

It provides reduction and stabilization of IOP throughout the treatment, improves the quality of life and prevents the progression of glaucoma.

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ISSUES IN THE DIAGNOSTIC MANAGEMENT OF SANDIFER'S SYNDROME IN A 3-YEAR-OLD MALE CHILD WITH ADENOTONSILLAR PATHOLOGY: *A CLINICAL CASE*

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ABSTRACT — Chronic adenoiditis has a high prevalence among children, specifically in preschool-age population and in midchildhood. Chronic adenoiditis often occurs against the background of somatic comorbidities. Severe hypertrophy of pharyngealand palatine tonsils causes hypoxic ventilatory response and, subsequently, leads to the development of obstructive sleep apnoea syndrome.

KEYWORDS — children, Chronic adenoiditis, obstructive sleep apnoea/hypopnea syndrome, Sandifer's syndrome, interdisciplinary follow-up, management.

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INTRODUCTION

In clinical practice, one patient might suffer from several diseases simultaneously. They differ in progression and degrees of impact on each other. Chronic adenoiditis is one of most prevalent diseases in preschool-age population [1]. Chronic intermittent hypoxia against the background of chronic adenoiditis is formed due to the syndrome of sleep apnoea/hypopnea. It is known that respiration impairment during nocturnal sleep is revealed in children of any age.

Prevalence of obstructive sleep apnoea/hypopnea syndrome (OSAHS) in children in overall population ranges from 0.0% to 5.7% [2]. These indices vary according to the age. At the age of two-six years, prevalence of snoring amounts to 10-14% [3], while prevalence of OSAHS reaches 3% [4]. Adenotonsillar pathology in preschool-age children may induce different nervous system pathologies including such impairments as learning disability, behaviour decline, the syndrome of central nervous system (CNS) hyperactivity, the attention deficit and hyperactivity disorder (ADHD), etc. [5]. A rare form of nocturnal hypoxemia against the background of OSAHS is impairment of the extrapyramidal system.

Early diagnostics of cases related to comorbidity between chronic adenoiditis and Sandifer's syndrome is of critical significance for correct diagnosis, symp-

tomatic treatment and disease prevention, taking into account that Sandifer's syndrome represents a multidisciplinary diagnostic and therapeutic challenge [6,7].

The purpose of the present study is to present a clinical case of Sandifer's syndrome in a child with adenotonsillar pathology complicated by OSAHS.

A CLINICAL CASE

A male preschool child Fyodor aged 3 was first examined by a neurologist of the Neurological Centre of Epileptology, Neurogenetics and Brain Research of the University Clinic (UCNC) in October 2016. The child suffered from stereotypically proceeding abrupt awakenings during nocturnal sleep with anxiety and crying; disorder of nasal breathing during nocturnal sleep, snoring and nocturnal enuresis; occasionally, dystonic head tilt with version and rotation to the left was registered as well as dystonic muscle tension in extremities and the neck during and after awakening; regular long-lasting release of mucus from nasal cavity. Prenatal period was not burdened.

Anamnesis vitae: the child was born at the gestational age of 40 weeks. At the age of six months, dystonic seizures were first diagnosed in his trunk and limb muscles. An examination to determine their origin was not performed. At the age of one year, seizures became more frequent and the child was hospitalised. Video-EEG-monitoring was conducted which verified the diagnosis of epilepsy. The child underwent antiepileptic therapy for one year. No epileptiform activity was revealed during subsequent video-EEG-monitoring. However, hyperexcitability, excessive salivation, nocturnal snoring dystonic tension in neck and limb muscles remained. That served as the reason to refer the parents to an epileptologist and an otolaryngologist.

Neurological status: the child's state was satisfactory, consciousness was clear, psychomotor and speech development corresponded to age norms. The child was hyperexcitable and impulsive. Attention deficit was observed. Cranial nerves: without lesions. No lesions have been revealed in motor, coordination and sensorial spheres. The patient had no meningeal signs and was continent.

At the otolaryngologic consultation, the patient's mother reported regular long-lasting release of mucus from nasal cavity, frequent episodes of acute respiratory viral infections up to one time per month; a new qualitative sign was occasional manifestation of eructation and musty smelling breath.

Objective status: nasal breathing was difficult. Excessive mucus secretion was observed. Examination by means of a zero-degree inflexible endoscope (endoscope tube diameter equalling 1.7mm) after topical anaesthesia and anemisation was used. It revealed that the nasal mucosa was cyanochrous, rears of inferior nasal conchae were enlarged, choanal lumens were blocked by 2/3 by hypertrophied tissue of pharyngeal tonsil; pharyngeal openings of auditory tubes were partially blocked by lymphoid tissue. The mouth was open during breathing; high-arched palate was observed; posterior pharyngeal wall mucosa was moderately hyperaemic; lateral pharyngeal bands were enlarged; palatine tonsils have first-degree hypertrophy; tonsillar lacunae were clean. Maximum sizes of posterior mandibular, submandibular, anterior and posterior cervical lymph nodes were 7.0/10.0/5.0 mm (over three groups) on both sides. Lymph nodes were elastic, non-tender and were not matted together.

In order to conduct differential diagnosis of Sandifer's syndrome, focal epilepsy and dyskinesia of non-kinesiogenic origin, the child underwent additional examination. Magnetic resonance imaging (MRI) of the brain (1.5 Tesla) showed that lymphoid tissue widened nasopharynx lumen by 2/3, the nasopharynx dome was blocked. No structural pathology of the brain was revealed; no cerebrospinal fluid dynamics impairment was found. Cardiorespiratory monitoring (for 8 hours) revealed four respiratory anomalies and two episodes of obstructive apnoea with maximum duration of 15 seconds. Two episodes of hypopnoea with maximum duration of 40 seconds were also observed; the apnoea-hypopnoea index (AHI) was 2.0 per hour (the normal value for children is 1 per hour). Desaturation index was 3 episodes per hour. Snoring was registered with the index of 30%. Mean oxygen saturation was 96% with the minimum of 88% which is a prognostic criterion for unfavourable course of the disease. Mean heart rate totalled 85 bpm, with the minimum of 51 bpm and the maximum of 196 bpm.

Epicrisis: ronchopathy, OSAHS of medium severity; pronounced respiratory sinus arrhythmia; transient nocturnal hypoxemia of medium severity. Nocturnal video-EEG-monitoring shoed that the structure of nocturnal sleep was defragmented; deep stages of slow-wave sleep were not reached, sleeping was of superficial character. Ultrasonography (US) of the stomach with an aqueous-siphon test (intake of 200 ml of water). Trendelenburg positioning for five minutes did not show the presence of gastroesophageal reflux (GR). However, signs of GR complicated by esophagitis with spontaneous reopening of esophageal hiatus were revealed during a fibrogastroduodenoscopy (EGD).

In general, it is noteworthy that onset of increased respiratory disease frequency in absence of confirmed

contacts in this child was registered simultaneously with the period of active motor performance and the onset of reflux manifestations forming neurological symptoms and the risk of aspiration.

On the basis of neurological, otolaryngologic and gastroenterological examination a diagnosis was verified: Sandifer's syndrome with mainly nocturnal abrupt dystonic attacks with involvement of limb, trunk, face and neck muscles; reactive (GR-associated) chronic adenoiditis; II degree hypertrophy of the pharyngeal tonsil, I degree hypertrophy of palatine tonsils; widespread hypertrophy of neck group lymph nodes on both sides of combined (reactive post-inflammatory) genesis.

Complication: ronchopathy, OSAHS of medium severity, pronounced respiratory sinus arrhythmia; transient nocturnal hypoxemia of medium severity.

A case conference with the participation of a neurologist, an otolaryngologist and a gastroenterologist was held and a collective decision of the otolaryngologist and the neurologist to perform a cold-plasma adenoidectomy as a salvage surgery was rendered.

One-year catamnesis: the child is registered with dispensary observation by a neurologist, an otolaryngologist and a gastroenterologist of the UCNC. General state of the child is satisfactory. Nocturnal sleep is normalised. No dystonic attacks or enuresis during sleep are registered. Pronounced syndrome of attention deficit and hyperactivity disorder has decreased significantly, socialisation of the child is not compromised at the moment. Nasal breathing is free. No relapses of neurological, gastroenterological or ENT-pathologies are observed within the framework of the interdisciplinary follow-up. Antiepileptic preparations were withdrawn more than one year ago.

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