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THE IMPACT OF BODY MASS INDEX AND AGE OF WOMEN ON DEVELOPMENT OF EATING DISORDERS

Ziuzin V.O.

Medical Institute of the Petro Mohyla Black Sea National University, Mykolaiv, Ukraine

<https://doi.org/10.35339/ic.10.2.zui>

ABSTRACT

Background. Obesity and overweight cause more than 1.3 million deaths each year, but even this figure may be an underestimate. According to the Global Nutrition Report, in 2021, 61.4% of men and 55.5% of women in Ukraine faced this problem. 90.0% of obesity cases are the result of lifestyle, eating disorders and physical activity.

The aim of the study was to evaluate the influx of indicators of the body mass index and age of women on the development of disordered eating behavior.

Materials and Methods. The study involved 240 female patients divided into 4 groups depending on the BMI: group 1 included 60 women with underweight, with Body Mass Index (BMI) average (18.0 ± 0.75) kg/m²; group 2 – 60 overweight women with BMI average (27.5 ± 0.98) kg/m², group 3 – 60 obese women with BMI average (32.2 ± 1.21) kg/m². Of the women of group 3, 40 had gynoid type obesity, 20 – abdominal type obesity. The control group consisted of 60 women with average BMI (23.5 ± 1.11) kg/m². The age of the patients ranged from 18 years to 75, average age was (46.5 ± 1.41) years. During the investigation, a variety of psychometric tests were used (Eating Attitudes Tests, Body Attitudes Test and Eating Disorder Examination Interview).

Results and Conclusions. In women of group 1 bulimia nervosa was recorded 8 times ($p < 0.05$) more often, and anorexia nervosa 2.7 times ($p < 0.05$) more often than in the control group. In patients of group 2, compulsive overeating was recorded 5 times ($p < 0.05$) more often, and in group 3 – 18 times ($p < 0.05$) more often than in the control group. Strong correlation was established between the young age (18–30 years) and bulimia nervosa ($r = 0.7$, $p = 0.02$), atypical bulimia nervosa ($r = 0.8$, $p = 0.001$), anorexia nervosa ($r = 0.76$, $p = 0.003$) and atypical anorexia nervosa ($r = 0.87$, $p = 0.004$).

Keywords: obesity, overweight, compulsive overeating, food behavior disorders.

Introduction

Obesity is a complex multifactorial disease characterized by excessive deposition of adipose tissue in the body. Globally, obesity and overweight cause more than 1.3 million deaths each year, but even this figure may be an underestimate [1]. In the European Region, the situation with overweight and obesity has investigated epidemic proportions. 63.0% of men and 54.0% of women are overweight. The highest rates of overweight

and obesity are found in Mediterranean and Eastern European countries. People with lower levels of education are more likely to be overweight [2]. According to the Global Nutrition Report, in 2021, 61.4% of men and 55.5% of women in Ukraine faced this problem [3]. Over 13 years, according to the State Statistics Service, the average weight of Ukrainians has increased by 2 kg. Mostly, the population over the age of 50 has recovered: in 2008, the average weight of adult Ukrainians was 73 kg, in 2021 – 75 kg [4]. Obesity, according to the State Statistics Service, affects 16.0% of the adult population of Ukraine. This is more than the world average (8.0%). According to the Ministry of Health, there is some dissociation between the urban and rural populations: in rural areas, obesity was detected in 18.0% of men and 36.0% of women, while in urban areas – 12.0% and 21.0% respectively. Overweight is

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present in 35.0% of men and 32.0% of women living in villages, and in 33.0% of men and 27.0% of women living in cities [5]. It is quite natural that the proportion of obese people is increasing among representatives of older age groups: for example, among women 55–64 years old, 38.0% suffer from this disease, while among women 18–24 years old – only 3.0% [6] (Fig. 1).

vian countries was equal to that of Europe. Point width ranged from 0.4 to 1.5 cm, and lifetime width ranged from 0.7 to 5.8 cm for disordered binge eating in women [10]. In the study, which included Argentina, Brazil, Chile, Colombia, Mexico and Venezuela, the breadth of food behavior disorder was 3.53 percent [11–13]. Thus, this particular study showed that the prevalence of disor-

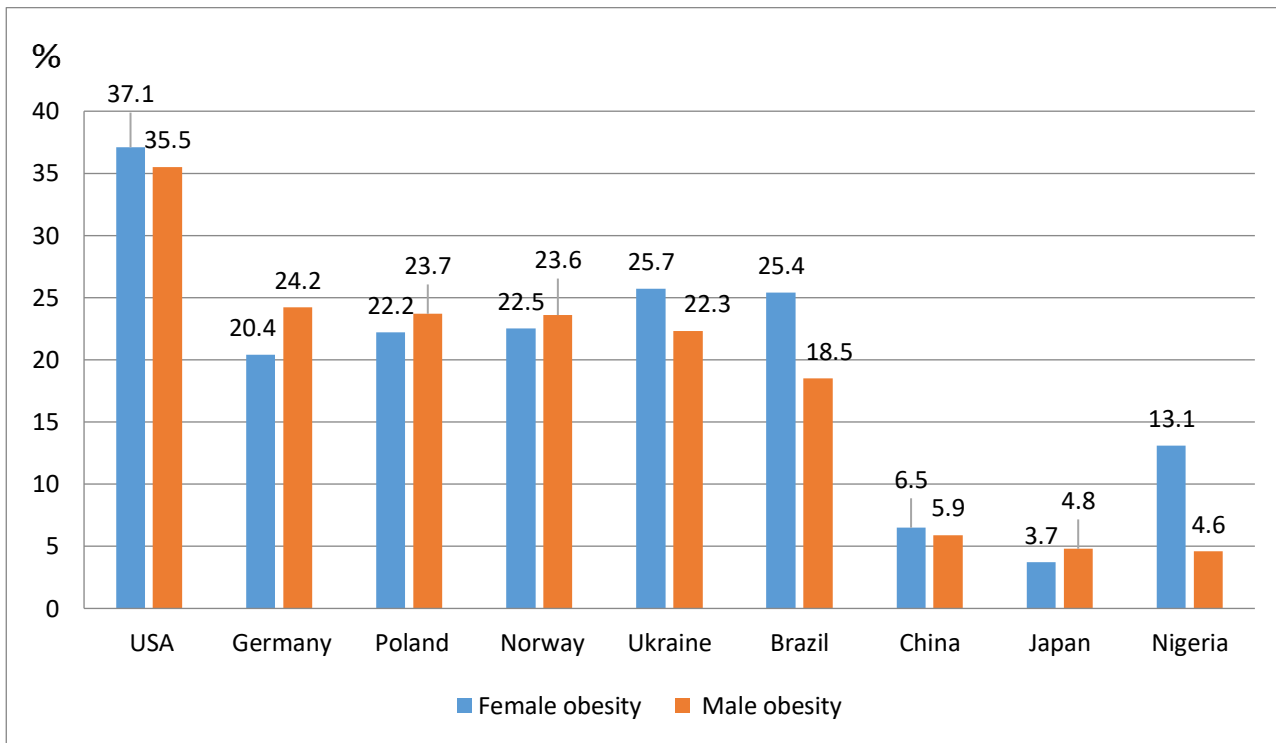


Fig. 1. Epidemiology of overweight and obesity in different countries during 2021–2022.

About 90.0% of obesity cases are the result of lifestyle, eating disorders and physical activity: long intervals between meals and excessive portions; overeating in the evening; eating before bed; a large amount of carbohydrates and fats (especially confectionery and animal origin) with a lack of fiber and dietary fiber; excess intake of calories compared to their expenditure; lack of physical stimulation of muscle tissue to participate in fat processing. This also includes family predisposition and psychogenic overeating. Evidence of the increasing eating disorders is observed in developing countries and among ethnic minorities. While further investigation of disorders reported, as a rule, is concentrated in Western America. This discord is growing in different cultures [7–9]. Currently, in the United States, food behavior disorder is present in 0.8% of adult men and 1.6% of adult women. In the study, which included Finland, Sweden, Norway and Iceland, the prevalence of disordered grub behavior in the Scandina-

dered food behavior in these Latin American countries is equal to that of Western countries [14].

The aim of the study was to evaluate the influx of indicators of the body mass index and age of women on the development of eating disorders.

Materials and Methods

During the study 240 female patients were examined at the University Clinic of Petro Mohyla Black Sea National University. All patients were divided into 4 groups depending on Body Mass Index (BMI): group 1 included 60 women with underweight with BMI average (18.0±0.75) kg/m², group 2 – 60 overweight women with BMI average (27.5±0.98) kg/m², group 3 – 60 obese women with BMI average (32.2±1.21) kg/m². Of women from the group 3, 40 had gynoid type obesity, 20 had abdominal type obesity. The control group consisted of 60 women with patients with average BMI (23.5±1.11) kg/m². The age of the patients ranged from 18 years to 75, average age was (46.5±1.41) years.

The examination of patients included detailed collection of patient history and complaints. During history taking, we specified the changes in the body weight over the past 2 years; eating habits, physical activity; taking medications; early diseases of the cardiovascular system (myocardial infarction or sudden death of the father or other first-degree male relatives ≤ 55 years, or the mother or other first-degree female relatives ≤ 65 years); identification and assessment of the impact of diseases associated with obesity (diabetes, hypertension, dyslipidemia, cardiovascular, respiratory and joint pathology, non-alcoholic fatty liver disease, sleep disorders, etc.). Physical examination included BMI calculation; WC (Waist Circumference) measurement; the examination was carried out for the presence of papillary pigmentary dystrophy of the skin (acanthosis nigricans) as a sign of insulin resistance; assessment of severity there are accompanying ones. Laboratory examination included measurement of total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, glucose, aspartate transaminase, alanine transaminase, uric acid, glucose tolerance test, with an increase in fasting glucose of more than 5.6 mmol/l, a family history of diabetes, indirect signs of insulin resistance. Data from instrumental research methods were taken from the patients' medical records.

The diagnosis of eating disorders was made by a psychiatrist after a thorough examination of the patients, in accordance with the American Family Physician criteria. To determine the type and triggers of eating disorders, during the investigation, a variety of psychometric tests were used (Eating Attitudes Tests (EAT), Body Attitudes Test (BAT), Eating Disorder Examination Interview (EDE).

Completing the EAT based on three criteria: 1) the total score based on the answers to the EAT-questions; 2) answers to the behavioral questions related to eating symptoms and weight loss; and 3) the individual's BMI calculated from their height and weight. Generally, a referral is recommended if a respondent scores "positively" or meets the "cut off" scores or threshold on one or more criteria. Regardless of the score, if a respondent feels that they are suffering from feelings that are interfering with daily functioning; they should seek an evaluation from a trained mental health professional.

The BAT is a self-reported questionnaire consisting of 20 questions. The patients are asked to score each statement 0–5, 0 meaning they do not relate to the statement at all, and 5 meaning the

statement frequently describes their sentiment. The answers to these questions are then analyzed and provide information regarding four factors that evaluate the patient's subjective view on their body: negative appreciation of body size, lack of familiarity with one's own body, general body dissatisfaction, and rest factor.

The Eating Disorder Examination Interview (EDE) is a semi-structured interview conducted by a trained clinician to assess the psychopathology associated with the diagnosis of an eating disorder. The EDE is rated through the use of four subscales and a global score. The four subscales are: restraint, eating concern, shape concern, weight concern. The questions concern the frequency in which the patient engages in behaviors indicative of an eating disorder over a 28-day period. The test is scored on a 7-point scale from 0–6. With a zero-score indicating not having engaged in the questioned behavior.

The patients' medical reports with compulsive eating behavior are usually characterized by the following: eating, over a period of time (for example, within 2 hours), an amount of food that is significantly more than most people would eat in the same period of time under the same circumstances. Patients with binge eating disorder complain of not feeling full while eating and have lost control over when to stop eating. The person eats much faster than usual. A person eats until a feeling of excessive and uncomfortable fullness of the stomach appears large amount of food without feeling physical hunger. A person eats alone because he is embarrassed by the amount of food he eats. The person feels disgusted with himself, depressed, or guilty about his overeating. There is distress (negative stress) due to binge eating. It occurs at least 2 days every week for 6 months.

The patients with bulimia nervosa are usually defined as having repeated episodes of binge eating (at least twice a week for a three-month period), in which large amounts of food are consumed in a short period of time. There was a constant preoccupation with eating, a strong desire or obsessive desire to eat. The patient attempts to counteract the fattening effects of food intake by one of the following: inducing vomiting; self-administration of laxatives; alternating periods of fasting; use of medications, in particular appetite suppressants; diuretics.

During a bulimic episode, a person with inappropriate compensatory behaviors regularly induces vomiting, uses laxatives, diuretics or enemas, fasts, or engages in excessive physical acti-

vity on a regular basis. Atypical bulimia nervosa is characterized by repeated episodes of overeating and excessive use of laxatives without significant changes in body weight. Typical concerns about body shape and weight may be absent.

The study was approved by the commission on ethics and bioethics of the Medical Institute of Petro Mohyla Black Sea National University. The study was conducted in accordance with the basic bioethical norms of Helsinki Declaration of the World Medical Association on Ethical Principles of Scientific and Medical Research, as amended (2000, amended in 2008), the Universal Declaration on Bioethics and Human Rights (1997), the Council of Europe Convention on Human Rights and Biomedicine (1997). All participants were informed about the aims, organization, methods of the study and signed an informed consent to participate in it, and all measures were taken to ensure patient anonymity.

Statistical processing of the findings was carried out by the methods of variation statistics implemented by the standard package of application programs SPSS 13.0 for Windows. Under the conditions of normal distribution, quantitative indicators were displayed in the form of mean (M) and standard deviation (S). Discrete values are presented in the form of absolute and relative frequencies (percentage of observation to the total number of examined. The obtained results were considered statistically significant at $p < 0.05$. The

relationship between indicators of the quantitative scale was evaluated using the Spearman correlation coefficient (r). The strength of the relationship was interpreted as follows: very weak – (0–0.3); weak – (0.3–0.5); medium strength – (0.5–0.7); strong – (0.7–0.9); very strong – (0.9–1.0).

Results and Discussion

The study recorded that in women with a body mass index below 18.0 kg/m^2 , bulimia nervosa was recorded 8 times ($p < 0.05$) more often, and anorexia nervosa 2.7 times ($p < 0.05$) more often than in the control group. In patients of group 2 (overweight), compulsive overeating was recorded 5 times ($p < 0.05$) more frequently, and in group 3, 18 times ($p < 0.05$) more often than in the control group. During the study, a direct positive correlation relationship was established between the BMI of patients and the type of eating behavior. In women of group 1, a strong correlation with bulimia nervosa ($r = 0.9$, $p = 0.002$) and anorexia nervosa ($r = 0.88$, $r = 0.001$) was established. In the group 2, the average correlation was between weight and compulsive overeating ($r = 0.7$, $p = 0.0001$), bulimia nervosa ($r = 0.7$, $p = 0.03$). In the group 3 of obese patients, a strong direct connection was established between compulsive overeating and BMI ($r = 0.83$, $p = 0.02$), while in patients in the control group (with an optimal index), a strong connection was recorded with healthy eating behavior ($r = 0.85$, $p = 0.001$) (Table 1).

Table 1. Structure of eating disorders in the examined patients depending on the body mass index

Eating behavior, eating disorder	Group 1, n=60			Group 2, n=60			Group 3, n=60			Control group, n=60		
	n (%)	r	p	n (%)	r	p	n (%)	r	p	n (%)	r	p
Compulsive overeating	5 (8.3)	0.3	0.06*	10 (16.7)	0.7	0.0001*	36	0.83	0.02*	2 (3.33)	0.2	0.2
Bulimia nervosa	16 (26.7)	0.9	0.002*	20 (33.3)	0.7	0.03*	8	0.5	0.2	2 (3.33)	0.42	0.05
Atypical bulimia nervosa	22 (36.7)	0.5	0.23	14 (23.3)	0.4	0.08	4	0.47	0.31	3 (5.0)	0.31	0.99
Anorexia nervosa	8 (13.3)	0.88	0.001*	7 (11.7)	0.3	0.10	5	0.32	0.41	3 (5.0)	0.4	0.81
Atypical anorexia nervosa	7 (11.7)	0.45	0.09	6 (10.0)	0.37	0.90	3	0.46	0.2	2 (3.34)	0.2	0.65
Healthy eating behavior	2 (3.3)	0.37	0.01*	3 (5.0)	0.41	0.01*	4	0.35	0.12	48 (80.0)	0.85	0.001

Notes: * – the difference is probable at $p < 0.05$.

A detailed collection of the patient’s medical history allows us to establish the main causes of behavioral disorders in women of different recurrent categories, such as: the influence of social factors – 109 (45.6%); environmental factors – 68 (28.4%); personal factors – 34 (14.0%), genetic factors – 16 (7.0%); presence of chronic somatic diseases – 12 (5.0%) (Fig. 2).

The study documented a strong correlation between young age (18–30 years) and bulimia nervo-

sa ($r=0.7, p=0.02$), atypical bulimia nervosa ($r=0.8, p=0.001$), anorexia nervosa ($r=0.76, p=0.003$) and atypical anorexia nervosa ($r=0.87, p=0.004$). In the age group of women 31–44 years of age, an average correlation was established with compulsive overeating ($r=0.6, p=0.03$), bulimia nervosa ($r=0.63, p=0.02$) and anorexia nervosa ($r=0.62, p=0.01$). In women aged 45 years and above, a stronger correlation was established with compulsive overeating ($r=0.8, p=0.002$) (Table 2).

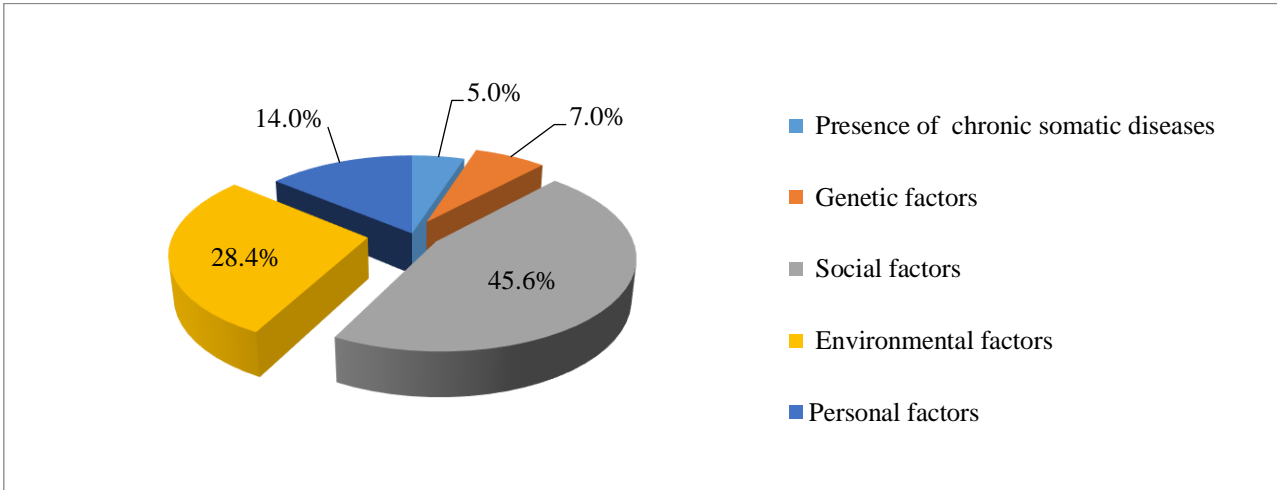


Fig. 2. Main causes of eating disorders in the clinical groups

Table 2. Structure of eating disorders in the examined patients, depending on the patients’ age

Eating behavior, eating disorder	Patients’ age, years											
	18–30			31–44			45–67			>68		
	n (%)	r	p	n (%)	r	p	n (%)	r	p	n (%)	r	p
Compulsive overeating	6 (10.0)	0.5	0.1	11 (18.3)	0.69	0.03*	36 (60)	0.89	0.002*	37 (61.7)	0.81	0.001*
Bulimia nervosa	14 (23.3)	0.7	0.02*	8 (13.3)	0.63	0.02*	6 (10.0)	0.1	0.21	5 (8.3)	0.2	1.32
Atypical bulimia nervosa	7 (11.7)	0.8	0.001*	3 (5.0)	0.49	0.001*	4 (6.7)	0.2	0.34	3 (5.0)	0.1	0.09
Anorexia nervosa	21 (35.0)	0.76	0.003*	14 (23.4)	0.62	0.01*	8 (13.3)	0.3	0.54	7 (11.7)	0.3	0.43
Atypical anorexia nervosa	8 (13.3)	0.87	0.004*	16 (26.7)	0.41	0.002*	4 (6.7)	0.01	0.58	5 (8.3)	0.4	0.44
Healthy eating behavior	4 (6.7)	0.4	0.06	8 (13.3)	0.2	0.05	2 (3.3)	0.2	1.03	3 (5.0)	0.45	0.32

Notes: * – the difference is probable at $p<0.05$.

Management of individuals with eating disorders included psychoeducation about the disorder, monitoring of body weight, mental and physical risks, any other risk factors, and was multidisciplinary with coordination between services. Family members were also involved. Changing body weight was the key to supporting other psychological and physical changes necessary for recovery. In the treatment of anorexia, the first priority was psychological help (of course, if the patient's condition allowed it, when hospitalization in the intensive care unit was not required). Cognitive-behavioral therapy (CBT), which was aimed at making the patient responsible for controlling his eating, showed high effectiveness in correcting eating disorders. Patients kept records of food intake and vomiting; tried to identify external stimuli or emotional changes that precede the emergence of a craving for overeating, in order to subsequently eliminate or avoid these factors. Treatment involved reducing dietary restrictions and developing cognitive and behavioral skills to overcome cravings or refusal to eat. Patients were taught to identify and change dysfunctional thoughts and attitudes about their body image, weight, and eating, as well as any dysfunctional thoughts and attitudes that contribute to negative emotions that lead to overeating or avoidance of food.

In our study, anorexia nervosa was characterized by loss of body weight 15% below normal, a BMI of 17.5 or below. Weight loss occurred as a result of the patients' refusal of "fatty food". Patients perceived themselves as "too fat", there was an obsessive fear of gaining weight.

Randomized trials by other authors have also shown superiority of cognitive-behavioral therapy over other types of psychotherapy and pharmacological interventions. On average, CBT helps approximately 50.0% of all patients get rid of binge eating and purging, while the percentage reduction in binge eating and purging in all patients who undergo CBT is typically 80.0% or more. CBT gives good and stable results: therapeutic changes persist for a year or more. Long-term prospective follow-up after CBT (mean duration 5.8 years) showed that approximately two-thirds of patients remained free of eating disorders. A peculiarity of CBT for bulimia is also its speed: the frequency of

attacks begin to decrease already after the first therapy sessions [14]. Thus, our results are consistent with the results of other authors.

Conclusion

The study determined, that in women of group 1 bulimia nervosa was recorded 8 times ($p < 0.05$) more, and anorexia nervosa 2.7 times ($p < 0.05$) more often than in the control group. In patients of group 2, compulsive overweight was recorded 5 times ($p < 0.05$) more often, and in group 3 – 18 times ($p < 0.05$) more often than in the control group. Strong correlation was installed between young age (18–30 years) and bulimia nervosa ($r = 0.7$, $p = 0.02$), atypical bulimia nervosa ($r = 0.8$, $p = 0.001$), anorexia nervosa ($r = 0.76$, $p = 0.003$) and atypical anorexia nervosa ($r = 0.87$, $p = 0.004$).

The study found that overweight young women are at risk for developing eating disorders; therefore, treatment of such patients should be handled by a team of multidisciplinary specialists.

Obesity is directly related to the patient's lifestyle, eating habits, and the influence of the environment. To achieve success in optimizing the population's weight: a range of measures is needed, such as limiting food advertising aimed at children, taxes on sugar-sweetened drinks and improving measures to control obesity. To achieve optimal body weight, age and initial BMI must be taken into account. Treatment of obesity and behavioral disorders requires a multispecialty approach, with the mandatory participation of a psychiatrist, general practitioner and endocrinologist.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

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PLASMINOGEN APPLICATION IMPROVES PLASTIC CLOSURE OF WOUND DEFECTS IN PATIENTS WITH CHRONIC DIABETIC WOUNDS

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ABSTRACT

Background. Chronic diabetic foot ulcers and wounds are significant complications associated with diabetes, comprising approximately 85% of purulent-necrotic lesions affecting the lower extremities. The development of these wounds is influenced by pathogenetic factors such as hyperglycemia, neuropathy, and existing infections, which contribute to metabolic disturbances, including tissue hypoxia and the activation of proteolytic enzymes known as matrix metalloproteinases (MMPs).

Aim. To explore the therapeutic potential of autologous plasminogen in facilitating the healing process of diabetic wounds through the modulation of MMP activity.

Materials and Methods. The study enrolled 45 patients diagnosed with chronic diabetic wounds, who were assigned to two distinct groups. The control group (n=25) received conventional treatment approaches, while the intervention group consisted of 20 patients treated with autologous plasminogen applications.

Results. After 18 days of treatment, a substantial reduction of 3.5-fold in MMP-2 and MMP-9 activity was observed within the intervention group, accompanied by complete wound closure in 16 patients. Additionally, four patients underwent autodermoplasty, successfully achieving wound defect closure through effective graft integration. In contrast, the control group exhibited consistently elevated MMP activity levels throughout the entire observation period.

Conclusions. The activity of matrix metalloproteinases (MMPs) in chronic diabetic wounds reaches dramatic levels, making spontaneous wound healing impossible. The application of autologous Pg allows modulation of this activity and creates favorable conditions for wound healing by reducing excessive MMP activity, improving blood supply, and resolving inflammatory processes.

Keywords: *chronic wounds, diabetes mellitus, matrix metalloproteinases, plasminogen, autodermoplasty.*

Introduction

Patients with diabetes mellitus are quite sensitive to any trauma due to the neuropathy, as well as a predisposition to slow or non-healing wounds. The primary presentations of tissue injury in the lower limbs among individuals with diabetes mellitus encompass chronic wounds and trophic ulcers, constituting approximately 85% of cases. The residual fraction comprises abscesses, phleg-

mons, osteomyelitis, and purulent arthritis, which manifest either due to trophic ulcers or as a consequence of traumatic events [1]. Consequently, the issue of effectively addressing wound defects through plastic surgical techniques becomes notably pertinent. Hyperglycemia serves as the principal pathogenetic mechanism contributing to the development of chronic diabetic wounds, as it exerts a toxic effect on tissues, causing metabolic disorders that lead to neuropathy, angiopathy, and immunosuppression [2].

These metabolic disturbances promote tissue hypoxia and subsequent activation of proteolytic enzymes. In physiological conditions, matrix metalloproteinases (MMPs) play a vital role in the degradation of the extracellular matrix (ECM), tissue remodeling, cell migration, and inflammation,

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thereby contributing to each phase of wound healing [3]. Proteases actively participate in the processes of wound healing, making the assessment of proteolytic activity a useful biomarker for wound healing status. Among all Ps, MMP-2 and MMP-9 are vitally important proteases, which are typically involved in the normal tissue remodeling during wound healing [4]. However, it has been reported that a significant increase in MMP activity is a key factor contributing to impaired wound healing in diabetic skin ulcers and other vascular complications. Moreover, excessive MMP activity has been shown as one of the most important risk factors for dermal graft failure during autodermoplasty procedure [5]. Therefore, the exploration of strategies aimed at modulating proteolytic activity is anticipated to yield advantageous outcomes in the management of recalcitrant wound healing cases.

Recent studies have identified plasminogen (Pg) as a crucial participant in the wound healing process that was designated as a "master regulator" of wound healing [6]. Currently, over 12 different cellular receptors for Pg have been identified, which are potentially associated with wound healing. This suggests that apart from fibrinolysis, Pg may act as a signaling molecule that regulates and coordinates the activity of monocytes/macrophages, keratinocytes, platelets, and other cells involved in wound healing [7]. Although many studies performed on animal models are accumulated to report beneficial effects of Pg application on healing process of both acute and chronic wounds, including in diabetic mammals so far there were no attempts made in clinical studies to explore Pg as a possible remedy to improve closure rates and quality of tissue reparation.

Therefore, the **aim** of this study was to investigate the effects of autologous Pg application on MMP activity, closure of chronic wounds, and success of autodermoplasty in patients with diabetes mellitus.

Materials and Methods

The study comprised a cohort of 45 individuals aged 45 to 81 years, diagnosed with diabetes mellitus, who received outpatient care at the Central Polyclinic of the Ministry of Internal Affairs of Ukraine between 2021 and 2023. These patients presented with neuropathic diabetic wounds of prolonged duration, exceeding 6 weeks, and were classified as wounds that are not at risk of amputation within the next year according SVS WIFI classification [8]. Written informed consent was obtained from all participants, who also provided

explicit authorization for the dissemination of research findings. Ethical considerations were rigorously observed, with all research procedures and protocols scrutinized and endorsed by the local ethics committee. Adherence to the ethical guidelines prescribed by the most recent iteration of the Helsinki Declaration (2013) was meticulously ensured throughout the course of the investigation.

The patients were randomly divided into two groups. The groups were representative in terms of age, complications, and comorbidities. The control group (25 patients) received treatment for diabetic wounds according to standard protocols, which included local application of antiseptics and wound dressings. All patients were administered glucose-lowering medications. In the intervention group (20 patients), in addition to standard wound care, autologous plasminogen was topically applied to the wound surface at a dose of 1.0 mg/mL of sterile buffered physiological solution every 2 days for a total of 20 days (10 applications in total). Biopsies from the wound bed in patients with diabetes (100 ± 3) mg were collected before the start of treatment (day 0) and on the 18th day of the current treatment period.

Native form of Pg (Glu-Pg) was obtained from fresh citrated plasma of donors (patients with diabetes from the study group) using affinity chromatography on Lys-Sepharose (GE Healthcare, Amersham, UK) in the presence of the serine protease inhibitor aprotinin (10 mg/mL) following the method described by Lijnen [9] with minor modifications. The purity of the obtained Pg preparations was evaluated by denaturing gel electrophoresis on a 10% polyacrylamide gel (SDS-PAGE). The gel electrophoresis results indicated that the Glu-Pg preparations isolated from donor plasma were electrophoretically homogeneous (purity level 99%). Prior to use, the Pg preparations were tested for spontaneous amidolytic activity using a photometric method with the specific chromogenic substrate plasmin S2251, and only those preparations that did not show spontaneous activity were included in the study. The protein preparations were concentrated, sterilized by ultrafiltration, frozen, and stored at -20°C until use.

The activity of MMP-9 in skin wound biopsies was evaluated by gelatin zymography and compared to the MMP-9 activity in biopsies taken from acute wounds. Gelatinolytic activity was assessed by separating proteins (50 μg per lane) on 8% polyacrylamide gel co-polymerized with gelatin (5 mg/ml). Following denaturing gel electrophoresis, the gels were subjected to two 30-minute

washes with cold 2.5% (i/v) Triton X-100 to eliminate SDS. Subsequently, they underwent five 5-minute washes with cold deionized water. The gels were then incubated for 16 hours at 37°C in a developing buffer (50 mM Tris-HCl, pH 7.6, containing 0.15 M NaCl, 5 mM CaCl₂, 1 mM ZnCl₂, and 0.02% Tween-20). Zymograms were stained using a 0.15% ethanol solution of Coomassie R-250. Destaining was carried out using a dye-free solution consisting of 30% methanol and 10% acetic acid. After destaining, the gel exhibited a uniform blue background, except for regions where MMPs migrated and digested the substrate. Gelatinolytic activity was identified as transparent bands against the stained gelatin background. The resulting MMP bands were visualized and subjected to quantitative densitometric analysis.

The statistical analysis of the gelatin zymography data was performed using the Mann-Whitney U test to assess differences between mean parameters. All variables were expressed as mean \pm standard error of the mean (SEM). A significance level of $p < 0.05$ was considered statistically significant for all tests. The statistical calculations were conducted using the "OriginPro" software (version 9.0 SR2 Pro English).

Results and Discussion

Conservative therapy often plays an independent role in the treatment of neuropathic diabetic wounds. According to some authors, the healing of foot ulcers reaches 80–90%, with approximately two-thirds of patients who do not require surgical intervention [10]. To achieve a positive outcome in such cases, adherence to treatment protocols, aseptic and antiseptic practices, and an unrestricted duration of treatment (up to 8 months) are necessary. However, chronic wounds pose a potential risk of further infection and the development of new purulent foci in the extremity. Therefore, the primary focus of treating these wounds is early closure of the wound defects to prevent complications and tissue destruction progression [11]. The primary requirements for undertaking plastic surgery involve achieving the patient's overall well-being, ensuring sufficient blood circulation to the soft tissues of the limb, and resolving any purulent inflammation present. Optimal conditions for plastic surgery include a wound with minimal bacterial colonization (below the critical level of 105 microbial bodies per 1 gram of tissue) and the presence of vibrant, moist granulation tissue with minimal exudation. The objective of the surgical procedure is to achieve

full closure of the wound defect and prevent deformities.

The following types of plastic surgeries are commonly performed: autodermoplasty (ADP) for extensive defects on the dorsal foot; tissue expansion or local tissue flaps for medium-sized defects on the shin; local tissue flaps in the ankle joint area and minor linear wounds on the dorsal foot; local tissue flaps for defects in "pressure points"; autodermoplasty for defects in the medial arch of the foot; rotation of dorsal flaps to close dorsal and plantar defects; rotation of plantar flaps to close lateral and dorsal defects of the foot.

The application of dressings in patients from the main group resulted in complete healing in 16 patients with wounds measured up to 50 cm² within 16–18 days of treatment. However, in 4 patients with larger wounds exceeding 50 cm² on the posterior surface of the shin and foot, the main objective was wound debridement and preparation for closure. Prior to the start of treatment, the wounds exhibited characteristic features: the wound surface was covered with fibrin, it was swollen and protruding above the skin surface, the granulation tissue was coarse-grained and had an unhealthy pale gray color, and there was moderate exudate with an unpleasant odor (*Fig. 1*).

After the application of autologous Pg dressings using the authors' method, complete debridement of the wounds from fibrin and necrotic tissue was observed, and a reduction in edema was noted starting from day 10 of treatment. The granulation tissue appeared fine-grained and had a "healthy" appearance, with minimal exudate. Pathogenic microorganisms were not detected in the bacteriological examination, and histological analysis showed the absence of a "biofilm." From day 14 onwards, progressive reduction in the wound area was observed, indicating favorable conditions for performing plastic surgery (*Fig. 2*).

The gelatinase activity analyzed by zymography assay in bioplates from chronic wounds before the Pg treatment was high, that is generally in agreement with earlier published data [12]. Levitation of MMP-9 levels, which is a typical characteristic of chronic wound processes, was observed on the zymograms (*Fig. 3*). However, a significant decrease in MMP activity in the wound tissues by 3.5 times was observed on day 18 of treatment ($p < 0.01$). Meanwhile, the MMP activity in acute wounds remained minimal throughout the entire treatment period, and by day 18, it exhibited a trace level (*Fig. 4*). Then, the wound defects were closed using full-thickness perforated skin grafts



Fig. 1. Diabetic trophic ulcer prior to treatment with autologous plasminogen.



Fig. 2. Diabetic trophic ulcer on the 12th day of treatment with autologous plasminogen.

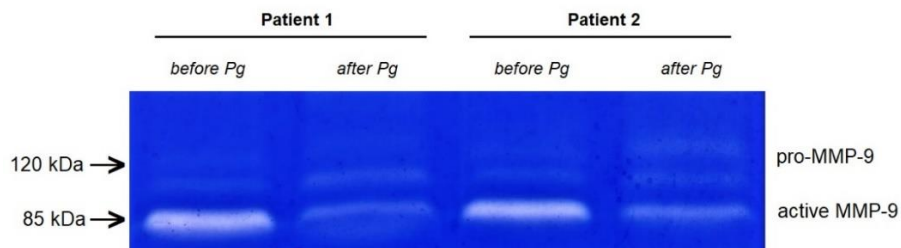


Fig. 3. Decrease activities of matrix metalloproteinases due to treatment by autologous plasminogen.

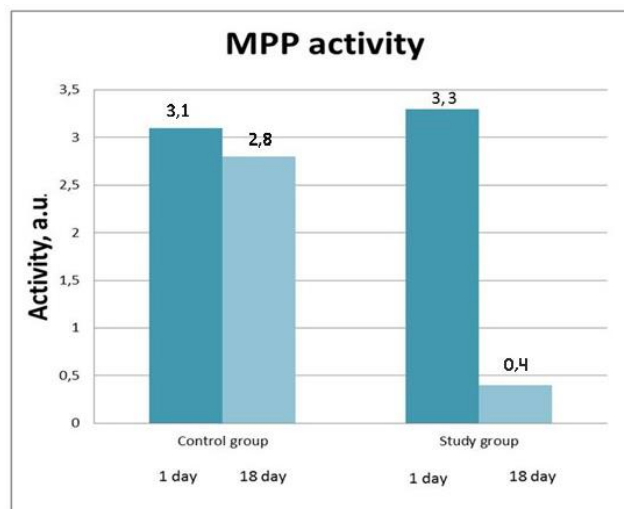


Fig. 4. Effect of plasminogen application on the levels of MMP-9 in chronic wound tissue of diabetic patients (typical gelatin zymography).

with the assistance of autodermoplasty (*Fig. 5*). All grafts successfully engrafted.

In the control group patients with traditional treatment, a decrease in signs of perifocal inflammation and cleansing of the wounds from fibrin and necrotic tissues was observed starting from day 20 of treatment. The level of matrix metalloproteinase (MMP) activity remained consistently high. Subsequently, the cleansing of the wound surface and reduction in wound area occurred gradually with the involvement of new forms of wound coverings and instrumental methods. Wound contraction occurred starting from day 30 of treatment. The prolonged and often unsuccessful healing of chronic diabetic wounds is attributed to the excessive activity of MMPs. Their aggressive action completely negates all treatment efforts for wound healing. Even complete cleansing of the wound from microbial components does not guarantee successful healing. Performing plastic surgery to close the wound surface will not be successful in this case, and will result in complete

graft lysis, until the protease activity is neutralized (*Fig. 6*). As demonstrated in our previous studies, despite the use of vacuum therapy in the treatment of diabetic wounds, the level of MMP activity in the wound exudate remains relatively high, even after vacuum therapy had been applied [13].

One of the mechanisms of Pg action in chronic wound processes primarily involves the elimination of tissue hypoxia by dissolving microthrombi in blood vessels through its fibrinolytic properties [14]. In addition, the conversion of plasminogen to plasmin is accompanied by increased activity of pro-inflammatory cytokines present in the wound tissues. The expression of these factors initiates inflammation and stimulates angiogenesis, which is a crucial component in overcoming the "vicious cycle" of chronic inflammation and transitioning the wound process to the proliferation stage thus pushing wound to heal.

Conclusion

The activity of matrix metalloproteinases (MMPs) in chronic diabetic wounds reaches dramatic levels,



Fig. 5. Graft survival on the 10th day after plastic closure of the wound.



Fig. 6. Graft necrosis on the 10th day after ADP in patient of the control group.

making spontaneous wound healing impossible. The application of autologous Pg allows modulation of this activity and creates favorable conditions for wound healing by reducing excessive MMP activity, improving blood supply, and resolving inflammatory processes. Local administration of autologous Pg represents a promising strategy for developing new therapeutic approaches that improve wound healing in patients with diabetes mellitus.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

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Consent for publication

All authors give their consent to publication.

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INTERNATIONAL PROGRAMS TO PROVIDE SCHOOL-AGE CHILDREN WITH NUTRITION

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ABSTRACT

A short scientific report is devoted to the global experience of organizing meals for schoolchildren. The main priorities in the formation of rations and the form of organization of supply have been determined. Children's nutrition is the most important component of the formation of a child's health, it contributes to the preservation of health, resistance to physical factors of the environment, high physical and mental capacity. Before the COVID-19 crisis, at least one in every two primary school students received daily school meals in 161 countries (equivalent to 388 million children). For millions of vulnerable children in poor countries around the world, free school meals are a vital component of their daily diet. A balanced school meal program is the key to optimizing the nutrition of the entire population of the country. School feeding programs play an important political role and are increasingly implemented by governments as a priority in national development strategies. Over the past decade, low-income countries have significantly increased their financial and policy efforts for school feeding, resulting in an increase in the number of school children receiving school meals. While school feeding programs in high- and middle-income countries are largely financed through domestic resources such as taxes and other sources, programs in low-income countries rely heavily on international donor support. According to the leading domestic hygienists, despite the ongoing conflict, one of the important priorities of our country is the continuation of the reform of school nutrition in order to bring it into line with international quality standards. Adhering to the basic principles of a complete and rational diet, you can achieve success even in conditions of limited resources.

Keywords: *hygiene of children and adolescents, children's health, world experience in the organization of schoolchildren's meals, preventive medicine.*

The World Food Program (WFP) is a branch of the United Nations dedicated to providing food assistance and is the largest humanitarian organization in the world. WFP primarily conducts school feeding programs in low and middle-income countries and provides additional support to national school feeding programs in politically stable countries that have established their own state programs. The school feeding strategy initiated by WFP for the period 2020–2030 aims to ensure healthy nutrition for every schoolchild through

an integrated and multi-sectoral approach [1–4]. Before the COVID-19 crisis, at least one in every two primary school students received daily school meals in 161 countries (equivalent to 388 million children). Globally, approximately 39 billion school meals were missed due to school closures during the pandemic and lockdowns in 2020 [5]. For millions of vulnerable children in poor countries around the world, free school meals are a vital component of their daily diet [5; 6].

Over the past few years, there has been a significant increase in the number of school feeding programs in low-income countries, but coverage remains low. For instance, between 2013 and 2020, the number of children receiving school meals worldwide increased by 9 percent. Low-income countries have significantly strengthened their financial and political efforts towards school feeding, leading to a 36 percent increase in the number of schoolchildren receiving meals [4; 7].

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While school feeding programs in high and middle-income countries are primarily funded through domestic resources, such as taxes and other sources, programs in low-income countries heavily rely on international donor support [4; 6]. Over the past decade, various countries have introduced state-run school feeding programs or are transitioning away from external program support in the short to medium term [8–10]. Other countries are seeking to establish or reinstate effective school feeding programs in response to the COVID-19 pandemic [5; 11]. In the context of the 2020–2030 school feeding strategy, the World Food Program (WFP), in collaboration with partners and governments, aims to ensure that all young schoolchildren have access to quality school-based nutrition, accompanied by a broader integrated package of health and nutrition services. In the School Feeding Strategy for 2020–2030, WFP outlines its vision for collaboration with governments and partners to jointly ensure access to high-quality school-based nutrition for all primary school children, complemented by a more comprehensive integrated package of health and nutrition services [4].

The World Health Organization emphasizes that school feeding programs are as important for children's health as vaccination programs [12]. Currently, governments are not inclined to supplement school feeding with other school interventions (such as promoting handwashing with soap before meals, deworming, nutrition education, agricultural diversification, improved water supply and sanitation, as well as micronutrient supplementation) to achieve long-term results [13]. Less than seven percent of governments implement school feeding exclusively with food items; all other countries combine school feeding with additional health and nutrition interventions [5; 8; 9]. In Africa, national school feeding programs aimed to improve access to education and higher academic achievement [14; 15]. Various studies show that school health and nutrition programs lead to improved learning outcomes.

In high-income countries, the primary focus is on the quality of school nutrition [1; 2; 8; 16; 17]. School feeding programs in economically developed countries are associated with health promotion, nutrition education, and aspects of sustainable development. High-quality free school nutrition is considered a fundamental approach to creating a fair and sustainable food environment [4]. According to a survey conducted by the World Health Organization (WHO) in 2016–2017, 142

out of 160 WHO member states (89%) implement some form of health and nutrition program in schools [18]. In WHO regions in the Americas, Europe, and the Western Pacific, these programs aim to reduce or prevent intentional weight gain and obesity. Conversely, in WHO regions in Africa and South-East Asia, efforts primarily focus on preventing undernutrition.

In six WHO regions, 119 countries reported having national dietary guidelines [18]. Food standards are essential tools to ensure the quality of nutrition and differ from nutrient-based dietary guidelines and standards. Dietary recommendations based on the consumption of local food items are widespread in all WHO regions, but many African countries still do not have national standards. Specific dietary recommendations for different population groups (e.g., preschool children, school-age children) have the greatest impact and are more practical to implement. In 49% of countries, qualified dietitians and nutritionists are responsible for planning school nutrition.

In Europe, all 27 EU member states, as well as the United Kingdom, Norway, and Switzerland, have national school nutrition policies [17–22]. These policies are mandatory in half of the countries and voluntary in the other half. Food standards are also most prevalent in European countries: over 90% use food standards to ensure a balanced menu, followed by portion size guidelines (76%) and nutrient-based meal standards (68%) [1; 2; 17].

In Ukraine, recommendations for school nutrition were previously regulated by the Cabinet of Ministers of Ukraine Resolution dated November 22, 2004, No.1591 "On the Approval of Food Norms in Educational and Children's Health and Recreation Institutions" [19]. Additionally, there were orders from the Ministry of Education and Science of Ukraine and the Ministry of Health of Ukraine dated June 1, 2005, No.242/329, and an order from the Ministry of Education of Ukraine and the Ministry of Health dated August 15, 2006, No.620/563, which established the procedure for organizing children's nutrition in preschools, general education, extracurricular educational institutions, and health resorts. The nutrition of privileged categories of students was regulated by the Cabinet of Ministers of Ukraine Resolution dated June 19, 2002, No.856 "On the Organization of Nutrition for Certain Categories of Students in General Education Institutions".

Hygiene standard "Draft Sanitary Regulations for General Secondary Education Institutions" one

of the appendices of which includes "Recommendations for the Healthy Nutrition of Children in General Education Institutions" has been approved at the legislative level. According to leading domestic hygienists, despite the ongoing war, one of the essential priorities for our country is to continue the reform of school nutrition, with the goal of aligning it with international quality standards. However, as the experience of international programs providing school-age children with nutrition shows, there are no dogmas in implementing the school nutrition system. By adhering to the basic principles of adequate and rational nutrition, success can be achieved even in conditions of limited resources.

Conclusions

1. The implementation of international programs for providing school-age children with food depends on the economic and social conditions and should be accompanied with other preventive activities.

2. The priority directions in the field of school meals are developing system of catering and promoting health diet.

3. Main challenges of the national nutrition programs for children and adolescents are resource limitations.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

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Statement of Ethics

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MECHANISMS OF FORMATION AND CLASSIFICATION OF SECONDARY IMMUNODEFICIENCY STATES IN UVEITIS

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ABSTRACT

Background. The role of immunological disorders in the pathogenesis of uveitis has been proven by numerous studies. However, there are different views on the timing and methods of immunocorrection. In our opinion, this issue should be solved on the basis of determining the mechanisms of the formation of immunodeficiency states in uveitis.

The purpose of this work was to develop a classification of secondary immunodeficiency states in uveitis according to the mechanism of formation.

Materials and Methods. The paper presents the results of the examination of 370 patients with uveitis (416 eyes; 179 were men, 191 were women, aged from 16 to 87 years; the duration of the disease ranged from 1 month to 32 years) who were treated in Kharkiv Regional Clinical Hospital, were under dispensary supervision at Kharkiv Regional Anti-Tuberculosis Dispensary and Kharkiv Regional Dispensary for Radiation Protection of the Population, or were examined, consulted and treated on an outpatient basis. The observation period was up to five years.

Results. Based on the study of immunological changes in patients with uveitis, the dynamics of immunological disorders in relapses of the inflammatory process in the uveal tract, clinical and immunological features of various forms of uveitis, and the results of correction of immunological disorders in patients with uveitis, a classification of secondary immunodeficiency states in uveitis according to the mechanism of their formation was proposed. On its basis, the principles of correction of immunodeficiency states in patients with uveitis were developed.

Keywords: *infectious uveitis, noninfectious uveitis, cellular immunity, humoral immunity, correction principles, immunological disorders.*

Introduction

The role of immunological disorders in the pathogenesis of uveitis has been proven by numerous studies [1–9].

However, there are different views on their correction, which has become an integral part of treatment in uveitis [10–16]. The timing and tactics of immunocorrection in uveitis, which some researchers recommend using in the remission stage, need to be clarified [14]. Meanwhile, there is convincing evidence of the high efficacy of immunocorrective therapy in the active stage of the disease [11; 12; 15; 17; 18].

In our opinion, this issue should be resolved on the basis of determining the mechanisms of the formation of immunodeficiency states in uveitis.

The Purpose of this work was to develop a classification of secondary immunodeficiency states in uveitis according to the mechanism of formation.

Materials and Methods

The paper presents the results of the examination of 370 patients (416 eyes) with uveitis who were treated in Kharkiv Regional Clinical Hospital, were under dispensary supervision at Kharkiv Regional Anti-Tuberculosis Dispensary and Kharkiv Regional Specialized Dispensary for Radiation Protection of the Population, or were examined, consulted and treated on an outpatient basis. Among these patients, there were 179 were men, 191 were women (aged 16–87 years). The duration of the disease ranged from 1 month to 32 years. The observation period made up to five years.

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To study the role of immunosuppression in formation of complicated forms of uveitis, we investigated the features of the clinical picture, course, and immunological disorders in 36 patients (45 eyes) with uveitis who were exposed to increased levels of radiation as a result of Chernobyl nuclear power plant accident (as an example of exogenous immunodepression), and in 39 patients (60 eyes) with uveitis of tuberculous etiology and pulmonary tuberculosis (as an example of endogenous immunodepression). 46 of them were men, 29 were women; ages from 26 to 87 years.

Statistical processing of the obtained results was carried out using a package of application programs (STATISTICA 9.0, USA). Informed consent to participate in the study was obtained from all patients.

Results and Discussion

The analysis of the mechanisms of the formation of immunodeficiency states in patients with uveitis showed that depression of the immune system can be caused by various factors.

Thus, the presence of immunodeficiency in patients with uveitis can be caused by adverse environmental factors, the most important of which is the increased level of radiation pollution [19–21].

Our studies have shown that exogenous immunodepression (in particular, due to exposure to high levels of radiation pollution) plays an integral role in the onset and development of complicated forms of uveitis. Thus, uveitis against a background of exogenous immunodepression (due to Chernobyl accident) in the patients we examined more often was complicated by uveal cataract (by 18.4%) and macular edema (by 14.9%) compared to patients who were not exposed to elevated levels of radiation.

Inflammatory diseases of the uveal tract often occur against a background of chronic inflammatory diseases of other organs and systems, the presence of which also causes immunodeficiency syndrome, which exists even before the onset of uveitis [22–25].

We have found that endogenous immunodepression plays an important role in formation of complicated forms of uveitis, in particular, in patients with uveitis of tuberculosis etiology (pulmonary tuberculosis). Thus, uveitis occurring against a background of endogenous immunodepression (tuberculosis etiology on the background of pulmonary tuberculosis) is more often complicated by uveal cataract (by 42.4%) and uveal glaucoma (by 10.9%) compared to uveitis in patients without chronic inflammatory diseases.

Thus, immunodeficiency states in the body can occur as a result of external and internal factors that are not related to uveitis. In our opinion, immunodeficiency states that are formed in the body before the onset of uveitis (conditionally "primary") can be considered one of the etiopathogenetic factors of its development.

According to many authors, infection plays the role of a triggering factor in the pathogenesis of uveitis, and the further course of the disease is determined by immunological and autoallergic mechanisms formed as a result of uveitis [3; 26; 27]. Immunodeficiency states arising from the inflammatory process in the ocular vascular tract have their own characteristics.

The first attack of uveitis in such patients occurs and sometimes progresses against a background of normal immune system parameters or transient adaptive immunological changes. However, the inflammatory process in the vascular membrane induces a functional depression of immunity with formation of suppressor factors in the inflammatory focus, a decrease in natural killer activity [28], and the activity of antibody-dependent killer cells.

The recurrence of the inflammatory process (which is common in [31.0–68.5]% of uveitis cases [29; 30]) leads to more severe disorders in the immune system with the gradual formation of suppressor immunodeficiency and the occurrence of more severe lesions [31] and complications. As a typical example of the occurrence of immunodeficiency syndrome due to uveitis, we present the results of observation and immunological examination of patient O., who was treated in the ophthalmology department of Kharkiv Regional Clinical Hospital for left eye iritis, which proceeded without complications against a background of normal immune status (*Fig. 1, 2*).

Two months later, patient O. came to the ophthalmology department of Kharkiv Regional Clinical Hospital with recurrent iridocyclitis complicated by macular edema with cellular immunity indices at the lower limits of normal. The second relapse of uveitis in patient O. occurred against a background of a significant decrease in the total number of T lymphocytes and T helper cells with an increase in the content of T suppressors and a decrease in the immunoregulatory index. During the third exacerbation of uveitis complicated by macular edema (a year after the "first attack" of uveitis), patient O. developed cellular immunodeficiency of the suppressor type. Thus, immunodeficiency conditions in the body can occur as

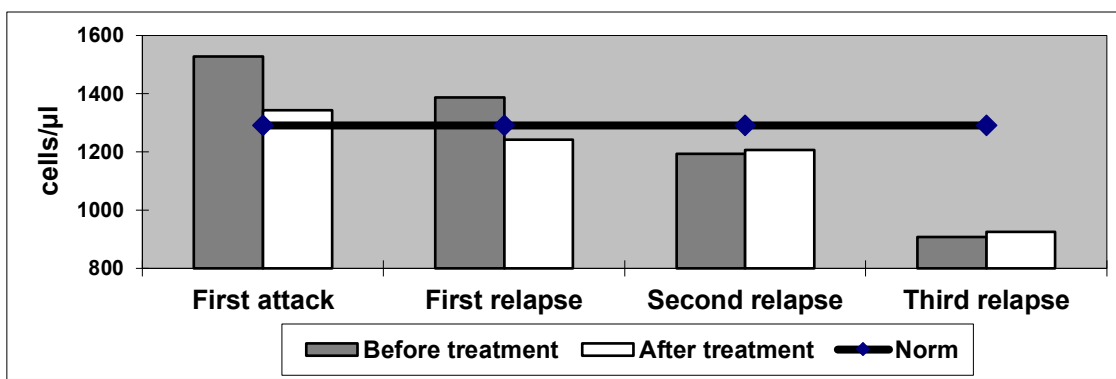


Fig. 1. Dynamics of the total number of T-lymphocytes in patient O.

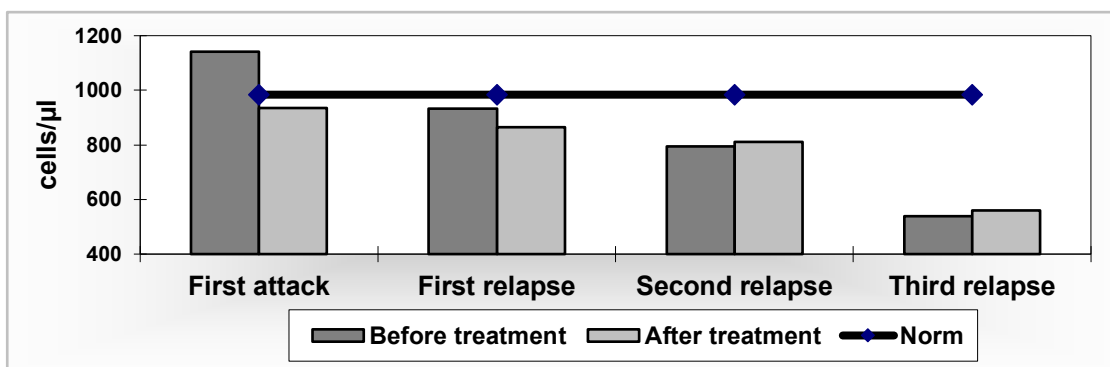


Fig. 2. Dynamics of the number of T-helper cells in patient O.

a result of uveitis. Several factors contribute to the possibility and presence of immunodeficiency states that form simultaneously with uveitis but are not a consequence of the inflammatory process in the choroid. First, immunodeficiency can be caused by infections that cause uveitis. Thus, according to the literature, retroviruses (including HIV-I and HTLV-I viruses), which are one of the most common causes of uveitis [32; 33], can play a key role in the occurrence of autoimmune reactions [34; 35].

Researchers have shown that complicated uveitis in HTLV-I infection is caused by immune-driven mechanisms, and further in the pathogenesis of uveitis infectious and autoimmune mechanisms are intertwined [34].

Second, immunodeficiency in uveitis can be formed as a result of a genetically determined inadequate response of the immune system to the inflammatory process. This position is supported by data about the role of immunogenetic factors in the pathogenesis of endogenous uveitis. Thus, it has been established that the immune response genes are linked to the major histocompatibility complex, and their functions are directly related to

the regulation of cellular interactions by the HLA histocompatibility system [36; 37], and the occurrence of autoimmune reactions is controlled, at least in part, by the genes of the major histocompatibility complex [38]. It has been shown that the presence of certain HLA antigens in patients with uveitis determines the peculiarities of the immune system and some clinical characteristics of uveitis [39]. An example of immunodeficiency that developed simultaneously with uveitis can be seen in the case report of patient S. with central chorioretinitis of the right eye of cytomegalovirus etiology, complicated by ophthalmic hypertension. Despite the therapy, the number of T lymphocytes, T helper cells, and immunoregulatory index decreased, and the deterioration of these parameters continued over the next 3 months (*Fig. 3, 4*).

A month after the discharge from the hospital, patient S. developed secondary immunodeficiency syndrome, and a significant improvement in immunological parameters was achieved only one year later (in the absence of exacerbations of the inflammatory process in the uveal tract).

Thus, immunodeficiency states in the body can form simultaneously with uveitis.

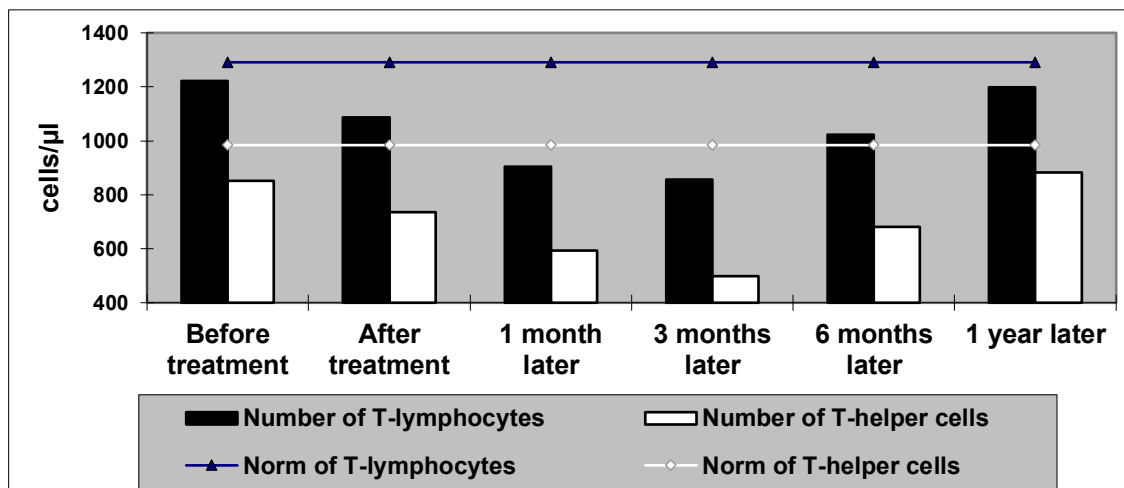


Fig. 3. Dynamics of T-lymphocytes and T-helper cells in patient S.

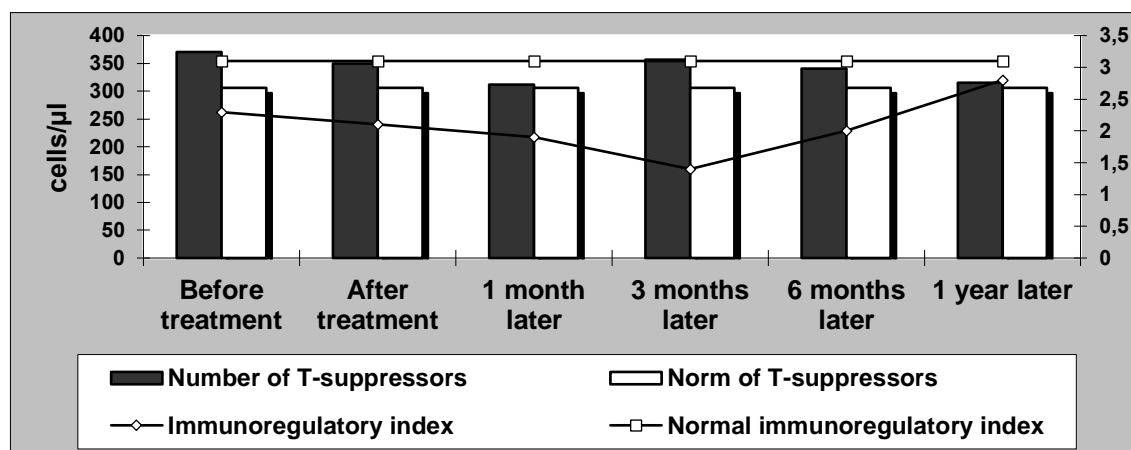


Fig. 4. Dynamics of T-suppressors and immunoregulatory index in patient S.

These features make it possible to diagnose the type of immunodeficiency in specific patients.

Based on the study of immunological changes in patients with uveitis, the dynamics of immunological disorders in relapses of the inflammatory process in the uveal tract, clinical and immunological features of various forms of uveitis, and the results of correction of immunological disorders in patients with uveitis, we propose the following classification of secondary immunodeficiency states in uveitis.

I. By the mechanism of formation.

1. Immunodeficiency states, "primary" in relation to uveitis:

- a) caused by the influence of environmental factors;
- b) caused by chronic infectious and other diseases.

2. Immunodeficiency states arising from uveitis.

3. Immunodeficiency states that form simultaneously with uveitis:

- a) caused by infections that cause uveitis;
- b) formed as a result of genetically determined inadequate response of the immune system to the inflammatory process.

II. By the degree of immune system depression:

1. minor;
2. expressed.

The proposed classification of secondary immunodeficiency states in uveitis also allows us to determine the timing for the correction of immunodeficiency states in patients with complicated forms of uveitis.

Immunodeficiency states "primary" to uveitis, caused by environmental factors or existing chronic diseases, are more likely to be of a suppressor or effector type and require adequate correction in the active phase of the inflammatory process since the correction of existing immunological changes in patients with complicated forms of uveitis will have a positive effect on the course of the inflammatory process and reduce the likelihood of relapses and chronicity of uveitis.

Immunodeficiency states resulting from uveitis may be transient, and the subsidence (under the influence of therapy) of the inflammatory process in the uveal tract may improve the immunological status. In such cases, immunocorrection in patients with complicated forms of uveitis is justified in the remission stage to prevent exacerbations of the inflammatory process.

Immunodeficiency states that develop simultaneously with uveitis require balanced and cautious therapy. In cases where the presence of immunodeficiency syndrome is due to infections that cause uveitis or due to a genetically determined inadequate immune system response, immunocorrective therapy, in the active phase of the disease, should only prevent the occurrence of profound changes in the immune system, since active immunostimulation can lead to exacerbation of the inflammatory process, and "residual" immunological changes can be corrected in remission.

When prescribing immunocorrective therapy based on peripheral blood parameters, the greatest attention should be paid to the type of T-cell subpopulation disorders based on the ratio of immunocompetent cells, since the type of these disorders [40] and the changes [41] are the same in the blood and intraocular fluid, unlike the content of immunoglobulins, which is due to the possibility of their local synthesis in uveitis [42; 43].

The principles of correction of the main types of immunologic disorders in complicated forms of uveitis were substantiated. Thus, researchers have shown the selenium origin of antibody-producing cells in the eye in experimental uveitis. Several studies have simultaneously determined immune-

competent cells (activated T lymphocytes with interleukin-2 receptors [44]) in both the anterior chamber fluid and peripheral blood of patients with uveitis. In patients with acute uveitis, the same type of immunological disorder was found [40] in the study of T lymphocyte subpopulations in the peripheral blood and anterior chamber fluid.

Studying the changes in T lymphocytes in the intraocular fluid, vitreous and peripheral blood in patients with uveitis of various etiologies, researchers [41] found that changes in aqueous humor significantly corresponded to similar changes in the peripheral blood, and the ratio of T helper and T suppressor cells in the blood, pre-chamber fluid and vitreous was almost the same.

Unlike indicators of cellular immunity, the content of immunoglobulins in aqueous humor, where they can appear as a result of plasma ultrafiltration [42], does not always correlate with their concentration in the blood serum, due to the possibility of local synthesis of immunoglobulins in uveitis [42; 43].

Conclusion

We have proposed a classification of secondary immunodeficiency states in uveitis according to the mechanism of their formation. On the basis of the proposed classification, the principles of correction of immunodeficiency states in patients with uveitis were developed.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclose.

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Consent for publication

All authors give their consent to publication.

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INFLUENCE OF TENSION AND DEFORMATION INDICATORS ON THE QUALITY OF REMOVABLE CONSTRUCTIONS ACRYLIC BASIS

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ABSTRACT

Background. The question of distribution of masticatory pressure is one of the main branches in qualitative manufacturing of removable constructions. With the development of software, as well as with the increase in the power of computer technology has also spread to the problems of biomechanics, in particular the biomechanics of the human oral cavity.

The aim of our study was to analyze the results of using the method of finite element techniques with the purpose to improve the quality of prosthetic treatment by correct modeling constructional denture elements.

Materials and Methods. The study involved 45 patients aged 44–73 years (mean age 59.2 ± 4.3) treated with complete laminar prosthetic constructions for the upper jaw and lower jaw. A powerful method was developed to solve the problems of the theory of elasticity – the finite element method. The main idea is that the body under the study is divided into a finite number of subdomains or elements on which the desired continuous function is approximated by a polynomial (consists of piecewise continuous functions). A two-dimensional quadrangular element with four nodes was chosen as the partition element. Dividing it into elements and further solving the problem was in the ANSYS Mechanical APDL package (USA).

Results. Regarding the calibration of the ultimate displacements of nodal points and as a result of the distribution of masticatory pressure under the basis of a complete removable dentures on the tissues of the prosthetic area, the average values of each plane were as follows: for section PM_1 – the plane with high pressure was $([675298.14 \pm 5.21] \text{ m}^2\text{K})$. Taking the PM_2 region, the values were slightly higher $([369743.3 \pm 3.9] \text{ m}^2\text{K})$ and $([735356.34 \pm 4.52] \text{ m}^2\text{K})$, respectively.

Conclusions. Our findings suggest direct relationship between the using of mathematical calculation of material volume, volume deformation, potential data and elasticity theory as auxiliary element in the manufacture of removable dentures and, as a result, direct influence on level of quality of following constructions.

Keywords: *orthopedic treatment, finite element method, complete removable dentures, tension theory, deformation.*

Introduction

It is common knowledge that due to the effect of the external forces or loads; the body changes its shape and such a change is called deformation. The internal forces that arise in the body during its deformation, and relate to the unit of the area of the elementary site on which these forces act is

called tension. The main task of the theory of elasticity is to find the tension and deformation of a particular body at given loads.

The question of distribution of masticatory pressure is one of the main branches in qualitative manufacturing of removable constructions. Development of software, as well as the increase in the power of computer technology influenced, the problems of biomechanics, in particular the biomechanics of the human oral cavity [1].

The mismatch of the denture base with the soft tissues of prosthetic area can lead to a violation of the functional integrity of the biomechanical structure and uneven absorption of the masticatory load. This can lead to increased tension of the

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mucous membrane and bone structure, which in future will influence the durability and comfort of using the orthopedic structure, and, as a result, on the quality of life of the patient [2].

Mainly, qualitative manufacturing of removable construction says that load from the antagonist teeth in the state of occlusion is transmitted on the basis of the prosthesis clearly along its vertical axis, and in sagittal movements – evenly distributed over all prosthetic surface, and during transversal movements of the lower jaw does not require blocking movements on the teeth-antagonists with the formation of loads, which are acting at an angle or perpendicular to the vertical axis of the dentition [3; 4].

The aim of our investigation was to improve the quality of orthopedic treatment of adontal patients by means of modeling of the structural elements of removable dentures using the idea of finite elements.

Materials and Methods

The work is a part of the comprehensive research program of Kharkiv National Medical University, Ministry of Health of Ukraine, Department of Orthopedic Dentistry "Restoring the quality of life of patients with major dental diseases of maxillofacial organs and tissues with the help of orthopedic treatment and rehabilitation" (State registration number 0122U000350; 2022–2024).

Orthopedic treatment of the patients with complete adentia was performed at Department of Orthopedic Dentistry on the base of the University Dental Center of Kharkiv National Medical University.

The study involved 45 patients aged 44–73 years (average age 59.2 ± 4.3) treated with complete laminar prosthetic constructions for the upper jaw and lower jaw.

Such parameters as mucosal thickness and cortical bone thickness were selected to measure the degree of distribution of masticatory pressure and deformation in patients with complete removable dentures (CRD) [5].

Our methods of studying the variation of tension and deformation allow to determine the correct design of artificial teeth on the basis of CRD in accordance with the atrophy of the alveolar process of the patient taking into account the thickness of the oral mucosa [6; 7].

At the stage of denture construction, we performed 3D scans of orthopedic structures using an extraoral scanner for dental models inEos X5 Dentsply Sirona (Ballantyne Corporate PICharlotte, NC 28277USA). Based on the 3D scans of CRD, a graphical 3D model of dentures was created, which helped us to determine the geometric parameters of the model (Fig. 1).

Due to the fact that we were interested in the internal stress distribution, it was decided to investigate our model in cross section. To do this, we identified 4 planes of sections that pass through the medial lines of the first premolar, second premolar and the first and second molars of the third quadrant of the mandible (Fig. 2, 3). The choice of these planes was due to the fact that these areas have the greatest masticatory load.

Soft tissues by their mechanical properties are hyperelastic materials for which the elastic deformation is greater than 1. In this case relationship between tension and deformation is nonlinear; it was calculated using the following formula for isotropic incompressible materials [8; 9]:

$$I_3 = \lambda_1^2 \times \lambda_2^2 \times \lambda_3^2 = 1 \quad (1),$$

where I – isotropic incompressible,
 $\lambda_1, \lambda_2, \lambda_3$ – relative elongation in directions parallel to coordinate axes.

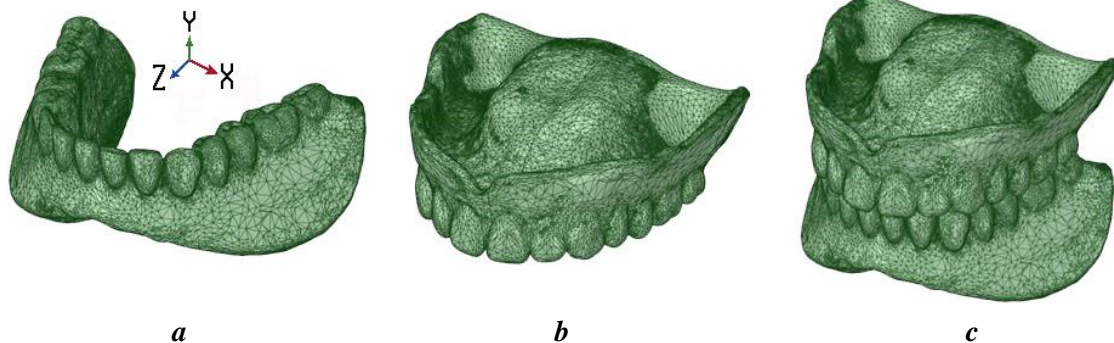


Fig. 1. 3D model of dentures: a) lower jaw; b) upper jaw; c) state of occlusion.

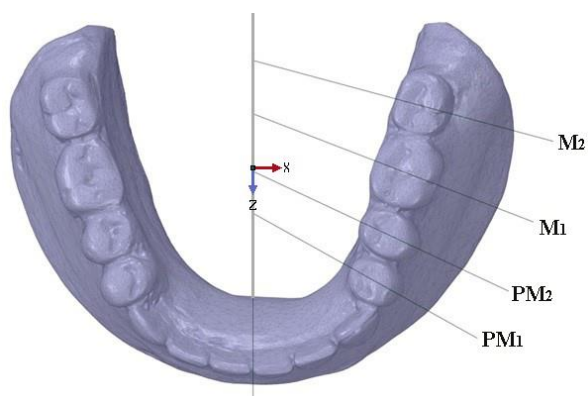


Fig. 2. Cross-sectional planes passing through the medial lines of the teeth of the third quadrant of the mandible: PM1 – the first premolar; PM2 – the second premolar; M1 – the first molar; M2 – the second molar.

The relative change in volume or volume deformation was determined by the formula:

$$J = \frac{V}{V_0} = \lambda_1 \times \lambda_2 \times \lambda_3 \quad (2),$$

where V_0 – starting volume,
 V – final volume,
 $\lambda_1, \lambda_2, \lambda_3$ – relative elongation in directions parallel to coordinate axes.

Volumetric deformation due to thermal expansion was determined by the formula:

$$J_{th} = (1 + \varepsilon_{th})^3 \quad (3),$$

where J_{th} – thermal expansion;
 ε_{th} – linear deformation of thermal expansion.

The finite element method [10] was taken into account. The main idea is that the body under the study is divided into a finite number of subdomains or elements on which the desired continuous function is approximated by a polynomial (consists of piecewise continuous functions). The finite element method is a flexible and accurate numerical method. In our work, this method was chosen to solve the problem.

Thus, when constructing a discrete model of a continuous value, the following was done:

1. A finite number of points is fixed in the area. These points are called nodal points or simply nodes.

2. The value of a continuous quantity at each nodal point is considered a variable that must be determined.

3. The definition domain of a continuous value is divided into a finite number of subdomains, which are called elements. These elements have common nodal points and collectively approximate the shape of the area.

4. A continuous quantity is approximated on each element by a polynomial, which is determined using the nodal values of this quantity. For each element, its own polynomial is determined, but the polynomials are selected in such a way that the continuity of the value along the boundaries of the element is preserved.

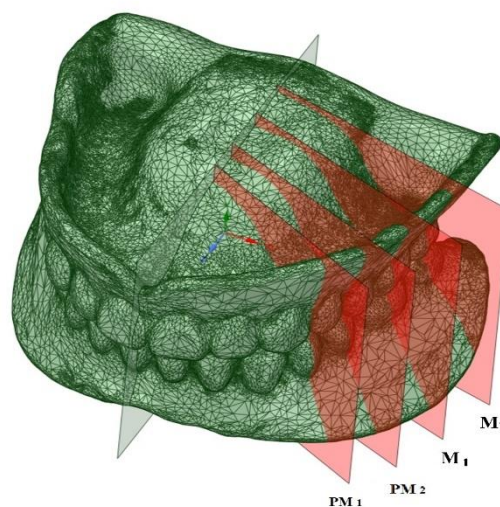


Fig. 3. 3D image of cross-sectional planes: PM1 – the first premolar; PM2 – the second premolar; M1 – the first molar; M2 – the second molar.

Results and Discussion

After determining the geometry of the solution areas, and the physical characteristics of the components of the model, we chose the type of elements into which we will divide the model. A two-dimensional quadrangular element with four nodes was chosen as the partition element. Dividing it into elements and further solving the problem was done in the ANSYS Mechanical APDL package. Fig. 4 shows the division into elements of the two-dimensional solution area [11].

At the next step, the boundary conditions were determined, where the red arrows show the external load (the load which is caused by the muscles of the lower jaw), the triangles indicate the type of boundary movements of the nodal points.

After solving the problem with the given boundary conditions, tension fields were obtained

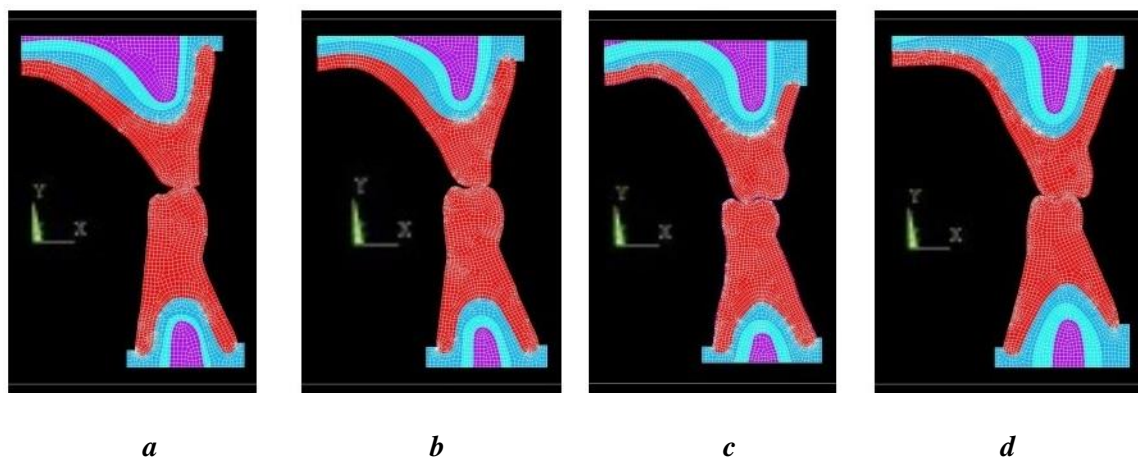


Fig. 4. Dividing the solution area into quadrangular elements:
a) section PM_1 ; b) section of PM_2 ; c) section M_1 ; d) section M_2 .

Note: Fig. 4 (a–d) show the mutually perpendicular x and y axes, which are not clear in the screenshots.

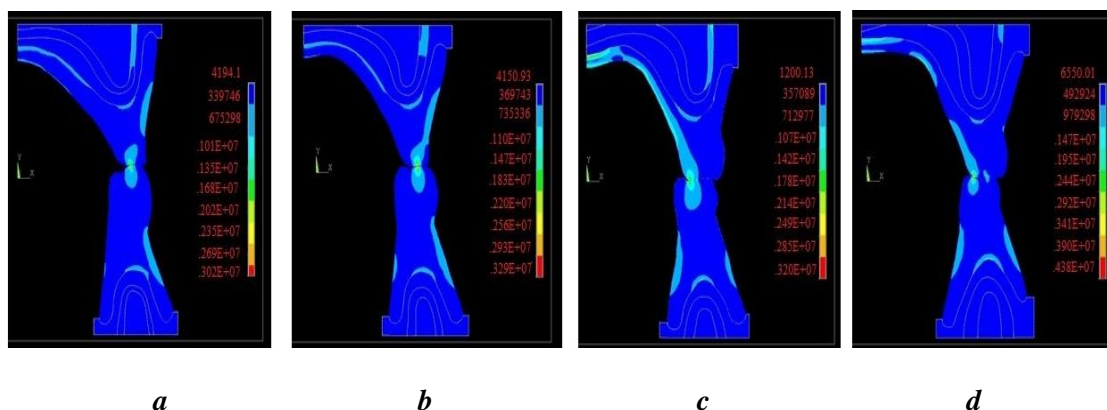


Fig. 5. Stress field in certain areas of the solution:
a) section PM_1 ; b) section of PM_2 ; c) section M_1 ; d) section M_2 .

Note: Fig. 5 (a–d) show the mutually perpendicular x and y axes, which are not clear in the screenshots.

for certain solution areas with the average value for PM_1 – $([4194.10 \pm 3.41] \text{ m}^2\text{K})$, PM_2 – $([4150.93 \pm 5.22] \text{ m}^2\text{K})$. Data on the average values of M_1 and M_2 were $([1200.13 \pm 4.1] \text{ m}^2\text{K})$ and $([6550.01 \pm 3.23] \text{ m}^2\text{K})$, respectively (Fig. 5).

Regarding the calibration of the ultimate displacements of nodal points and as a result of the distribution of masticatory pressure under the basis of a complete removable dentures on the tissues of the prosthetic area, the average values of each plane were as follows: for section PM_1 – the plane with high pressure was $([675298.14 \pm 5.21] \text{ m}^2\text{K})$. Taking the PM_2 region, the values were slightly higher $([369743.3 \pm 3.9] \text{ m}^2\text{K})$ and $([735356.34 \pm 4.52] \text{ m}^2\text{K})$, respectively.

Section M_1 had the result of a total plane with a lower degree of load $([357089.2 \pm 1.7] \text{ m}^2\text{K})$, a plane with high pressure – $([712977.2 \pm 3.4] \text{ m}^2\text{K})$. The largest values were shown by the segment M_2 with the values of the groups $([492924.12 \pm 2.15] \text{ m}^2\text{K})$ and $([979298.1 \pm 3.3] \text{ m}^2\text{K})$.

The obtained data were used to substantiate and develop methods for mathematical calculation of material volume, volume deformation, potential data and elasticity theory as an auxiliary element in the manufacture of removable orthopedic structures and, as a result, to improve the quality of orthopedic treatment of patients in the clinic of orthopedic dentistry.

Analyzing the above-mentioned research methods for the development and introduction of a new alloyed material for the manufacture of removable structures of dental prostheses for patients with secondary dentition, it can be noted that the volume of the conducted research fully reveals the positive properties of the developed material and its practical significance in the complex orthopedic rehabilitation by complete removable dentures.

Conclusions

1. Our findings suggest direct relationship between the use of mathematical calculation of material volume, volume deformation, potential data and elasticity theory as auxiliary element in the manufacture of removable dentures and, as a result, direct influence on level of quality of following constructions.

2. Analyzing the dynamics of the obtained results, we can propose the developed theories for using during the laboratory stages of removable dentures manufacture.

3. Detailed modeling calculation of all aspects of adaptation of prosthetic area tissues to remo-

vable prosthesis can be reflected in the subsequent manufacture of structures using 3D technologies.

Prospects for further research: development of a computer program taking into account the deformation and tension during stages of complete removable dentures manufacturing in the clinic of orthopedic dentistry.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

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Consent for publication

All authors give their consent to publication.

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HARD TISSUE DENSITY OF PERMANENT TEETH AS A RADIOMETRIC BIOMARKER OF THEIR QUALITY

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ABSTRACT

Background. The use of radiographic methods for examining patients with the ability to determine the density of examined tissues opens up wide opportunities for individually predicting damage to hard tissues of teeth, as well as determining risk groups for the development of their pathology at early stages, which requires a detailed study of the mineral density indicators of hard tissues of teeth of different groups within the norm, taking into account their age, sex, ethnic, and other characteristics.

The aim of the study was to determine the density indicators of hard tissues of permanent teeth of different groups in the cervical area and compare them.

Material and Methods. The density of hard tissues was determined by analyzing radiographs of 320 intact permanent teeth of 10 patients. Radiographs were made using a Siemens Sirona (XIOS XG Supreme, Germany) dental radiography unit with Trophy Radiologie software (version 7.0, Slovakia). The images were processed using Gendex VixWin Pro software (version 3.5, USA). The density was measured in Conditional Unit of Grayness (CUG). The results were presented as Me (25%; 75%), where Me represents the median, 25% denotes the 25th percentile (first quartile), and 75% denotes the 75th percentile (third quartile).

Results. Incisors, canines, and premolars exhibited the highest density in the dentin area; the lowest density was observed in incisors and premolars for cementum and in canines for enamel. In molars, enamel had the highest density, while cementum had the lowest. Significant differences in enamel density were observed among incisors and premolars, incisors and molars, canines and premolars, canines and molars, and premolars and molars. Significant differences in dentin density were found among incisors and canines, incisors and premolars, incisors and molars, canines and premolars, and canines and molars. Significant differences in cementum density were observed among incisors and canines, incisors and premolars, incisors and molars, canines and premolars, and premolars and molars.

Conclusion. The density indicators of enamel, dentin, and cementum established for groups of permanent incisors, canines, premolars, and molars are different for different tooth groups with characteristic density patterns.

Keywords: *enamel, dentin, cementum, incisors, canines, premolars, molars.*

Introduction

Due to the significant prevalence of lesions of hard tissues of teeth with carious and non-carious etiology, as well as the constant tendency to increase their number and rejuvenate this group of

pathological processes, the search for ways of their early detection and prevention is particularly relevant [1]. Today, various methods of early diagnosis of caries and non-carious lesions of teeth are known. Boytsanyuk S.I., Kuznyak B.V. & Kuznyak L.V. (2014) propose a method for diagnosing tooth decay at an early stage using laser-induced fluorescence and the "DIAGNOdent" device [2]. This method also allows for the rapid and effective diagnosis of hidden caries. Studies by other authors are devoted to the development of methods for predicting and early diagnosis of lesions of hard tissues of teeth by determining their

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chemical composition, as well as the composition of oral fluid, since it has been proven today that the development of pathological processes in hard tissues of teeth are associated with mechanisms of ion exchange between oral fluid and enamel and dentin [1; 3; 4].

Today, one of the effective and widely used methods in clinical practice for detecting changes in the quality of mineralized tissues is determining their mineral density during patient radiographic examination [5–8]. In our opinion, the use of this method opens up wide possibilities for individual prediction of lesions of hard tissues of teeth, as well as determining groups of risk of developing their pathology based on the detected changes in the density of the investigated tissues and trends in its dynamics. A necessary condition for this is a detailed study of the normal indicators of mineral density of hard tissues of intact teeth of different groups, taking into account their age, sex, ethnic, and other features.

The aim of our study was to determine the indicators of density of hard tissues of formed permanent teeth of different groups in the cervical area and compare them.

Materials and Methods

The density of hard tissues of the cervical region was determined by processing radiographs of 320 intact permanent teeth ($n=10$ for each tooth of the permanent bite) taken on a dental radiographic apparatus Siemens Sirona (XIOS XG Supreme, Germany) with Trophy Radiologie software (version 7.0, Slovakia). The images were processed using the using Gendex VixWin Pro software (version 3.5, USA). The Conditional Unit of Grayness (CUG) was taken as the unit of measurement of density. The indicators of density of hard tissues of teeth in the cervical region were determined separately for enamel and cement on the proximal and distal surfaces of the crowns and roots, respectively, for dentin – in the projection of the tooth neck in the interval between the tooth

cavity and the lateral edge, so in this area the indicator was determined for dentin itself and the tissues that were layered on it (*Figure 1*).

To ascertain the conformity of the obtained data to the normal distribution law were used: an analysis of the distribution histogram, coefficients of skewness and kurtosis, the Shapiro-Wilk test. Since the established indicators of density of hard tissues of permanent teeth of different groups differ from the normal distribution characteristics, they are presented in the form of Me (25%; 75%), where Me is the median, 25% is the 25th percentile (first quartile), and 75% is the 75th percentile (third quartile). The reliability assessment of the difference between the means of samples was carried out using non-parametric methods: the Wilcoxon U-test (Mann-Whitney) and the Kruskal-Wallis method for comparing multiple samples.

The research was carried out as part of the planned scientific work of the Department of Normal Anatomy and the Department of Operative Surgery with Topographic Anatomy of Danylo Halysky Lviv National Medical University, "Morphofunctional features of organs in pre- and post-natal periods of ontogenesis, under the influence of opioids, dietary supplements, reconstructive surgeries, and obesity" (state registration number 0120U002129). The patients signed an informed consent to participate in the scientific research. The Bioethics Committee of Danylo Halysky Lviv National Medical University (protocol No.5 dated June 22, 2020) has determined that the research was conducted in accordance with the World Medical Association's Code of Ethics (Helsinki Declaration).

Results and Discussion

The indicators of enamel, dentin, and cement density established for groups of permanent incisors, canines, premolars, and molars indicated their difference for different groups of teeth, as well as characteristic features of the ratio (*Table*).

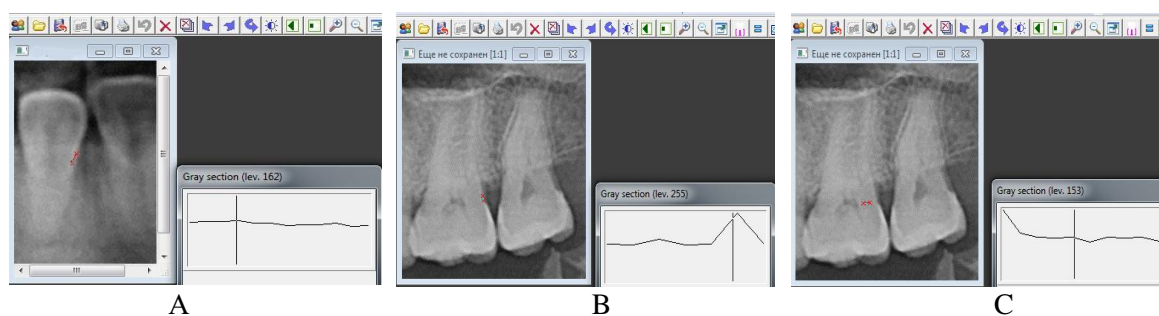


Fig. 1. Determination of density of hard tissues of permanent teeth: A – enamel, B – cement, C – dentin.

Table. Indicators of density of hard tissues of permanent teeth of different groups (CUG)

	Incisors	Canines	Premolars	Molars
Enamel	112.33 [99.00; 124.75]	118.50 [105.00; 137.75]	146.00 [131.00; 162.00]	168.00 [154.00; 182.75]
Dentin	125.00 [110.25; 139.00]	139.00 [125.00; 153.75]	159.50 [145.00; 173.00]	165.50 [152.00; 179.00]
Cement	105.00 [94.00; 119.00]	126.00 [110.00; 141.00]	122.00 [110.00; 137.00]	133.50 [121.00; 148.75]

It has been determined that in incisors, canines, and premolars the dentin area has the highest density. Meanwhile, in incisors and premolars the lowest density is observed in cement, while in canines, it's in the enamel. A different correlation of the investigated indicators is characteristic for molars, where the enamel has the highest density and cement has the lowest (*Table*).

The comparison of density indicators of the investigated hard tissues of incisors, canines, premolars and molars allowed establishing the significance of the difference between the teeth of different groups.

Upon pairwise comparison of enamel density indicators, a significant difference was found between incisors and premolars ($p < 0.001$), incisors and molars ($p < 0.001$), canines and premolars ($p < 0.001$), canines and molars ($p < 0.001$), premolars and molars ($p < 0.001$). The difference between enamel density indicators of incisors and canines is less significant ($p < 0.1$) (*Figure 2*).

Pairwise comparison of dentin density indicators of teeth from various groups revealed significant differences between incisors and canines, incisors and premolars, incisors and molars, canines and premolars, canines and molars ($p < 0.001$). The difference in dentin density indicators between premolars and molars is less significant ($p < 0.05$) (*Figure 3*).

The results of comparing cement density indicators of teeth from various groups showed a significant difference between incisors and canines ($p < 0.001$), incisors and premolars ($p < 0.001$), incisors and molars ($p < 0.001$), premolars and molars ($p < 0.001$). The difference between cement density indicators of canines and molars was less significant ($p < 0.005$), and no significant difference was found between canines and premolars (*Figure 4*).

The analysis results of the investigated indicators showed a similar correlation between enamel density and dentin density of teeth from different groups – the lowest density indicators are in inci-

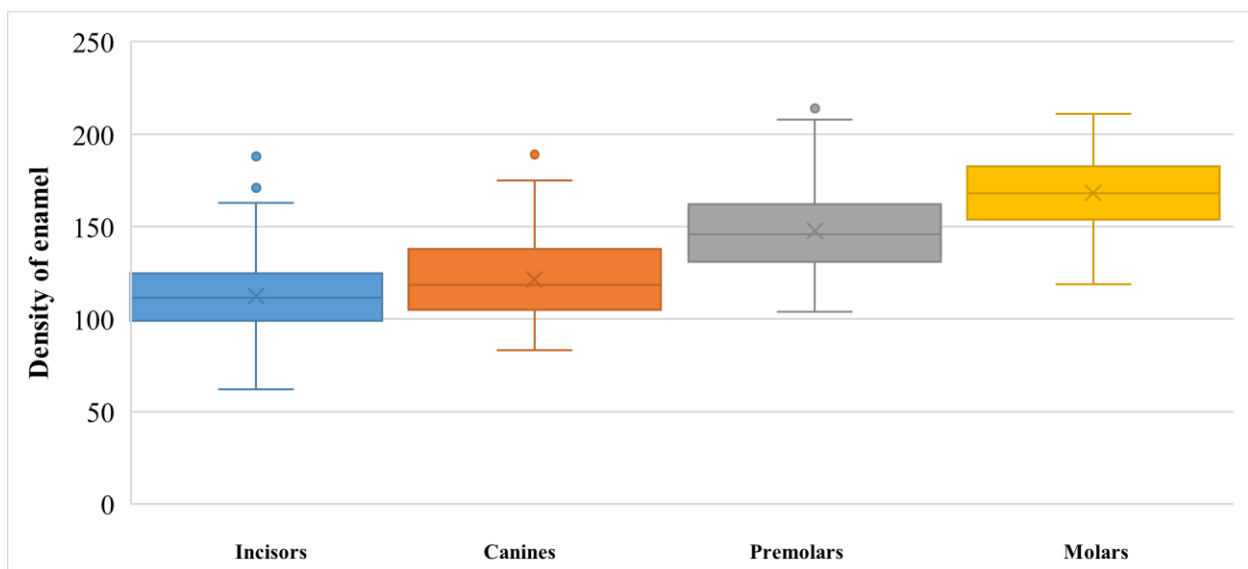


Fig. 2. Comparison of enamel density indicators of teeth from different groups.

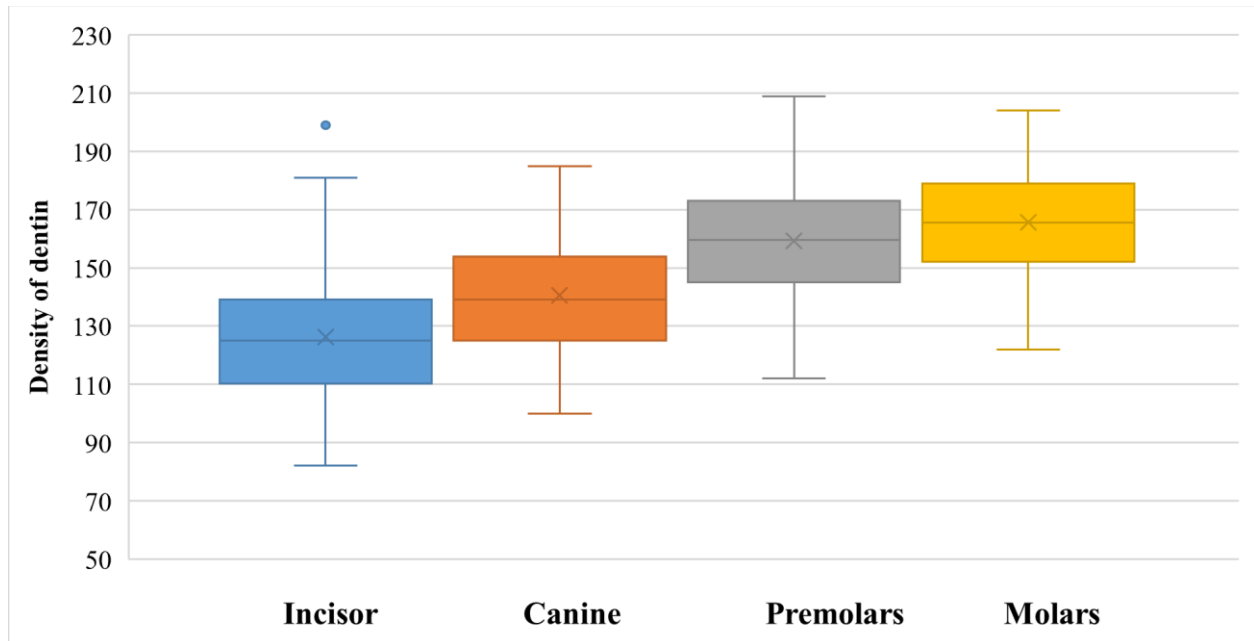


Fig. 3. Comparison of dentin density indicators of teeth from different groups.

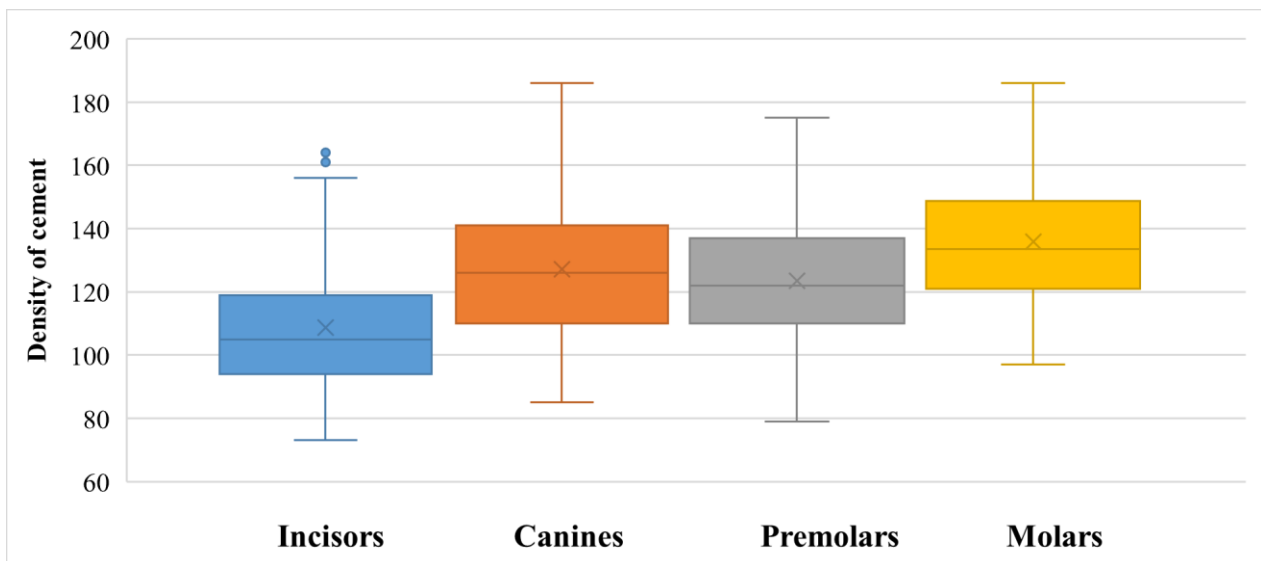


Fig. 4. Comparison of cement density indicators of teeth from different groups.

sors in both cases, increasing in canines, then in premolars, and highest in molars. The relationship of cement density indicators is somewhat different – similar to enamel and dentin, the lowest investigated indicator is in incisors, highest in molars, and the density indicators of canines and premolars occupy an intermediate position, but with a reverse correlation – the cement density in canines is higher than in premolars (Table, Figures 2–4).

The data obtained from this study could serve as a basis for developing a scale of normative quality indicators for the hard tissues formed by permanent teeth of different groups during their radiological examination. However, when conducting examinations and measuring density indicators of the investigated tissues, it is necessary to take into account that absolute indicators determined during patient examinations on different devices and using different image processing pro-

grams may significantly differ from each other. Therefore, the analysis of the relationship between the investigated indicators, the change of which can be interpreted as the first manifestation of pathology, is of primary importance, in our opinion.

Conclusions

1. The density indicators of enamel, dentin, and cement established for groups of permanent incisors, canines, premolars, and molars differ among the various tooth groups with characteristic correlation features.

2. In incisors, canines, and premolars, the dentin area exhibits the highest density; the lowest density in incisors and premolars is observed in cement, while in canines, it is enamel. In molars, enamel demonstrates the highest density, while cement exhibits the lowest.

3. The density indicators of enamel show a significant difference between incisors and premolars, incisors and molars, canines and premolars, canines and molars, and premolars and molars.

4. The density indicators of dentin show a significant difference between incisors and canines, incisors and premolars, incisors and molars, canines and premolars, canines and molars, and premolars and molars.

5. The density indicators of cement exhibit a significant difference between incisors and canines, incisors and premolars, incisors and molars, premolars and molars, and canines and molars.

6. The density of enamel and dentin is lowest in incisors, gradually increasing in canines and

molars and highest in molars. Cement density is lowest in incisors, slightly higher in premolars and canines, and highest in molars.

Prospects for Further Research

Further investigation into the qualitative and quantitative characteristics of the hard tissue of intact teeth from different groups, as well as studying the dynamics of their changes during the development of pathological processes using modern non-invasive and accessible radiological methods, will contribute to the development and improvement of new methods for their early diagnosis, effective treatment, and prevention, with subsequent practical implementation.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included. The authors confirm that artificial intelligence technologies were not used in the creation of this work.

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NEUROPROTECTIVE MECHANISMS OF PHYSICAL ACTIVITY

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<https://doi.org/10.35339/ic.10.2.mel>**ABSTRACT**

It is known that the adaptive capabilities of the brain are not unlimited and deteriorate over time. It is a proven fact that aging is one of the main risk factors for the occurrence of neurodegenerative disorders, mainly due to poorer immune protection and recovery of the body. Therefore, scientists have recently been paying attention to the search for additional methods of management of neurodegenerative pathologies for their more effective prevention. Among the identified methods, special attention is paid to physical activity, the results of which investigation indicate a powerful neuroprotective effect, however, the mechanisms of this phenomenon have not yet been conclusively proven. Therefore, in this systematic review, the main neuroprotective mechanisms of exercise were described and demonstrated using the methods of analysis and systematization of literature sources from PubMed, Web of Science, Elsevier, and Google Scholar databases. As a result of the study, it was established that a significant protective effect on the nervous system is achieved thanks to neuroendocrine regulation due to the influence on the hypothalamic-pituitary-adrenal axis. Another factor is the development of stress due to physical exertion, although the mechanisms of this phenomenon are still a subject of debate among scientists. However, it was proved that the consequence of such influence is the optimization of the work of neurotransmitters, in particular, in the locus coeruleus, as well as the activation of the antioxidant system, which allows to disrupt the number of free radicals in the brain structures. Relatively new is the role of moderate-intensity exercise in increasing the expression of neurotrophins – key factors of neuroplasticity, in particular BDNF, IGF-1, NGF and VEGF, which expands the possibilities of potential effects on the brain and its neuroprotective properties. The obtained results allow the use of physical activity as an additional therapy in the treatment and prevention of neurodegenerative pathologies, however, further practical research is needed to find a specific algorithm and schedule of classes with high application efficiency.

Keywords: *physical activity, neurotrophins, neuroprotection, brain-derived neurotrophic factor, antioxidants.*

Introduction

Neuroprotection is the prevention of cell death by necrosis or apoptosis due to the improvement of its adaptation mechanisms to changes in the external or internal environment. This term is often used to describe neuroplasticity – the ability of nervous structures to change under the influence of stimuli, which also leads to an increase in the adaptive capabilities of the brain and the body as a whole [1]. The concept of neuroprotection has

attracted the attention of scientists as one of the points of influence in the treatment of neurological and psychoneurological diseases, including neurodegenerative ones [2]. It has been found that over time the body's adaptive capabilities are lost, and aging is one of the main risk factors in the occurrence of Alzheimer's and Parkinson's diseases, not to mention dementia disorders and psychorganic syndrome [3]. For example, according to 2019 statistics, about 50 million people in the world suffer from dementia, while every year this indicator increases by 10 million new cases [4]. In Ukraine, the share of people of retirement age is approximately 25% of the population, with a tendency for this indicator to increase annually. According to Fedotova M. S. et al. (2021) as of 2021, the average prevalence rate of dementia in Ukraine was 99.72 persons per 100,000 population,

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and Alzheimer's disease was 5.34 persons per 100,000 population [5].

In addition, although the exact influence of stress factors and war on the susceptibility to the development of dementing disorders is not proven, studies by foreign scientists on the impact of war on the structure and function of the brain indicate a potential increase in the proportion of dementing disorders as a result of a full-scale invasion [6]. A separate topic is the development of various types of neurodegeneration in military personnel as a result of injuries to the central and peripheral nervous systems, which also significantly increases the share of neurodegenerative disorders in the structure of nervous system lesions and increases the urgency of finding and implementing the latest methods of treatment and rehabilitation of patients with these pathologies [7]. The algorithm of prevention and treatment of such disorders includes operative, medicinal and non-medicinal methods. Among the latter, physical activity has long been considered one of the most effective methods of managing dementia and post-traumatic consequences, and early activation has become a routine practice in the work of a doctor of physical rehabilitation medicine [8; 9].

On the basis of previous studies, it was found that physical activity (PA) has a beneficial effect on human cognitive functions and its neuroprotective capabilities [10; 11]. For example, it has been proven that the regular use of PA in the treatment of neurological diseases was associated with better blood supply to the affected areas of the brain and hippocampus, compared to untrained individuals [10]. At the molecular level, this was accompanied by an increase in superoxide dismutase (SOD), endothelial nitric oxide synthase (eNOS), vascular endothelial growth factor (VEGF), neurotrophins and a decrease in the production of harmful free radicals in the hippocampus region of the brain, which are mainly involved in memory [11]. Studying the mechanisms of PA neuroprotection will improve the possibilities of rehabilitation of patients with neurodegenerative disorders and become an impetus for creating more optimal methods of influencing the restoration of the function of nervous structures.

The Purpose of the work was to analyze and systematize the currently known neuroprotective mechanisms of exercise for their further use in future research.

A systematic literature review was conducted in March-June 2023. All literature sources were analyzed according to PRISMA recommendations

[12]. Sources from four databases (PubMed, Web of Science, Elsevier, and Google Scholar) were used to search for studies by keywords.

The inclusion criteria were:

- original studies and meta-analyses on the impact of physical activity on cognitive functions and/or neuroregeneration;
- review works describing possible neuroprotective mechanisms;
- research describing/studying the impact of physical activity on the immune system and antioxidant and neurotrophin systems
- works on the analysis of methods of treatment of neurodegenerative disorders.

Preclinical and in vitro studies, case series, and clinical cases were excluded from the review. Scientific works based on the use of questionnaires and questionnaires without further statistical data processing and all works that did not meet the inclusion criteria were also excluded. All retrieved publications were further screened and any studies not relevant to the topic were excluded. Among the reviewed articles, 43 works were selected for further analysis and inclusion in a systematic review.

Results and Discussion

According to the American College of Sports Medicine (ACSM), physical activity significantly reduces the frequency of diagnosis of metabolic syndrome (hypertensive disease, type II diabetes and obesity) and bone and joint disorders ($p < 0.05$) [13]. In addition, statistical data indicate a 20–30% reduction in the risk of ischemic stroke and a 10–20% risk of cardiovascular diseases, regardless of the patient's gender [11].

A similar effect is achieved thanks to a number of mechanisms. For example, systematic exercise leads to hypertrophy and proliferation of myocardial cardiomyocytes with the development of an "adapted" heart, leading to optimization of ATP utilization in cardiomyocytes, increased cardiac output, and improved oxygen delivery to tissues, including the brain. In addition, at the molecular level, PA leads to an increase in the concentration of C-type natriuretic peptide and endothelial natriuretic peptide, whose positive effect in the prevention of heart failure and other cardiovascular diseases has already been sufficiently studied [15].

With this in mind, the ACSM today recommends a program that includes aerobic, strength, flexibility, and balance training for the elderly and patients ≥ 50 years of age with chronic disorders. Aerobic training should be performed ≥ 5 days per week for 30 minutes of moderate intensity or ≥ 3

days per week for 20 minutes of high intensity [13]. However, is such a schedule of physical activity appropriate for neurological pathologies?

It is known that the etiology of neurodegenerative disorders is characterized by its multifactorial nature [16; 17]. Numerous endogenous (age, gender, genetic polymorphisms) and exogenous (smoking, obesity, hypodynamia) factors can both contribute to the development of the disease and prevent it [18]. It was found that among non-medicinal agents, physical exercises have the most pleiotropic effect, due to their influence on the cardiovascular, nervous, and immune systems at both the cellular and molecular levels [9].

The influence of physical activity on neurodegenerative and other neurological disorders has been studied for a long time [9–11]. During this period, several possible points of influence of PA on the brain were identified, which is demonstrated in more detail in the figure (Fig. 1). For example, improving the rheological properties of blood and accelerating blood flow as a result of systematic physical activity, which contributes to reducing the risk of acute cerebral blood circulation disorders, was studied as early as the 20th century [19]. At the same time, relatively recent works by Amidfar M. et al. (2020) and Baranowski B.J. et al. (2020), which indicate an increase in the concentration of neurotrophins, in

particular BDNF, and antioxidants in the intercellular spaces of the brain, which potentially improves the adaptive capabilities of the brain and reduces the risk of developing Alzheimer's and Parkinson's diseases [20; 21].

Therefore, based on the available modern data, scientists put forward a number of hypotheses regarding the possible mechanisms of the neuroprotective function of physical activity, which are described below.

Neuroendocrine regulation

According to the research of Hackney A.C. (2006), with sufficient intensity and duration of physical activity, they can play the role of an activator of the neuroendocrine system and its adaptation to stress. In response to submaximal loads, the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system are activated, resulting in the release of hormones from the adrenal glands (cortisol, adrenaline) and the hypothalamus (vasopressin, corticolipin, and beta-endorphin), which contributes to greater utilization of metabolic substrates. The result of this is improved blood circulation, optimization of vascular tone and better delivery of oxygen to tissues [22].

At the same time, physical activity has an effect on neurotransmitters, namely on the central dopaminergic, serotonergic and noradrenergic systems. Tai F. et al. (2020) found that systematic

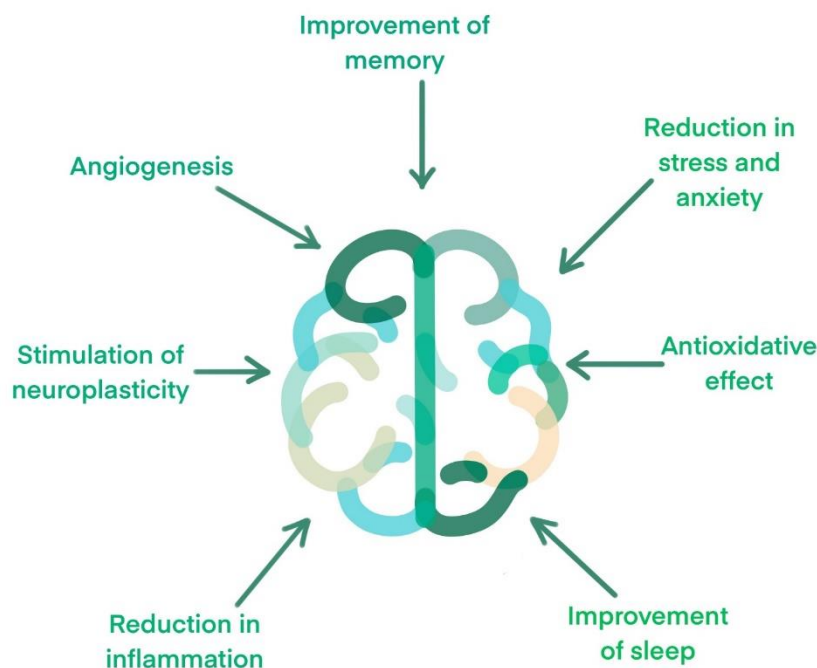


Fig. 1. General effects of physical activity on the human brain.

physical activity significantly increases the release of mediators in these systems and the extracellular concentration of dopamine, norepinephrine, serotonin, and neurotrophins, which is primarily explained by an increase in serum calcium levels in the blood as a result of exercise [23].

Neural adaptation in response to uncontrolled stress is associated with the effect on neurotransmitter systems. Sciolino N.R. et al. (2012) found that neuroprotection occurs through the expression of galanin in the locus coeruleus, which hyperpolarizes noradrenergic neurons, thereby reducing the excessive release of norepinephrine that causes feelings of fear and anxiety. Since the main source of the mediator for the frontal cortex and the amygdala is the locus coeruleus, the inhibitory effect of PA on this area of the brain leads to the optimization of norepinephrine levels and the prevention of anxiety-like behavior [24]. In addition, norepinephrine in normal concentrations is involved in memory consolidation and recovery, which especially plays a role in the case of patients prone to neurodegenerative disorders [25].

The influence of PA on the serotonergic system depends on the region of the brain and the intensity of training. For example, running at a moderate pace for a month reduced 5-HT levels in the hippocampus, while 7 days of high-intensity training led to increased levels of the mediator. This indicates the potential antidepressant and anxiolytic effects of exercise, which was also found in studies by Mahalakshmi B. et al. (2020) [9].

Immune-inflammatory regulation

It is known that sharp physical activity is accompanied by an increase in the levels of pro-inflammatory cytokines, which is explained by the reaction to a sudden stress factor [26]. However, Flynn M.G. et al. (2007) found that regular physical exercises of moderate activity, on the contrary, are associated with a decrease in the levels of the main markers of the inflammatory process in the body, which is explained by the immunomodulatory effect of PA [27].

For example, Koh Y. et al. (2018) in their study found that daily gymnastics of moderate and low intensity led to a decrease in the expression of cell adhesion molecules - one of the key factors in "luring" immune cells to the focus of inflammation. At the same time, high-intensity exercises, on the contrary, increased the intensity of these markers. The mechanism of this phenomenon consists in the epigenetic regulation of the transcription of genes responsible for the synthesis of cell adhesion molecules and inflammatory cytokines, as

well as the effect of physical activity on the antioxidant system [28].

Thus, the systemic immunomodulatory effect of exercise is the result of a combination of regulation of the activity of pro-inflammatory cells, neuroendocrine effects, activation of metabolism and reduction of visceral fat mass, and an increase in the levels of antioxidants in the blood.

Optimizing the function of antioxidant systems

It is known that the brain accounts for approximately 20% of the total use of oxygen and glucose by the body [29]. Accordingly, the degree of generation of free radicals in the brain is also significant, which is fully compensated by the work of antioxidants (enzymes and other substances capable of neutralizing free forms of oxygen). However, with age, their effect decreases and the level of oxidative damage to the nervous system increases, which is currently considered one of the main elements in the pathophysiology of neurodegenerative diseases [30].

In recent years, a number of studies have demonstrated an inverse correlation between different degrees of physical activity and the state of oxidative stress in the body. Thus, according to research of Li T. et al. (2015) high-intensity training leads to temporary stress in the body and an initial increase in the level of oxidative stress, since muscle cells are the main source of free radicals during exercise. However, it promotes the activation of compensatory systems and increases the expression of antioxidants, in particular catalase, glutathione peroxidase and superoxide dismutase, which are present in the body for a long time and contribute to the reduction of oxidative stress not only in muscles, but also in other systems, in particular, the brain [31]. This is confirmed by the work of Bojarczuk A. et al. (2022), who found a statistically significant difference in a higher level of antioxidants in athletes compared to untrained individuals [32].

However, the concept of using high-intensity loads is not appropriate in the elderly, who are the main risk group for the occurrence of neurodegenerative disorders. In this case, low-intensity exercises with their systematic application can also be useful, as according to the same study by Li. T. et al. (2015) leads to a compensatory increase in antioxidant levels, however, more evenly than during high-intensity exercise [31]. The effectiveness of this type of load is explained by the theory of hormesis, highlighted in the work of Radak Z. et al. (2008), which is graphically demonstrated in the figure (*Fig. 2*) [33].

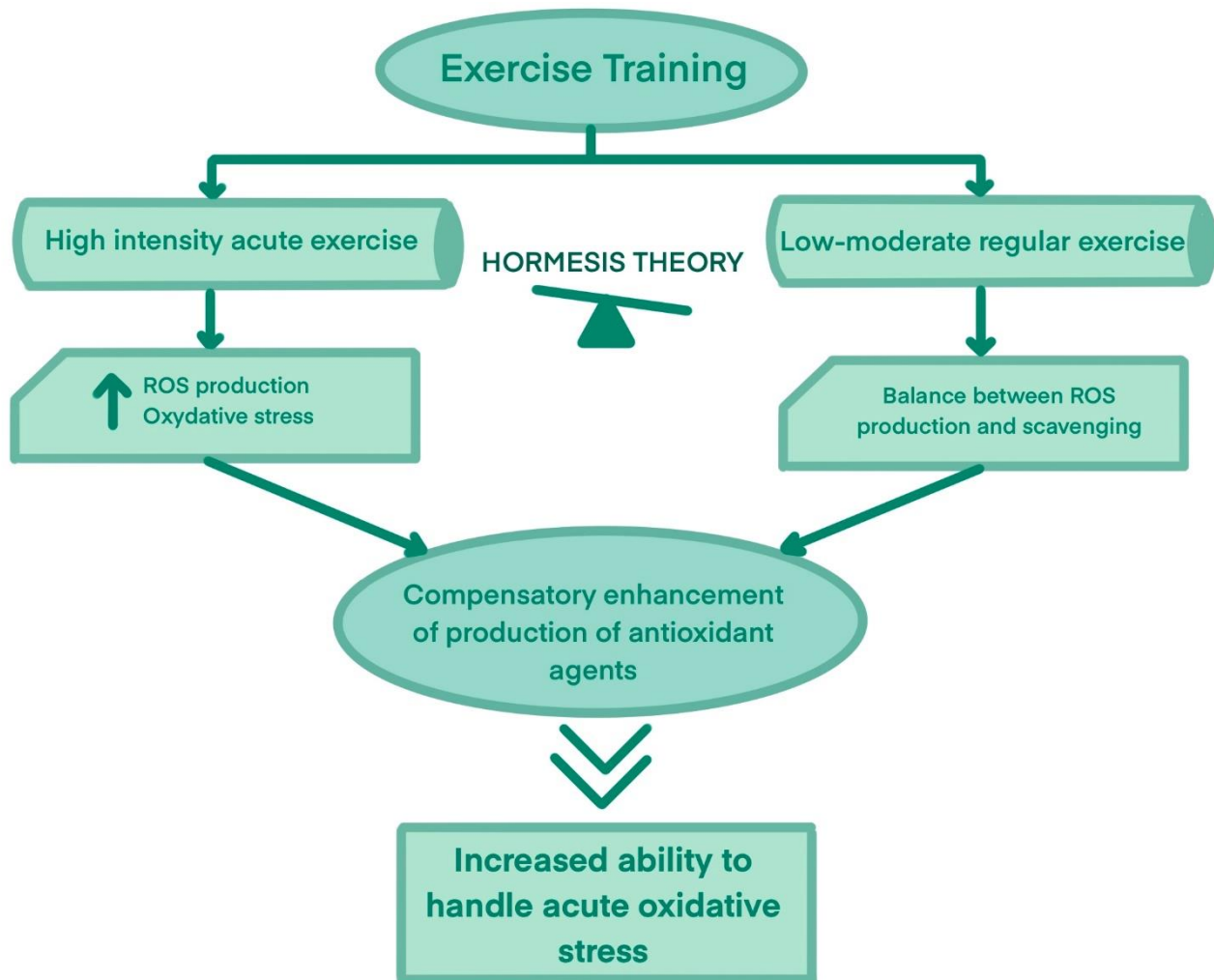


Fig. 2. Schematic representation of the theory of hormesis in the context of physical activity [33].

According to the work of scientists, a low dose of any agent that is harmful at high altitudes causes an adaptive beneficial effect on the cell or organism. In the context of physical activity, their low intensity will lead to a gradual increase in antioxidants as a compensatory response to moderate physical stress, without the occurrence of oxidative stress, while high intensity, on the contrary, will promote its development, resulting in the activation of antioxidants [33].

Thus, it is more appropriate to use low-intensity exercises in the elderly, taking into account their comorbidity, while in young patients with an organism adapted to loads, it will be appropriate to use high-intensity exercises in combination with low-intensity ones for better adaptation of the body.

Influence on neuroplasticity

Neuroplasticity is the ability of the nervous system to adapt in response to endo- and exoge-

nous stimuli through structural and functional restructuring.

Relatively recently, it was discovered that in response to physical activity, proteins-neurotrophins are released, the main effect of which is not carried out by neural networks of the brain. Basically, they have neurotrophic activity (stimulate synaptogenesis, growth and differentiation of new neurons), which significantly increases the neuroprotective potential of a specific individual. Their effect on the brain was primarily detected after an ischemic stroke, as it was found that after ischemic stroke, the concentration of neurotrophic factors such as BDNF and IGF-1, as well as the substance VEGF, which is one of the main proangiogenic factors, in the impression zone increases significantly [34]. Recent studies also indicated their role in the prevention of neurodegenerative disorders, in particular, Alzheimer's disease and other types of dementia [35–41].

In particular, Kuga G.K. et al. (2017) found that under physiological conditions, BDNF, IGF-1, and VEGF transduce intracellular signals in hippocampal neurons to maintain their integrity and function. However, with mutations in the genes encoding the specified factors, the risk of dementia disorders increases significantly, which was demonstrated in [35]. In addition, Lovatel G. A. et al. (2013) found that IGF-1 dysfunction leads to a decrease in aversive memory and an increase in inflammatory markers, in particular, interleukins 1, 4 and tumor necrosis factor [36].

At the same time, it was established that the use of physical exercises reliably improves the neuroprotective capabilities of the body [36; 37]. For example, in the same study Lovatel G. A. et al. (2013), the use of daily running for 20 minutes for a period of 2 weeks reduced the level of pro-inflammatory markers and increased IGF-1 signaling in hippocampal neurons. At the same time, Lin T. W. et al. (2015) found that 10 weeks of regular treadmill training can delay the development of Alzheimer's disease. This is because exercise promoted synaptogenesis, specifically increasing the dendritic chain of CA1 and CA3 neurons, which led to improved memory associated with the amygdala and hippocampus. At the same time, the scientists found an increase in BDNF/TrkB signaling molecules (p-AKT, p-PKC and p-TrkB) in the hippocampus and amygdala, as well as a decrease in amyloid- β levels in these areas, which further indicates a positive neuroprotective effect of neurotrophic factors [37].

In addition to BDNF and IGF-1, exercise also regulates the expression of VEGF, which is responsible for endothelial cell proliferation and angiogenesis, which is critically necessary for neurotrophic and neuroprotective processes in the brain, as revealed by Ben-Zeev T. et al. (2022) Scientists found that exercise-induced increases in VEGF concentrations led to improved neurogenesis and microangiogenesis, as well as increased levels of ciliary neurotrophic factor neurotrophin (CNTF) fibroblast growth factor 21 (FGF21), whose effects on the brain are currently poorly understood [38]. In addition, studies have been described on the neuroprotective effect of neuron growth factor (NGF) and neurotrophin-4, which contribute to the induction of growth and remodeling of the innervation of motoneurons of the spinal cord and brain, however, their proof of their role in neuroprotection and the connection with physical activity is still not sufficiently studied, which can be a topic for further research [39–41].

A separate neuroprotective mechanism of exercise is its effect on autophagy – the breakdown and circulation of the body's own substances, mediated by lysosomes. Physiologically, this process is necessary for the destruction of damaged intracellular components and the use of the obtained substrate for obtaining energy or the synthesis of new structures [42]. Thanks to the work of Rocchi A. et al. (2017) found that defects in the normal course of autophagy are associated with stress sensitivity and neurodegenerative disorders. For example, a mutation in the Beclin 1/Becn 1 gene is accompanied by a significant increase in β -amyloid in brain cells, which physiologically is also an autophagic substrate. At the same time, researchers found that voluntary physical activity of moderate intensity is a physiological inducer of autophagy, which is accompanied by a protective effect similar to the work of Beclin 1/Becn 1 regarding the preservation of memory function and the onset of dementia, however, the exact mechanism of this phenomenon is still not well understood [43].

Thus, due to the effect of physical activity on the system of neurotrophins and autophagy, a pronounced neuroprotective effect is potentially achieved, which can reduce the tendency to develop neurodegenerative and other psycho-neurological diseases.

Conclusions

Our findings indicate that regular physical activity of moderate and active intensity reliably leads to the improvement of the cognitive skills of athletes and their adaptability to the occurrence of neurodegenerative disorders. In particular, it was found that due to physical activity neuromuscular transmission, synthesis of neurotrophins, autophagy is optimized, the expression of serotonin, dopamine and norepinephrine mediators improves, which leads to a reduction in the risk of neurodegeneration, as well as a number of other neuropsychological pathologies, for example, depression and anxiety disorders. The obtained results allow the use of physical activity as an additional therapy in the treatment and prevention of neurodegenerative pathologies, however, further practical research is needed to find a specific algorithm and schedule of classes with high application efficiency.

DECLARATIONS:

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**THE USE OF PSYCHOLOGICAL AND PSYCHIATRIC METHODS
IN DETERMINING VALEOLOGICAL COMPETENCE FORMATION
IN NON-MEDICAL STUDENTS OF UKRAINE**

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ABSTRACT

Background. Valeological competence is the ability to lead a healthy lifestyle. Teaching the basics of a healthy lifestyle in higher education institutions of Ukraine is regulated by higher education standards. Valeological competence is formed in non-medical students during the teaching of valeological disciplines. At the Ukrainian Engineering Pedagogics Academy (Kharkiv) such a valeological discipline is "Health Pedagogy", at the National Technical University "Kharkiv Polytechnic Institute" (Kharkiv) and at the National University of Civil Defense of Ukraine (Kharkiv) – "Fundamentals of Medical Knowledge and Health-Saving". Confidential questionnaires are used to assess the success of the formation of the motivational-value and personal components of valeological competence, the list of questions of which allows studying the behavior patterns of non-medical students.

Aim. To establish the conformity of the questions of the questionnaires, which are used to study the formation of the motivational-value and personal components of the valeological competence in non-medical students, to the existing psychological and psychiatric methods.

Materials and Methods. The bibliosemantic method and the system analysis method were used in the study.

Results. Correspondence was established between the questions used to assess the success of the formation of the motivational, value and personal components of valeological competence, with the questions of such psychological and psychiatric methods questionnaires by Rogers K. and Diamond R. (social-psychological adaptation), Boyko V.V. (level of emotional burnout), Burtyanskyi D.L. and Krystal V.V. (levels of socio-pedagogical and sexual-behavioral adaptation of a married couple or sexual partners), Navran L. (satisfaction with married life or life with a sexual partner) and the CAGE-AID screening test for alcohol and/or drug addiction.

Conclusions. The questions of the questionnaires used for assess the success of the formation of the motivational-value and personal components of valeological competence in non-medical students, correspond to existing psychological and psychiatric methods, the modification of which to the needs of assessing the formation of the components of valeological competence requires further research.

Keywords: *qualitative factor-criterion model, health-saving, valeological education.*

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Introduction

The importance of health care cannot be doubted. Disease prevention is a priority direction of the state policy of Ukraine and takes place with the participation of medical workers, civil servants, mass media, professional medical and social non-governmental organizations, and teachers.

However, doctors mostly put effort into secondary and tertiary prevention, because they communicate mainly with citizens who already have the disease. The primary prevention of diseases at the system level is carried out precisely in the institutions of the education system [1–3].

The tool for healthy lifestyle forming in the education system is valeological disciplines, which form the valeological competence of students and establish a commitment to safe behavior and a healthy lifestyle for the entire future life. Teaching the basics of a healthy lifestyle in higher education institutions of Ukraine is regulated by higher education standards. However, each institution of higher education independently chooses the disciplines through which valeological competence will be formed. In the Ukrainian Engineering Pedagogics Academy (Kharkiv) it is "Health Pedagogy", in the National Technical University "Kharkiv Polytechnic Institute" (Kharkiv) and the National University of Civil Defense of Ukraine (Kharkiv) – "Fundamentals of Medical Knowledge and Health-Saving" [4; 5].

The creation of new valeological disciplines for non-medical students conveys a wealth of simple medical information from medical disciplines. First for everything, Anatomy, Physiology and Hygiene. Simplification of information will require special methods of balancing, scaling and aggregation [6–9], which allow one to condense the enormous number of complex terms without losing the integrity of the information, logics and interconnections between themes of discipline, violation of the principles of evidence-based medicine [10–13].

When creating programs of new valeological disciplines, the need to develop competencies provided for by national education standards is taken into account [3; 14–20], as well as the principle of adaptability [21; 22], thanks to which it is simplified to supplement the discipline with information about new achievements in the theory and practice of health care, to build individual educational trajectories of students and to transition to new forms of education (distance synchronous, mixed distance-auditory). Requirements for adaptability, the framework of the competence approach, the transition to learning according to the Bologna model [23; 24] have a significant impact on the system of evaluating students' success in forming the necessary competencies, including valeological. But our research shows that the issue of competence assessment has not been studied enough [25; 26]. In particular, this refers to the comprehensive as-

essment of non-cognitive components related to motivation and the value system, and not to the triad of "knowledge-ability-skills".

To assess the success of the formation of motivational, value and personal components of valeological competence when teaching the discipline "Health Pedagogy", we use the qualitative model of competence formation [27; 28] and confidential questionnaires, the questions of which make it possible to study the behavior patterns of education seekers, the dynamics of their changes, and ultimately to conclude on the success of achieving the goal of forming valeological competence for leading a healthy lifestyle and health care [26–28]. However, in accordance with modern requirements for the verification of psychological and pedagogical methods used in the pedagogical process [19; 29], it is necessary to verify the effectiveness of the scales used to assess the formation of motivation and values.

The **purpose** of the study is to establish the correspondence of the questions of the questionnaires, which are used to study the formation of the motivational-value and personal components of the valeological competence of the non-medical students to the existing psychological and psychiatric methods.

Materials and Methods

The bibliosemantic, comparative method and the system analysis method were used in the study [30]. The search for methods of evaluating motivation and values, as well as activities based on the life principles of mentally healthy people, was performed in the Google Scholar and PubMed scientific databases. The choice of methods for comparison was based on the principles of realism, flexibility, confidentiality and evidence [31; 32].

Results and Discussion

The programs of valeological disciplines "Fundamentals of Medical Knowledge and Health-Saving" and "Health Pedagogy" consist of 14 identical topics [6; 26], but differ in the additional psychological and pedagogical block (didactics, motivation for maintaining health, activation of cognitive activity for the formation of valeological competence, control of valeological competence formation, feedback) in the last one.

In the program of disciplines "Health Pedagogy" [5; 33] and "Fundamentals of Medical Knowledge and Health-Saving" there is a topic about mental and psychological health, within which issues of mental health, mental diseases, borderline states, psychological balance, stress resistance, logical and emotional intelligence, men-

tal and psychological development of a person in connection with age. The program also includes separate issues of neuro-linguistic programming (in particular, techniques for transforming negative emotions into neutral and positive ones, representative systems, diagnostics and getting out of the Karpman triangle, etc.) [34; 35]. Working with one's own emotions involves observing one's own feelings, studying one's own behavior patterns, psychological roles, habits, thoughts, and motivations. The connection between discipline materials, exercises and control questions with Between the discipline material and the method of diagnosis of socio-psychological adaptation by K. Rogers and R. Diamond [36], a self-diagnostic questionnaire with a survey scale and a rating of answers from 0 ("this does not concern me at all") to 6 ("it's definitely about me"). The results of the survey indicate the possibility of adaptation to a new environment, circumstances, rules of conduct, etc. The rating scale for responses to 101 depersonalized statements assesses adaptability, lying, acceptance of self and others, emotional comfort, internal and external control, dominance, and escapism. In the self-diagnosis of one's own psychological state and the risks of psychological adaptation disruptions within the valeological disciplines [37], the restoration of psychological comfort and balance, self-assessment of the effectiveness of psychological relief and increased stress resistance are especially important, which confirms a significant similarity with the methodology of K. Rogers and R. Diamond.

Questions for students in the courses of valeological disciplines on professional burnout correspond to the method of diagnosing the level of emotional burnout by Boyko V.V. (1996) [38; 39], who considered this process "a mechanism of psychological protection in the form of complete or partial exclusion of emotions in response to psychotraumatic influences". Burnout is accompanied by "emotional exhaustion, a decrease in the level of professional activity, dissatisfaction with the activity, as well as an inadequate assessment of one's professional capabilities". A person who is burning out goes through the stages of "tension", "resistance" and "exhaustion". For diagnosis or self-diagnosis, it is necessary to read 84 judgments and answer "yes" or "no" to each of them. Finding someone who is burning out is in the "tension" stage is evidenced by such signs as experiencing psycho-traumatic circumstances, dissatisfaction with oneself, the feeling of being "caged", anxiety and depression. About being in

the stage of "resistance" – inadequate emotional response, emotional and moral disorientation, expansion of the sphere of economy of emotions and reduction of professional duties. About being in the stage of "exhaustion" – emotional deficit, emotional detachment, personal detachment (depersonalization), psychosomatic and psychovegetative disorders. The task of a teacher of valeological disciplines is to teach students of higher non-medical education the principle of self-diagnosis of emotional burnout and to determine the moment when a burned-out person should seek specialized medical or psychological help [40–42].

A significant number of questions on the topic of sex education and family planning, which the teacher of the valeological discipline must ask the students when they complete their independent tasks, are confidential, because they concern their sex life, personal health, the health of a sexual partner or partners. To determine the progress in the formation of valeological competence, the teacher needs frank and honest answers. They can be obtained only under the condition of a guarantee of confidentiality and the student's trust in these guarantees [31]. Questions about sexual practices complement well questions about the attitude of sexual partners to each other, the harmony of marital relations. These questions overlap with the methodology of the questionnaire by Burtyanskyi D.L. and Krystal V.V. (1982) regarding the levels of socio-pedagogical and sexual-behavioral adaptation of a married couple [43–48]. Answers to the 17 questions of the questionnaire are evaluated on a scale from +2 to –2, in which +2 means complete psychological adaptation and sexual harmony, 0 – the absence of any meaning of adaptation and harmony, –2 – psychological maladjustment and sexual disharmony. Additional conclusions about satisfaction with married life or life with a sexual partner can be made using a questionnaire Navran L. (1967) [43; 49] about communication skills. Answers to 25 questions of the questionnaire about non-verbal communication of partners are evaluated on a scale from 1 (if the answer is "never") to 5 (if the answer is "very often"). Based on the results of the survey, it is possible to determine how happy a husband and wife are in marriage, and how happy sexual partners are in a relationship.

High confidentiality requirements also apply to questions of chemical dependency. Especially about the use of drugs, which, unlike alcohol and tobacco, are not legal. Of the large number of existing questionnaires for such questions to determi-

ne the risks of chemical addictions, in our opinion, the majority of overlaps in questions are present in the Screening test for the diagnosis of alcohol and/or drug addiction (Cut, Annoyed, Guilty, Eye-opener, CAGE-AID) [50]. Similar tests with fewer questions are used during visits to doctors when alcohol and drug problems are first detected. In cases of a positive CAGE-AID test (2 or more positive answers to the questions of the questionnaire), the valeological discipline teacher should privately recommend that the student seek professional help from a narcologist.

Conclusions

The questions of the questionnaires offered to those seeking higher education, which are used to assess the success of the formation of the motivational-value and personal components of valeological competence, correspond to existing psychological and psychiatric methods, the modification of which to the needs of assessing the formation of the components of valeological competence requires further research. But it is the study of the motivational, value and personal components of competence that allows the teacher of the valeological discipline to diagnose dangerous conditions for the student's health and to provide recommendations for seeking professional medical or psychological help.

As a result of the research, we established the correspondence of the questions used in the study of the formation of valeological competence of non-medical students with the questions of questionnaires by Rogers K. and Diamond R. (social-psychological adaptation), Boyko V.V. (level of emotional burnout), Burtyanskyi D.L. and Krystal V.V. (levels of socio-pedagogical and sexual-behavioral adaptation of a married couple or sexual partners), Navran L. (satisfaction with married life or life with a sexual partner) and the CAGE-AID screening test for alcohol and/or drug addiction.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Data Transparency

The data can be requested from the authors.

Statement of Ethics

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**PECULIARITIES OF PROFILING AND PROBLEMS
OF TEACHING BIOLOGICAL AND BIOORGANIC CHEMISTRY
FOR STUDENTS STUDYING UNDER THE EDUCATIONAL
AND PROFESSIONAL PROGRAM "PEDIATRICS"**

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ABSTRACT

Background. The methodical article covers to problematic issues of higher education in general, and medical education in particular, as well as specialized teaching of biological and bioorganic chemistry in medical institutions of higher education, for students studying in the specialty "Pediatrics" and the importance of mastering the relevant skills and abilities taking into account the chosen specialization in the field of medicine.

The aim of the study was to analyze, systematize and develop general approaches to the further improvement of specialized educational materials in biological and bioorganic chemistry for level 2 (master's degree) students majoring in specialty 228 "Pediatrics".

Materials and Methods. General scientific research methods, namely analysis and synthesis were used. Scientific literature, educational programs and normative documents of higher medical education were investigated. Bibliosemantic method and system analysis method were used.

Results. The issues of professional competence formation of future doctors studying under the educational and professional program (EPP) "Pediatrics" were considered, taking into account the age characteristics of metabolic processes and regulation of biochemical processes. The problems and relevance of the level of formation of the professional competence of teachers of medical institutions of higher education and its development in our time, taking into account the socio-economic and political situation and the ongoing russian aggression, were discussed. The effectiveness of the profiling process largely depends on the creation of optimal methods of learning, which include the preparation of profiled EPPs, work programs of educational disciplines and syllabuses created on their basis. Owing to the study of issues of age-related biochemistry, peculiarities of biochemical processes in childhood, students' motivation to learn the educational material increases and a stable interest in the chosen profession is formed.

Conclusions. One of the tasks for the integration of the higher school into the European educational space is to increase the level of competence of pediatricians studying by EPP "Pediatrics" from the point of view of the teaching staff's mastery of innovative teaching methods and readiness for their implementation in the pedagogical process due to profiling of various sciences for their more thorough study.

Keywords: *specialized teaching, age biochemistry, pediatrics, quality of medical education.*

Introduction

Despite the rather long existence of an independent state, Ukraine still, unfortunately, has not

been able to overcome the socio-economic crisis, which is certainly deepened by the ongoing russian aggression. The crisis is also clearly evident in the system of higher education, in particular medical education. Steps to reform university education have been taken a long time ago, but they are so superficial and poorly coordinated that they do not solve urgent problems [1]. The decline in the quality of education and the residual principle of its financing, the breakdown of information links, the backwardness of the material and technical base

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of higher education, the outflow of teaching staff abroad, which is connected both with the ongoing military aggression and with a sharp devaluation of the status of teaching and scientific activity, as well as inadequate material support and social protection of the teaching staff and students of education – all this creates real threats to the national security of the country in the future after our victory [1]. As a result, as of now, higher education in general and medical education in particular in Ukraine is becoming uncompetitive, inferior to the level of education in developed countries and practically not recognized by the European community. Such an unfavorable situation requires well-thought-out and systematic reforms to give the opportunity to realize the enormous intellectual potential that exists in our society.

The fact is indisputable that, even at the current stage of development of the Ukrainian state, taking into account the ongoing Russian aggression, education, in particular, higher medical education, should remain a development priority as the future "cornerstone" around which the state will be built after our victory. The extremely difficult modern conditions in which our state finds itself pose the task of revising the goals and responsibilities of education [2]. The directions of the development of the education system are aimed at accelerated development in comparison with other areas of society, since education is related to the development of human potential and, at the same time, prepares leaders and specialists to ensure reforms in other areas of human activity [3]. The need for accelerated development of the education system, as is accepted in the developed countries of the world, is the basis of the concept of the educational process in new realities and provides an opportunity for all participants of the educational process to obtain the highest level of competence [4; 5]. The proof of the transition to a new model of education is the rejection of the passive role of participants in the process, the recognition of only an active position and, for this purpose, the determination of the personal trajectory of education by each student, which gives the opportunity to work fruitfully in the conditions of the newly formed information society [6].

Modernizing the Ukrainian higher education system according to the European model is the most acceptable method of reforming it today, where, in particular, in higher medical education, emphasis is placed on practical-oriented teaching and clear profiling of future specialists [7]. It is necessary to finally eliminate the post-Soviet lega-

cy with its overloading of the theoretical component of education at a higher medical school. State should contribute in every way to the creation and development of powerful university clinics based on European models, which will allow to significantly improve the quality of medical care for the population, ensure the competitiveness of future medical specialists on the domestic and international labor markets [8].

It is clear that most of the processes at the tissue and cellular levels of living matter have already been deciphered and further research is highly relevant only if they are carried out at the molecular and submolecular levels. Therefore, the significance of biological chemistry as the main fundamental discipline is indisputable, and the development of models for its further structuring and profiling are priorities for a higher medical school [9].

The aim of the study was to analyze, systematize and develop general approaches to the further improvement of specialized educational materials in biological and bioorganic chemistry for level II (master's degree) students majoring in specialty 228 "Pediatrics".

Materials and Methods

General scientific research methods, namely analysis and synthesis were used. Scientific literature, educational programs and normative documents of higher medical education were studied. Bibliosemantic method and system analysis method were used.

Results and Discussion

Biological chemistry is still one of the leading fundamental disciplines in the system of higher medical education. At the current stage, it is developing at a rapid pace and has achieved great success in such sections as molecular biology, biochemical genetics, genetic engineering, and so on [9]. In this regard, a modern doctor must be a professional, armed with advanced scientific knowledge, able to make decisions and act in non-standard conditions, be communicative, have a creative and proactive approach to work. These requirements become especially relevant in the training of future pediatricians, because the main integral indicator according to WHO recommendations, which characterizes the quality of medical care in developed countries, is, namely, child mortality, in particular, the number of deaths in the age group of children under one year per 1,000 newborns.

To educate and train a highly qualified pediatrician in the course of teaching biological chemistry, it is necessary to take into account scientific

data from other experimental disciplines, taking into account age characteristics. Pediatricians deal with children's bodies, which are constantly developing and transforming. During the ontogenetic development of a person, there are changes in the metabolism of substances and energy, both quantitatively and qualitatively. Each age period corresponds to a state of metabolism that provides an optimal ratio of plastic and bioenergetic processes. With age, the ratio between the main phases of metabolism (anabolism and catabolism) gradually changes. In certain age periods, children are especially vulnerable, sensitive, and their resistance, in particular immunological, may be reduced. It is necessary to remember the peculiarities of the development and energy supply of the functioning of the central nervous system at various stages of the development of the child's body, and, especially, in early childhood, when the basis for the so-called higher nervous activity is formed. All this should be taken into account by pediatricians, because they are responsible for the mental and physical health and development of the child, and it is during childhood that a person acquires the "main margin of strength" that should serve him throughout his life.

Profiling (profilization) in the teaching of biological chemistry for students studying by EPP "Pediatrics" is a necessary, most promising and, at the same time, difficult direction in the implementation of the educational process. Pediatric students must learn about the peculiarities of the course of biochemical processes in normal and pathological conditions, taking into account the anatomical and physiological features of the child's body in each of the periods of its development. Also, the study of the peculiarities of metabolism in childhood, even in the presence of relevant information in the educational literature available to students, taking into account the lecture hours, created certain difficulties in the assimilation of this material. Therefore, it was extremely necessary to prepare high-quality methodological materials of the management type, in particular, appropriate work training programs for disciplines and syllabuses, for the correct organization of students' work, with the aim of creating conditions for the most effective assimilation of topics, which contain the necessary amount of specialized educational material for the students of the EPP "Pediatrics". In this regard, the Department of Biological and Bioorganic Chemistry of Poltava State Medical University has developed a working curriculum for biological and bioorganic che-

mistry and the corresponding syllabus on the basis of the EPP "Pediatrics", which include profile questions featuring the peculiarities of the chemical composition and exchange processes in the children's body. In the practical classes, specialized questions from pediatrics containing elements of age-related biochemistry are considered, in particular, data are given on the need for food substances, nuances of their digestion and absorption, features of energy, carbohydrate, lipid and protein metabolism, maintenance of water-electrolyte balance, regulatory action of vitamins and hormones. The age-related features of the biochemical composition of blood, urine and other biological fluids in normal and pathological conditions are discussed. For example, when considering the topics of the "Enzymology" section, the issues of qualitative and quantitative characteristics of the enzyme spectrum in different age groups are highlighted. At the same time, it is emphasized that in early childhood, a number of enzyme systems are not fully formed, in particular, this applies to the enzymes of the gastrointestinal tract. All this requires the pediatrician to pay close attention to the organization of proper feeding of children in early childhood. Issues of changes in the activity of the isoenzyme spectrum of lactate dehydrogenase, creatine phosphokinase, alkaline and acid phosphatases, etc., which ensure the processes of metabolic and diagnostic differentiation of cells, are considered. All this allows us to conclude that the formation of enzyme systems in ontogeny proceeds at different speeds depending on age. Vitamins are involved in the functioning of a number of enzymes. Data related to the needs of individual vitamins at different age periods of a child's life, their characteristics, as well as the biological role of water-soluble and fat-soluble vitamins in children are considered in practical classes with students studying by EPP "Pediatrics". At the same time, assessing the role of each of these vitamins in metabolic processes, the causes of vitamin deficiency, as well as hypervitaminosis in childhood and the clinical manifestations of the resulting pathologies are discussed. In the practical classes devoted to the consideration of neurohumoral regulation of metabolism, information is given about the peculiarities of the synthesis and secretion of hormones of the hypothalamic-pituitary system, hormones of the thyroid, pancreatic, parathyroid, and adrenal glands. When considering topics from bioenergetics, the specifics of the energy needs of individual organs at different periods of a child's life are emphasized,

and the issues of energy supply of the central nervous system at the age of one year are carefully considered at the molecular level.

When considering the topics devoted to the exchange of proteins and amino acids, the leading role of these substances as the main plastic material in the growing body is noted, data on the daily need for proteins and essential amino acids in different age periods are given. We also pay attention to the digestion and intracellular metabolism of amino acids in children. We emphasize that the main and most complete source of proteins and amino acids in early childhood is mother's milk, we emphasize the priority of breastfeeding. In practical classes on carbohydrate metabolism, we pay attention to the peculiarities of the metabolism of glucose and other monosaccharides (fructose, galactose) in different periods of childhood. Emphasis is placed on the value of lactose in breast milk in the first months of a child's life. On the basis of the acquired knowledge, we are trying to form the clinical thinking of future pediatricians regarding the molecular mechanisms of the occurrence of various disorders of carbohydrate metabolism, both at the stage of digestion (malabsorption syndrome, maldigestion, etc.), as well as at the stage of intracellular metabolism of monosaccharides (fructosemia, hereditary fructose intolerance, galactosemia, glycogenoses and aglycogenoses). In topics devoted to lipid metabolism, we consider the peculiarities of the digestion of individual classes of lipids, the difference in the lipoprotein spectrum of blood and cholesterol metabolism in children of different age groups. We emphasize that water-electrolyte exchange in children is characterized by high lability, immaturity of its regulation mechanisms, especially in early childhood. Considering the sections "Biochemistry of blood" and "Biochemistry of urine", we draw the attention of students to the peculiarities of the physicochemical properties and chemical composition of these biological fluids at different times of the child's ontogenesis, we discuss the functions and biological role of individual components of blood and urine, their significance in the

diagnosis of children's diseases age. All this will undoubtedly help the future pediatrician to correctly use biochemical indicators of blood and urine in the diagnosis and treatment of specific nosological units of children's pathology. We emphasize that the main questions of the clinical and biochemical characteristics of the pathological conditions of various organs and tissues (diseases of the liver, kidneys, connective and muscle tissues, hemostasis and anti-hemostasis systems, the central nervous system and the cardiovascular system, etc.) will be considered during the study of the elective component "Clinical Biochemistry", which is included in the EPP "Pediatrics".

Conclusions

Therefore, knowledge of the peculiarities of metabolism in the child's body, which are considered as profile questions in the study of the discipline "Biological and bioorganic chemistry", will help the future pediatrician in assessing the state of metabolic processes in the norm and in pathology, will provide a general idea of the formation of metabolic processes in different age periods of ontogenesis.

Prospects for further research

This study will allow to determine the optimal steps on the way to the formation in the future of a new practical-oriented elective component "Clinical biochemistry of children's age" for students studying in specialty 228 "Pediatrics".

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

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