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EDITORIAL

Dear Colleagues!

The annual medical forum Euromedica-2015 has been recently held in Hannover. Among our participants there were medical doctors from Germany as well as a big delegation of specialists from Eastern Europe and Central Asia as well as our regular attendees, Russian-speaking doctors from Germany and other European countries, who arrive traditionally at our annual Doctors' Ball.

The speakers stressed a great importance of cooperation between medical specialists from Eastern Europe, especially from Russia, Ukraine and Germany, which should not be a subject of political disputes but on the opposite, to encourage our countries to draw closer.

The new issue of the journal has been formed by an international team of authors – representatives of medical science from Germany, Russia, Ukraine, Georgia, Uzbekistan, Tajikistan, Armenia and Azerbaijan. Some of the countries are currently in the state of military confrontation – Russia and Ukraine, Armenia and Azerbaijan.

It is obvious that publishing articles from the countries with a different level of health care and medical education might be criticised for a not adequate quality of some articles. However, the editorial board sees as one of its priorities alongside with maintaining a high quality of publications to create a general platform for international collaboration of medical scientists from Europe and Asia irrespective of their political and economic views. This is, in our opinion, the only way to improve the quality of medical services and to reduce the level of suffering in these countries, which strongly motivates our work.

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CONTENTS

ISOLATION OF HEPATITIS C VIRUS IN CULTURED LEUKOCYTES FROM HUMAN BLOOD

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ABSTRACT — The article presents the results of the author's long term research on use of human leukocyte cultures for the isolation of hepatitis C virus and studying its characteristics.

KEYWORDS — hepatitis C virus, chromosomal alterations, mitotic activity, electron microscopy (EM), buoyant density.

INTRODUCTION

Our previous data [1] established that human and animal hepatitis viruses actively replicate in the organs rich in reticular cells and lymphoid elements (liver, spleen, lymph nodes, bone marrow), and viremia especially in transmitted parentherally transmitted hepatits is connected both with the blood plasma and leukocytes [2]. In our present study, a blood leukocyte culture was used for isolation of the viruses from patients with C hepatitis.

MATERIALS AND METHODS

The method of cultured leukocytes was based on the technique by Moorhead et al. [see in refs. [3, 4]. Venous blood was collected into sterile tubes containing 1 or 2 drops of concentrated heparin. Blood samples were centrifuged at 1000 rpm 10 min or left for 18 hrs at 4° C. The plasma was removed, and the leukocyte film was collected off the surface of erythrocytes. Leukocytes were then suspended in cultural medium 199 containing 25–30% of the autologous plasma to a final concentration of 2–3 or 6–7 million cells per 1 ml. An equal amount of leukocytes from healthy donors was added followed by PHA to a final concentration of 0.1–0.2 mg per 10 ml of cell suspension. The cells were incubated in an atmosphere with 2.5–5.0 CO_2 at 37° C.

For EM studies, cells were taken off the glass mechanically or with versene solution and washed off by centrifuging in medium 199 (1500 rpm). After that cells were fixed either with 1.6% glutaraldehyde for 1 hr followed by 1% osmium at 40 C for 45 min, or with 3% glutaraldehyde in 0.1 M cacodylate buffer (pH 7.2). (Osmium fixator was prepared in acetate-veronal buffer, pH 7.2) [3, 4]. Slices were prepared using LKB-8800 A microtome and contrasted with 1% uranyl acetate in 70 % methanol for 15 min at room temperature followed by 1.5 % lead citrate for 10 min at room temperature. For negative contrasting, concentrated virus was placed on a net with a formvar underlayer dusted with coal and exposed to electric field. Contrasting was achieved by 3% phosphone-tungsten acid (pH 7.2). A 5EM-7A microscope was used.

An indirect immunofluorescensce on blood smears was used. Patients were diagnosed based on the clinical survey data and the results of morphologic research of blood and bone marrow samples.

The buoyant density of the leukocytic hepatitis virus and its RNA were measured in cesium and sucrose gradients [4,5].

The amounts of RNA of hepatitis C and G viruses were measured by RT-PCR as previously described [1,4,5].

Phytohemagglutinin (PHA) was obtained from Sigma.

Leukocytes from the blood of healthy donors were stimulated with PHA in a final concentration of 0.02 mg/ml. PHA-stimulated leukocytes were infected with the virus and serially passaged. The support medium was RPMI-1640 with 20% of authologous donor serum and PHA (0.02 mg/ml).

The method is described in details in [4].

RESULTS

Previously, in patients diagnosed with hepatitis as well as in virus-bearing donors, a high percentage (up to 48%) of lymphocytes with chromosome alterations was observed (Fig. 1). In a special set of studies we tested the possibility of passageing of the viral agents from those blood samples in leukocyte cultures from healthy donors.

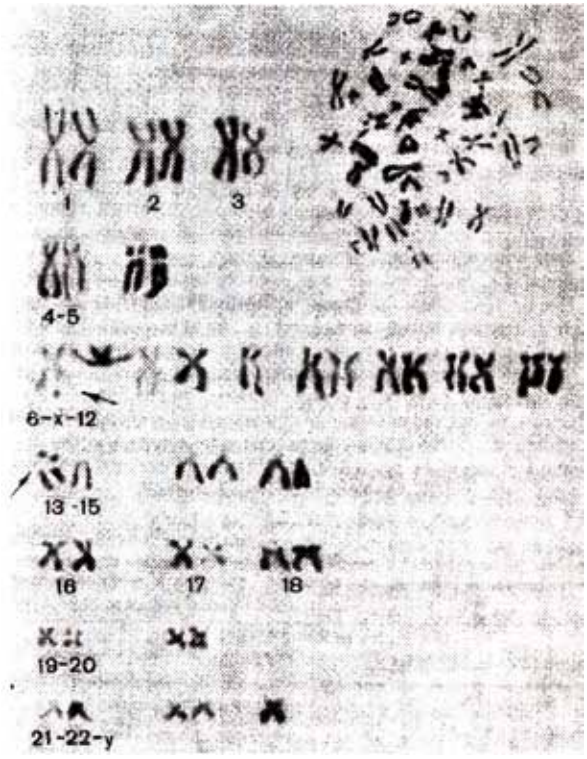

Fig. 1. *Chromosomal alterations (indicated with arrowheads) in leukocyte culture from a 'non A non B' hepatitis patient*

We also marked a decrease of mitotic activity in leukocytes from patients with viral hepatitis, especially over the first days of the disease [3, 5]. This phenomenon was observed in leukocyte cultures also at later stages of infection. It is considered a virus-specific cytopathic activity, like alterations in chromosomes. In collaboration with A. Shubladze, I. Dementyev and J. Shahgildyan, we tested the infectious agents from blood sera by several features: chromosome altering activity in cultured leukocytes, decrease of mitotic activity in those cultures and delay of blast transformation in PHA-stimulated cultured lymphocytes.

Blood sera from patients with hepatitis obtained on days 3 to 5 of jaundice were added to cultured lymphocytes from healthy donors. 72 hrs later the cultures were studied cytologically and cytogenetically. Some cultures were used for serial passages. With the rise of the passage level, the initial sera were diluted 20 times. The sera form healthy donors and non-infected lymphocyte cultures were passaged in parallel as controls. The results are shown in Tables 1 and 2. They indicate a consistent decrease of the mitotic activity and blast-transformation capacity in the process of passageing of the initial material (a 2- to 3-fold at passage 3). The number of lymphocytes with alterations in chromosomes (increased as early as at passage 1) rose 3 to 6 times at passage 3 of the infected material compared with the controls. It is important that no contaminating virus was detected in the sera samples over 3 serial passages in human embryo kidney cells as well as the material from passage 15 in lymphocytes.

Thus, the obtained results indicate to the possibility of in vitro passageing of the agent contained in hepatitis patients blood sera. In addition to our previous data [1], the agent's cytopathic activity was manifested in inhibition of the mitotic activity and blast transformation of lymphocytes as well as chromosomal alterations. The viral nature of the agent was confirmed by the results of a cytogenetic study of leukocyte cultures from viral hepatitis patients and convalescents. Also, the cytoplasm of lymphocytes in infected cultures showed a specific fluorescence in the immunofluorescent assay using an immune serum against the virus. The electron microscopic (EM) study detected peculiar viral particles in leukocyte cultures from patients (Fig. 2, 3). Similar particles were detected in blood sera from patients at the early stage of hepatitis [1, 5].

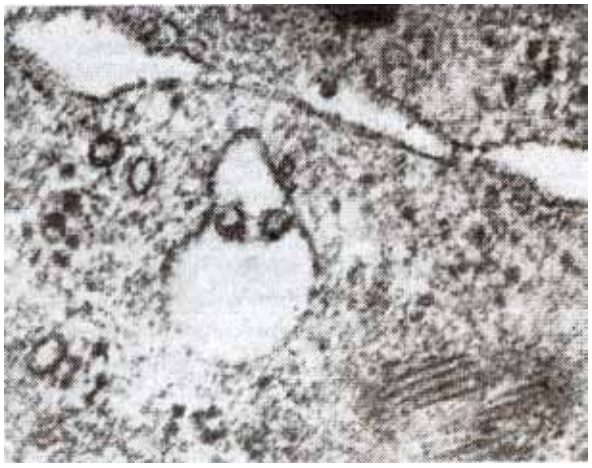

Fig. 2. *Slice of a leukocyte culture from hepatitis C patient. Vacuoles contain virus-like particles. X 200,000*

A series studies on the virus was carried out. Currently we have several isolates of the virus designated as 'leukocytic hepatitis virus (LHV)' obtained from the patients sera over the first days of the disease [1, 3, 4, 5].

Virus-like particles measuring ca. 50–55 nm were detected in slices of infected cultured leukocytes examined by EM, and in the peak fractions of 3H-uridine labeled cesium chloride gradient. The inner component of those particles represented electron

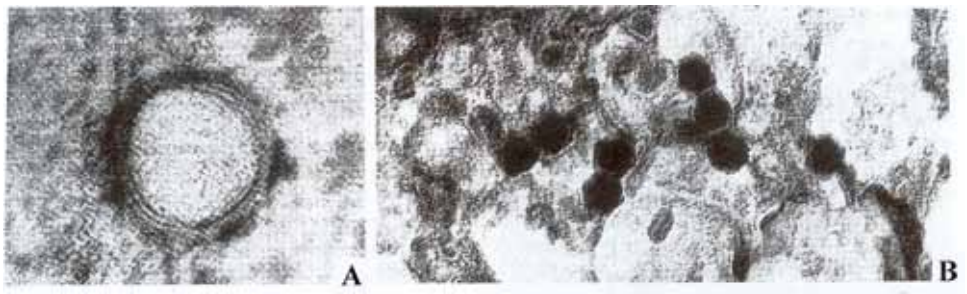

Fig. 3. *Leukocytic hepatitis virus. Negative contrasting. A – Blood serum of a viral hepatitis patient, B – Multiple particles in a PHA-stimulated leukocyte culture, passage level 12. X 400,000.*

dense nucleoid covered with a bilayer envelop 4 to 5 nm thick. Similar particles were found by negative contrast staining of sera from hepatitis patients purified from proteins on sefadex column [3]. LHV is non-pathogenic for small laboratory animals, green african monkeys and lacks hemagglitinating properties with erythrocytes from chickens, sheep, geese, mice, dogs, monkeys and humans. LHV has no shared antigenic determinants with HBVs antigen. The specificity of LHV was proved in a survey of 500 paired sera in complement fixation test, leukocytes migration delay and cutaneous assay. Cutaneous assay using formalin-inactivated LHV was clinically applied and proved positive in 15% of patients with hepatitis in the acute stage and in 75% of individuals with active chronic hepatitis [1, 5]. In the assays when the control antigen was applied (non-infected cultured leukocytes), negative results were obtained. The buoyant density of the two studied LHV strains is 1.26 g/ml (Fig. 4). Replication of LHV in human embryo kidney cell cultures in the presence of 3H-uridine resulted in accumulation of structures with the indicated density. Extraction of RNA from virions from the peak fractions of cesium chloride density gradient and subsequent research of it in sucrose gradient consistently isolated the higher-weight RNA with a sedimentation constant of 40-50S [2, 3, 5]. EM studies with negative contrasting of the virus and LHV-infected cultured leukocytes as described previously [4], revealed numerous spheric and oval particles 50 to 55 nm in size (Fig. 3). The inner component, electron dense nucleoid, is covered with a 4 to 5- nm-thick envelop. Non-infected leukocyte cultures did not contain such particles. Previously, we observed particles similar in size and structure in EM of slices of leukocytes from viral hepatitis patients (Fig. 4) [1].

DISCUSSION

The conducted research has shown that PHA-stimulated cultured leukocytes from healthy donors may successfully be applied for study of the etiology of parenteral viral hepatitis. EM study of negative contrasted LHV samples as well as cultured leukocytes from hepatitis patients without hepatitis B antigenemia detected viral particles of a hexagonal shape 50 to 65 nm in size with a double envelop 5 nm thick. It allowed us to classify LHV as a Flaviviridae family member. In LHV, RNA of hepatitis C virus (1A subtype) was detected. The sedimentation constant LHV in cesium chloride density gradient (1.26 g/ml) was similar to that of hepatitis virus G particles (1.18–1.23 g/ml) [6]. However, no hepatitis virus G RNA was detected by RT-PCR in LHV [4, 7]. Instead, RNA of hepatitis C virus (1A subtype) was detected in one of the isolates of LHV after its passageing in PHA-stimulated cultured leukocytes by RT-PCR [4,5]. In addition, RNA the NS non-structural protein of hepatitis C virus was regularly detected (66.7%) in leukocytes of patients with hepatitis [7, 8, 9].

Therefore, the conducted research showed the effectivity of using PHA-stimulated cultured leukocytes from healthy donors for studying etiology of parenterally transmitted viral hepatitis.

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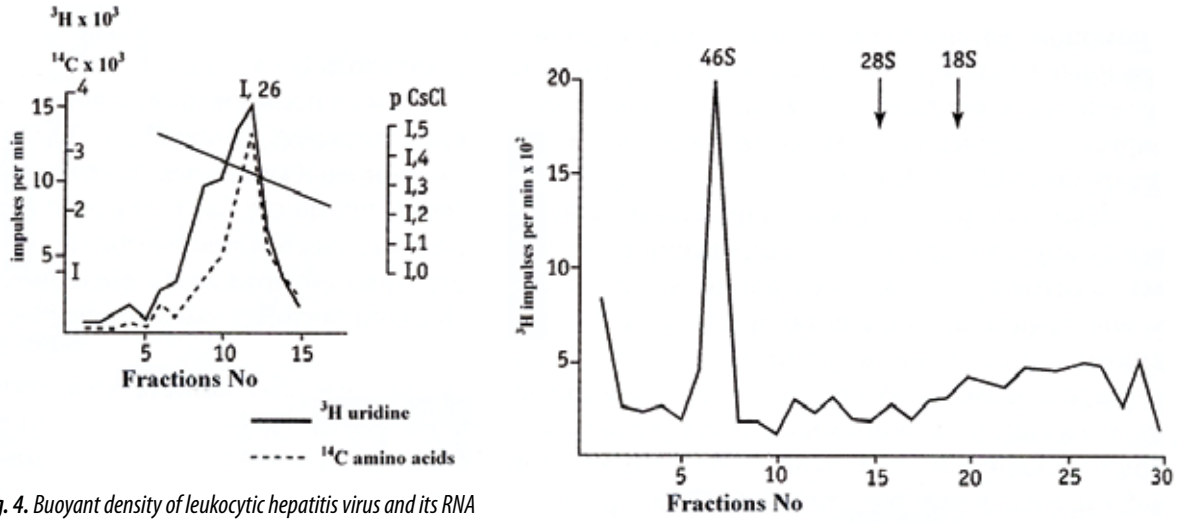

Fig. 4. Buoyant density of leukocytic hepatitis virus and its RNA

Table 1. *Mitotic activity and chromosome alterations as a result of passageing of the agent from the blood sera of the viral hepatitis patients. (The serum agent was passaged in cultured leukocytes from healthy donors)*

Dilution	Passage	Donor Sh.					Donor M.					
		1B		2B			1B		2B		H	
		1	2	1	2	1	1	2	1	2	1	2
Dilution	Initial stock	28	12/4	28	12/4		29		29	4.2	29	4/2
0.5·10^{-1}	1	16.7	25/10	13.3	_		18	12/4	20	16/8		_
0.25·10^{-2}	2	10	24/12		20/8		20	20/20	24	14/12		_
0.125·10^{-3}	3	15	20/8		21/12		24	32/32	13.4	28/24	28	8/0

1B and 2B: blood sera from viral hepatitis patients on days 3 and 5 of jaundice, H: blood serum from a healthy donor.
1 — mitotic activity, in per mille;
2 — Percentage of cells with chromosome alterations (the numerator is the total of cells with alterations, the denominator is the number of cells with coarse alterations)

Table 2. *Delay of lymphocyte blasttransformation in leukocyte cultures infected with the material from patients with hepatitis*

Dilution	Passage	Donor Sh.						Donor M.			
		1B		2B		H		1B		2B	
		48h	72h	48h	72h	48h	72h	48h	72h	48h	72h
	Initial stock	90.4	96.9	90.4	96.9	90.4	96.9	65.8	89.7	65.8	89.7
					78.3*	89.7	96.5	_	_	28.6*	68.3*
0.5·10^{-1}	1	55.8*	77.1	66.3*	78.3*	90.1	92.7	33.0	39.9*	40.3*	61.9*
0.25·10^{-2}	2	63.0*	78.8*	66.0*	71.8*	97.7	93.2	30.1	49.8*	_	_
0.125·10^{-3}	3	65.8*	78.6*	66.5*							

1B and 2B: blood sera from viral hepatitis patients on days 3 and 5 of jaundice, H: blood serum from a healthy donor.
Figures indicate the numbers of blastocells as percentage to the total cell numbers. Asterisk is a reliable difference from the control

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OUR EXPERIENCE OF ULTRASOUND DIAGNOSIS OF CONGENITAL HEART DISEASES

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ABSTRACT — Congenital heart disease (CHD) is the most common disorder of newborns.Most forms of CHD can be detected in utero, especially the severe ones with considerable fetal and postnatal morbility and mortality. Although there has been a great improvement in the diagnosis of CHD both prenatally and postnatally due to the availability of echocardiograpy. The goals of fetal echocardiograpyare to exclude CHD and, when present, to diagnose the specific malformations of the heart.

We report about 2392 cases of fetus's CHD during an period between 2012–2014 years. All cases were verified. Most of them were severe CHD. The number of diagnostic mistakes is 81 (3,4%) from 2392 cases. Echocardiography reveals major congenital heart diseases with a high of accuracy (the number of diagnostic mistakes is 3,4%). Ultrasound of fetus's heart will determine whether the fetus has the type of structural abnormality and detaliesspecifical CHD. This information is very important for choice of surgical repair after birth.

Congenital heart disease (CHD) is the most common disorder of newborns, affecting one out of every 100 babies. CHD is 6 times more common than chromosomal abnormalities and 4 times more common than neural tube defects [3].

About 25% of all infant deaths resulting are due to congenital malformations and one third of these deaths are of infants with cardiac abnormalities. Most forms of CHD can be detected in utero, especially the severe ones with considerable fetal and postnatal morbility and mortality.The prenatal diagnosis of major CHD requires furtherassessment for extracardiac (about 65%) and chromosomal (about 43%) abnormalities [1,2].

Although there has been a great improvement in the diagnosis of CHD both prenatally and postnatally due to the availability of echocardiograpy. The goals of fetal echocardiograpyare to exclude CHD and, when present, to diagnose the specific malformations of the heart. Echocardiography will determine whether the fetus has the type of structural abnormality and detaliesspecifical CHD. This information is very important for choice ofsurgical repair after birth.

THE STAGES OF FETAL ECHO

The early transvaginal fetal echocardiogram can be performed at 12 weeks of pregnancy (for exclude major heart malformations for groups of risk.). But early transvaginal fetal diagnosis will be repeat over 2 weeks. The optimal transabdominal fetal echocardiogram can be performed at 16 to 22 weeks of pregnancy. By this time , details of the fetal cardiac anatomy can be well visualized, such as the atrioventricular and ventriculoarterial connections.

Fetal echocardiographic images may be difficult after 32–34th weeks of gestation because of fetal rib shadowing, fetal position, or maternal body habitus.

METHODS OF SCREENING OF MAJOR FETAL HEART ANOMALIES

Definition of fetal CHD was attempted from multiple scan planes including four-chamber, long- and short-axis as well as aortic arch and ductal arch views. We use 3–4 Dimensional Fetal Echocardiograms for diagnosis complex CHD after 2 dimensional echo. Optimal 3-Dimensional Fetal Echocardiograms were obtainedbetween 22 and 27 weeks

of gestation. 3-D echocardiography enables more detailed evaluation of dynamic fetal cardiac function.

Doppler color flow mapping and pulsed Doppler interrogation were used to facilitate identification of great vessel relationship, location and severity of ventricular outflow obstruction. Initial fetal echocardiograms were obtained between12 and 39 weeks of gestation (median 24.5 weeks). Major cardiac malformations should be followed serially by fetal echocardiography as progressive alterations in flow may affect growth of cardiac structures over time: for example, very often, after prenatal diagnosis of hypoplastic left-heart syndrome (HLHS) couples have been offered termination of pregnancy.

But termination of pregnancy should not be proposed when it is only a small left ventricle (on echo), because many of those patients end up with only coarctation of the aorta. A second echo should be carried out in these cases.

Methods of the echocardiographic identification of fetal CHD are:

— postnatal echocardiography,
— angiography,
— surgery or autopsy.

RESULTS

A total of 2392 fetuses were obtained during an period between 2012–2014 years with a prenatal diagnosis of CHD were enrolled.

CHD usually are diagnosed during the first echo.

The number of echocardiographic studies was ranging from one to four examinations. Maternal age was from 17 to 41 years old.

— 29 % of fetal echocardiograms were obtained before 18 weeks of gestation.
— 48% of fetal echocardiograms were obtained between 18–28 weeks of gestation.
— 23% of fetal echocardiograms were obtained between 29–39 weeks of gestation.

The number of diagnostic mistakes is 81 (3,4%) from 2392 cases. The results of our patient's cohort are presented in tables 1, 2.

DISCUSSION

Fetal echocardiography has opportunity to study the most important parameters of fetal heart with major congenital defects for postnatal surgical repair.

Important parameters of fetal echocardiography in last weeks (32–34 weeks of gestation) are:

— left/right ventricular diastolic dimensions in M-mode, B-mode (right–to–left ventricular disproportion: cardiomegaly, dilatation of right ventricle, right atrium or left chambers of heart; hypoplastic right or left heart);
— atrioventricular and semilunar valves'sdimentions (valve's stenosis/atresia or dilatation);
— study of ejection fraction (fetal heart contractility including its ability to fill and to eject blood to the body and back to the placenta);
— inefficient of fetal circulatory (pericardial effusion, atrioventricular regurgitation, fetal non-immune hydrops, fetal arrhythmias;
— ultrasound diagnosis of anatomical details of specific CHD.

ULTRASOUND DETAILS FOR SPECIFIC CHD BY THE PLANNING OF THE DELIVERY AND THE POSTNATAL CARE

Most important Ultrasound details for major CHD are:

ForConotruncal anomalies (fig. 1, 2):

— fetal echocardiographic definition of the great artery relationship;
— left ventricular diastolic dimension;
— dimension of foramen ovale (restrictive foramen ovale-early closure of a flap valve in the fetal heart and restriction of flow across the foramen ovale);
— dimension of ductusarteriosus (duct closures);
— type ofcoronary arteries;
— the location of associated ventricular septal defect;
— the presence/absence of ventricular outflow tract obstruction with the other diagnostic modalities.

For Pulmonary atresia:

— the presence/absence ofventricular septal defect;
— intracardiac anatomy;
— presence and size of the branch pulmonary arteries;
— source of pulmonary blood supply;
— side of the aortic arch.

For Hypoplastic left/right heart (fig. 3):

— mitral/tricuspid vulvar anomaly (congenital Parachute mitral valve, stenosis/ atresia);
— aortic valve or aortic root disease;
— stenosis/atresiapulmonary artery,right ventricular outflow obstruction;
— dimension of foramen ovale and ductusarteriosus.

CONCLUSIONS

1. Echocardiography reveals major congenital heart diseases with a high of accuracy (the number of diagnostic mistakes is 3,4%).

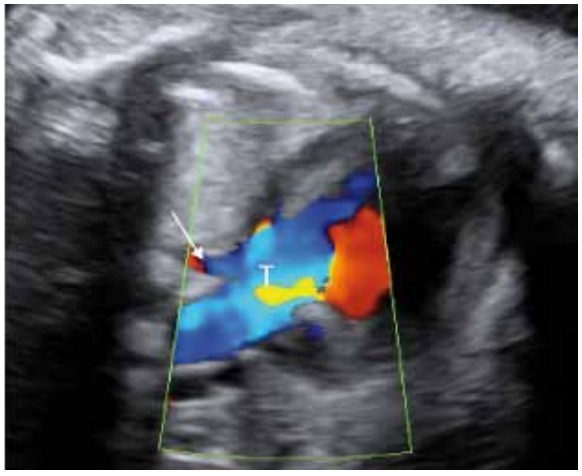

Fig. 1. *30 week of gestation Truncus Arteriosus (T) CDW. Source of Pulmonary atery (arrow)*

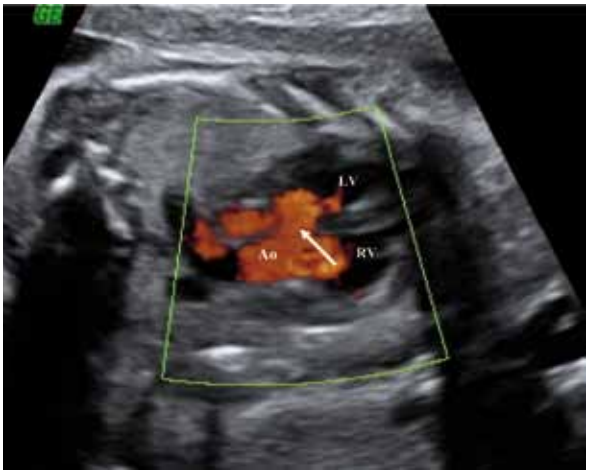

Fig. 2. *22 week of gestation. Tetralogy of Fallo. Power Doppler. Subaortic Ventricular septal defect (arrow)*

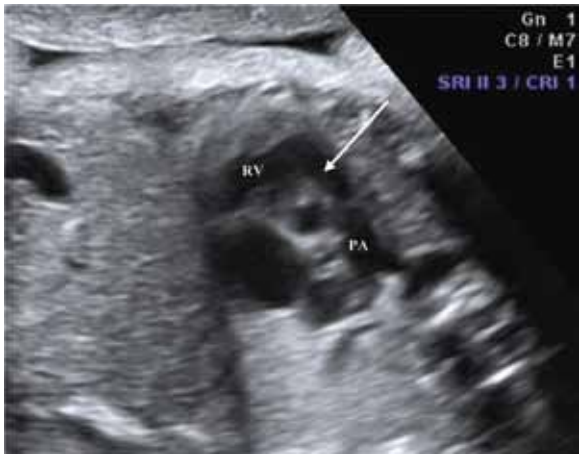

Fig. 3a. *22 week of gestation. TF. B-mode. Stenosis of pulmonary atery (arrow)*

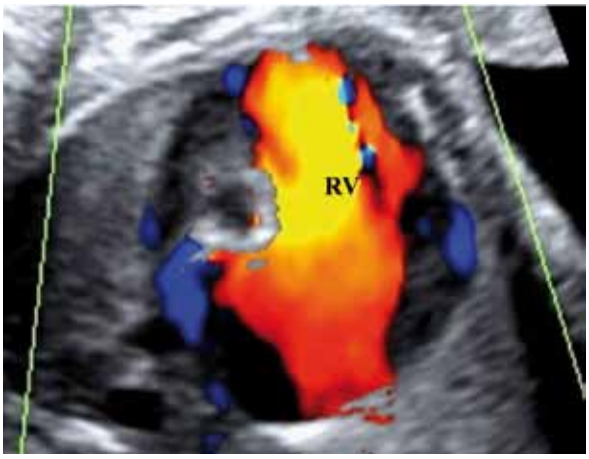

Fig. 4. *32 week of gestation. Color Doppler. Hypoplastic left heart*

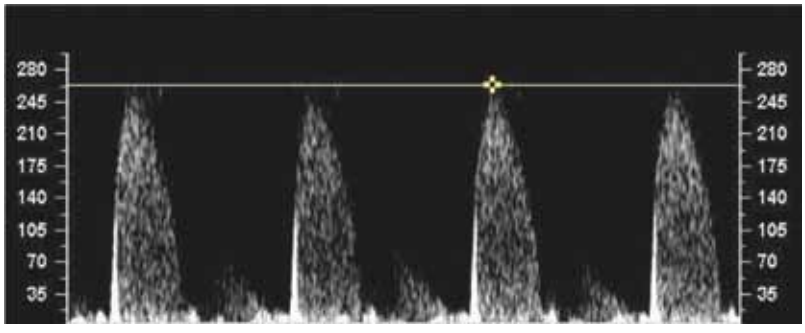

Fig. 3b. *22 week of gestation Pulse Doppler. Flow into PA*

2. Echocardiography will determine whether the fetus has the type of structural abnormality and detaliesspecifical CHD, that is very important for choice of *surgical repair* after birth.
3. Prenatal Echocardiography allows analyzed many factors influence the outcome of fetuses with CHD:research of morphological details for specific CHD, diagnosis of extracardiac malformations and chromosomal anomalies.

Table 1.

NAME OF CARDIAC ANOMALIES	N (abs)	(%)
Atrioventricular canal	163	6,8
Hypoplastic left heart	161	6,7
Tricuspid atresia	49	2,1
Conotruncal anamolies	409	17,1
Pulmonaty atresia+VSD/intact ventricular septum	43/17	1,8/0,7
Ventricular septum defects	914	38,2
Coarctation/interruption of the aorta	57	2,4
Anomalous pulmonary venous connection	12	0,5
Valvar anomalies	63	2,6
Single ventricle	65	2,7
Potential atrium septum defects	61	2,5
Cardiac tumors	25	1,1
Congenital coronary atery anomalies	5	0,2
Other complex heart defects	348	14,6
ALL	2392	100

Table 2.

OUTCOME	N (abs)	(%)
The termination of pregnancy	698	29,2
Intrauterine fetal death	4	0,2
Nejnetal death soon after birth	39	1,6
Fetal evalution (small VSD)	619	25,9
Surgical repair before 1 year	604	25,2
Surgical repair after 1 year	223	9,3
Are followed up by doctors, SR is planned in the future	205	8,6
ALL	2392	100

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EFFICIENCY EVALUATION FOR INTEGRATED APPROACH TO CHOICE OF ORTHODONTIC AND PROSTHETIC TREATMENTS IN PATIENTS WITH REDUCED GNATHIC REGION

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ABSTRACT — The results of morphometric, photostatic, teleradiographyc research together with an analysis of tomograms of temporo-mandibular joints as well as studies of the functional status in the dentofacial region stand proof that there is a reason for employing an integrated approach to treating patients with dentition defects in the lateral segments presenting cases of reduced gnathic region. The efficacy of orthodontic and prosthetic treatment can be seen from the outcomes obtained so far — normalization of the teeth position and dentition on the whole, restoration of the gnathic region's height, recovered chewing function and aesthetic features.

KEYWORDS — gnathic region, orthodontic treatment, prosthetic treatment, teleradiography, tomography, electromyography.

The recent years have witnessed a special emphasis placed on comprehensive treatment offered to adult patients suffering from reduced gnathic region; this is due to high prevalence and, therefore, a high need for specialized treatment [14]. Until recently, the orthodontic treatment for adults was not much common; however, according to W. Proffit (2012) nowadays adults account for around 15% out of the entire body of orthodontic patients, while there is also a growing respective trend among those over 40 [12].

In their scientific endeavor dentists are guided by individual variability in the dentofacial region. It stands a proven fact that one of the indicators for evaluating self-regulation in the dentofacial system is the morphometric parameters matching the size of the teeth to the dental arches. Therefore, prior to performing prosthodontic and orthodontic treatments on patients with dentition pathology it is advisable to employ biometric methods in order to determine and personalize the topographical features of anatomical structures in the dentofacial region [2,4,6,7].

A factor of paramount importance that has its impact on the position of the teeth in the row is the right match between the size of permanent teeth and the dental arches' parameters. Cases of discrepancy here may result in crowded teeth or interdental spacings. The issue of interdependence between the teeth size and the parameters of the dental arches, jaw bones, and the craniofacial complex as a whole has become of specific relevance lately due to the advances in orthodontic treatments for patients with dentition pathology [1,3,13].

The introduction of newer nonremovable orthodontic appliances has expanded significantly the treatment options when dealing with dentofacial anomalies. Such appliances can be effectively used to bring back to normal the shape and dimensions of

dentition, to correct the growth and development of the apical bases in the jaws and jaw bones, to reach a stable myodynamic equilibrium, as well as for reasons of aesthetical and functional improvement in the dentofacial system [9,10,11].

Nevertheless, despite all the improved methods of diagnostics and a significant increase in the number of treatment strategies one cannot but admit that there are still numerous issues related to orthodontic and prosthodontic treatment of adult patients that remain unresolved and rather questionable [5,8].

There is still a need for investigation into functional disorders in the dentofacial region under this pathology. Experts also stick to different opinions when it comes to the option of integrated treatment for this group of patients – some propose surgical and prosthodontic intervention; others, however, believe that in order to ensure a comprehensive chewing function as well as to meet the patient's aesthetic requirements prosthetic repair should be preceded with an orthodontic treatment. There is no common understanding as to the methods and terms of orthodontic treatment for cases of different forms of reduced gnathic region, the construction of temporary and permanent prosthetic devices, as well as the manufacturing materials to be used. There are no clear recommendations for the comprehensive treatment of patients with various forms of reduced gnathic regions. In case these issues are resolved it could improve integrated (orthodontic and prosthodontic) treatment for this pathology.

Purpose – producing a rationale for an integrated approach to treating patients with dentition defects in the lateral segments and with reduced gnathic region.

Integrated orthodontic and prosthodontic (prosthetic) treatment was performed in 111 patients (46 men and 67 women) who developed dentoalveolar gnathic reduction due to the loss of their posterior teeth. The pathology in question was associated with abnormal occlusion in the sagittal, transversal and vertical directions and increased teeth abrasion, which was proven by the anamnesis data and the results of clinical and laboratory research.

The main objective of the comprehensive treatment here was to improve the position of the jaws, which was evaluated based on the results from photostatic, teleradiographyc examinations as well as an analysis of tomograms in the temporo-mandibular joints, and following the functional status of the dentofacial region.

The outcomes of the morphometric study revealed improved morphological parameters of the face upon completion of the comprehensive treatment (Table 1).

The outcomes showed that the parameters like zy-zy, gl-n, gn-me, and the height of the nasomaxillary complex (n-inc) virtually underwent no change. As a rule, changes in the gnathic region occurred between the points of inc-spm and inc-me, which increased the height of the gnathic part of the face also improving the morphometric face height.

The improved facial profile was noted not only through a visual-rank evaluation but also in a photostatic study. A lateral teleradiography showed no change in the position of the maxilla during the comprehensive treatment while it also was within the respective age norm; however, at the same time the mandibula moved in sagittal direction, which led to a change and, that is to say, normalization in the ANB angle. The gonial angle remained within the range of 119–123 degrees (just like prior to the treatment); the gnathic angle, however, (between the mandibular flat and the spinal flat) went up to 23–27 degrees thus increasing the height of the lower part of the face and normalizing the aesthetic profile (Fig. 1).

The study outcomes demonstrated that such comprehensive treatment resulted in changed key teleradiographyc parameters. Table 2 offers a view on the teleradiographyc data.

The outcomes show a significantly reduced ANB angle, and after the comprehensive treatment was completed its indicators went normal. The treatment resulted in normalization of the interincisal angle, which measured within 134–138 degrees.

The mandibular angle virtually suffered no change; yet at mandibular protrusion and restored occlusal relationships the gonial angle (between the mandibular flat and the spinal flat) was within the age norm (24–30 degrees).

Using an X-ray examination of the temporomandibular joints in most cases we identified, prior to the treatment, disturbed topographic relations of the joint's elements. The joint heads of the mandibula were displaced distally up; there was a widening of the joint space in the anterior part, and its narrowing in the posterosuperior part. One of the major stages of the orthodontic treatment for these patients was gradual dosed mesial movement of the lower jaw aiming at normalizing position (Fig. 2).

The main criterion for measuring the sagittal mandibular shift in each case was the position of the mandibular head in the glenoid cavity; we were seeking its position at the base of the articular tubercle, which we pursued through tomograms of the temporo-mandibular joints. In the cases where after a mesial shift the mandibular head was situated at the top of the articular tubercle or was found on the lower half of the rear slope of the tubercle we performed some correction of the orthodontic appliances in order to reduce the amplitude of the sagittal mandibular shift to permissible limits (Fig. 3).

Table 1. *Face measurements in patients*

Morphometric parameters	Facial dimensions (mm) in humans	
	Before treatment	After treatment
n-me (face height)	108.5 ± 3.13	112.96 ± 2.26
gl-me	118.88 ± 3.29	123.34 ± 2.34
n-inc (height of the nasomaxillary complex)	73.57 ± 2.52	74.45 ± 2.24
sn-inc (height of the dentoalveolar part of the maxilla)	18.39 ± 2.17	19.27 ± 1.62
n-sn	55.18 ± 3.39	55.18 ± 3.39
sn-gn	47.30 ± 2.06	51.76 ± 1.59
inc-me (height of the mandibula)	34.93 ± 2.32	38.51 ± 1.87
sn-spm (intergnathic height)	31.35 ± 3.45	37.41 ± 2.14
gn-me	6.02 ± 1.19	6.02 ± 1.19
Inc-spm (height of the dentoalveolar part of the mandibula)	12.96 ± 1.89	18.14 ± 1.27
gl-n	10.38 ± 2.62	10.38 ± 2.62
zy-zy	135.57 ± 6.79	135.57 ± 6.79

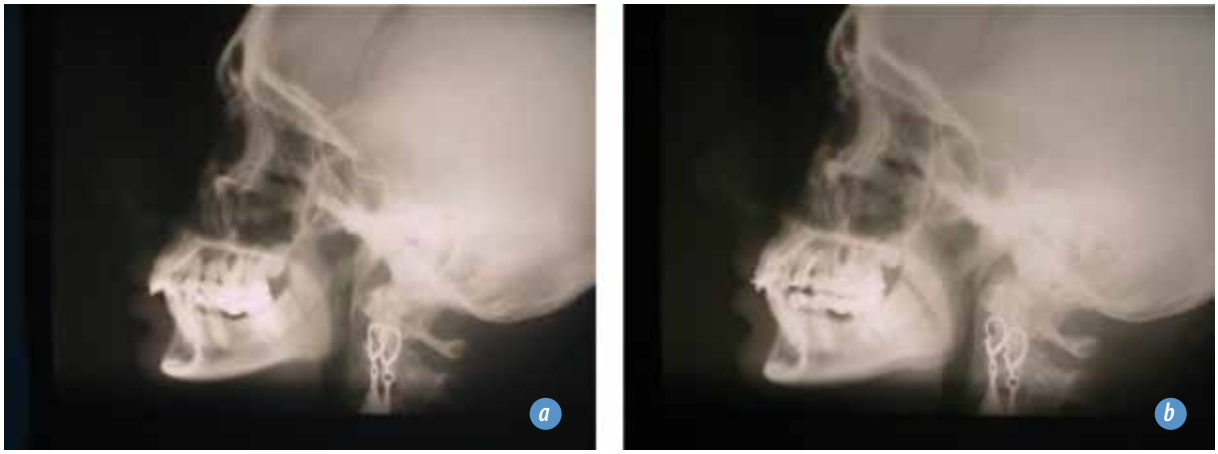

Fig. 1. *Lateral teleradiography, patient S., 44 yrs old, prior (a) and into the treatment (b)*

Table 3 contains the major tomography results.

Once the treatment was complete and there was an increase in the height of the gnathic part of the face (by 4.43 mm) there was also a forward shift of the mandibular head (D1) by 0.5 mm and a reduction in the distance of D2 by 0.2 mm, D3 by 0.1 mm, and widening of the joint space in the posterior part (D4) by 0.5 mm.

The efficacy of orthodontic treatment in the group under investigation was also identified based on the improved position of the teeth roots, which had a significant impact on the occlusal relationship between the dental arches of the upper and lower jaws. The number of occlusal contacts after the comprehensive treatment almost doubled.

Such comprehensive treatment led to improved shape and sizes of the dental arches as well as restored occlusal relationship (Fig. 4).

While studying the indicators of the patients' chewing efficiency we could conclude that the true indicators of the significant improvement in the chewing efficiency and reduced chewing time were due to the period of complete adjustment (4–6 months after only) to the temporary prostheses through the stages of orthodontic treatment, and were related to the normalization of the mandibular position. Until

Table 2. *Major teleradiographyc parameters in patients*

Major teleradiographyc parameters	Outcomes	
	Before treatment	After treatment
Facial angle ANSe	85.6 ± 1.1	85.1 ± 1.8
ANB	6.7 ± 0.9	1.9 ± 0.7
Gnathic angle	21.6 ± 2.4	26.8 ± 3.1
Gonial angle	120.6 ± 1.3	120.8 ± 1.5
Interincisal angle	152.6 ± 4.8	136.4 ± 3.2
Facial convexity angle (n-ss-spm), deg.	171.7 ± 4.35	168.9 ± 4.24
Height at skeletal points (sna' – me'), mm	66.76 ± 5.58	70.96 ± 4.68
Height at skin points (sn'-Kme'), mm	71.5 ± 6.8	75.4 ± 6.45
Position of mandibular angle, vertically (go-x), mm	67.7 ± 7.8	68.5 ± 7.3
Position of mandibular angle, sagittally (go-y), mm	1.76 ± 0.15	2.70 ± 0.33
Position of mandibular head, vertically (co-x), mm	9.7 ± 2.1	10.1 ± 2.1
Position of mandibular head, sagittally (co-y), mm	16.1 ± 3.4	16.2 ± 3.7

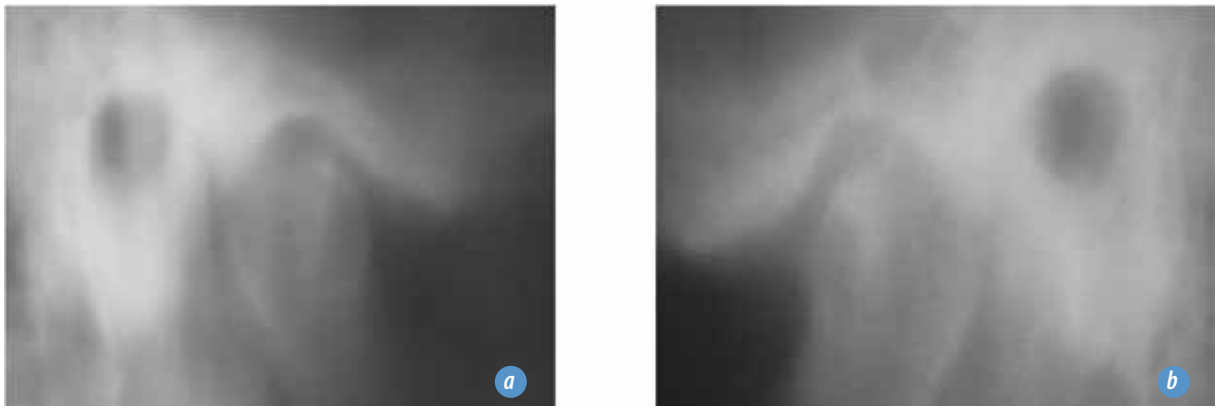

Fig. 2. *Position of elements in temporo-mandibular joints; patient S., age – 44; right (a) and left (b) before treatment*

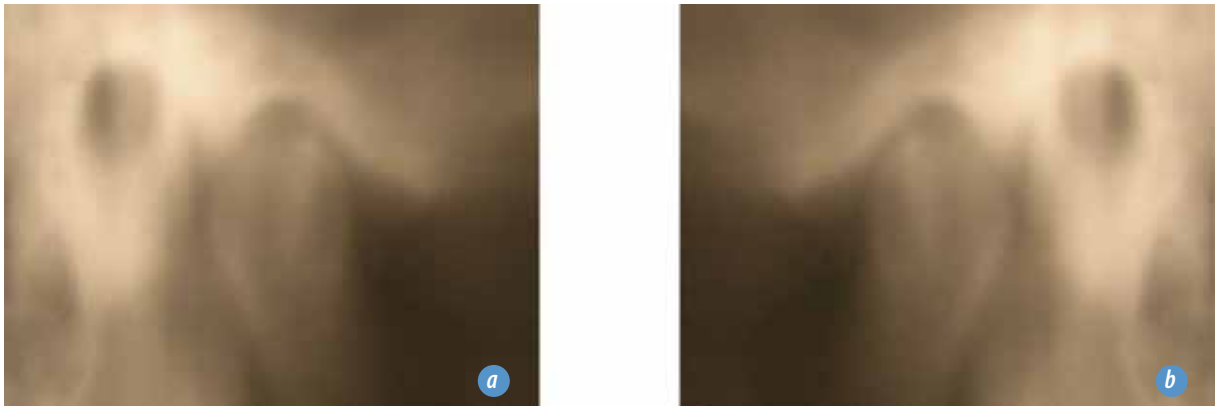

Fig. 3. *Position of elements in temporo-mandibular joints; patient S., age –44; right (a) and left (b) after treatment*

Table 3. *Major tomogram data for temporo-mandibular joints*

Major tomogram data for temporo-mandibular joint (TMJ)	Outcomes	
	Before treatment	After treatment
Pm/Pr, deg.	123.9 ± 4.98	123.9 ± 4.98
A-B, mm	18.25 ± 1.5	18.25 ± 1.5
D1, mm	2.65 ± 0.7	2.15 ± 0.6
D2, mm	3.3 ± 0.7	3.1 ± 0.8
D3, mm	3.65 ± 0.9	3.55 ± 0.6
D4, mm	2.4 ± 0.7	2.9 ± 0.9
D, mm	9.9 ± 1.0	9.85 ± 1.0
a, deg.	47.9 ± 4.2	47.9 ± 4.2

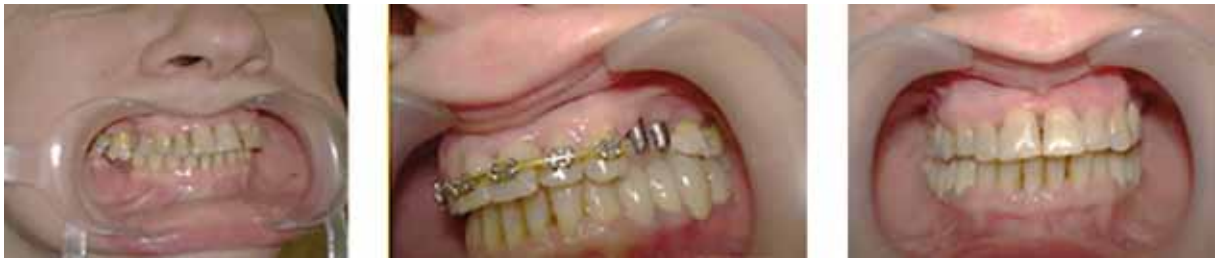

Fig. 4. *Patient, before (a), into (b) and after (c) treatment*

that point the indicators were rather controversial and unreliable, which could be accounted for by the specificity of adult patients' dentofacial region adjustment to the new position of the mandible.

Table 4 offers a view on the results of studying the temporal muscles tone (g) in the patients of Group 1, Subgroup1.

The results suggest that the temporal muscles resting tone at the normalized height of the gnathic part of the face and the adjustment to the prosthetic appliances was significantly decreased both in males and females. The tension tone was significantly increased in both sexes. The temporal muscles tone indicators approached the thresholds obtained from people with physiological occlusion, which served proof of the comprehensive treatment efficiency.

To see the results of studying the masseter muscles tone (g), please refer to Table 5 below.

The study showed that after the comprehensive treatment and normalized height of the gnathic part of the face the masseter muscles tone approached the threshold indicators for the normal tone, which demonstrated the efficiency of the treatment. The tone of the masseter muscles in males was significantly higher than that of females.

The spontaneous activity in the resting phase in masseter muscles was identified in 38.4% ± 5.7% of the patients prior to the treatment and in 30.8% ± 7.4% of them after the treatment.

The functional activity of the masseter muscles when chewing and highest possible compression of the jaws was 49.2 ± 2.8% below the norm before the treatment while after the treatment this share was 63.4 ± 2.8%.

The functional activity of the temporal muscles when chewing and highest possible compression of the jaws was 65.2% ± 34.8% lower than the normal index before the treatment; after the treatment, however, this index was 71.8% ± 3.3%.

The quantitative factors could be described with an increase in the average time of one dynamic cycle (DC) of up to 0.85–0.90 sec. The temporal parameters of electromyograms (EMG) can be seen in Table 6.

The outcomes obtained from this study show that the bioelectric activity of the jaw muscles significantly increased in both sexes. The bioelectric activity phase (BEA) in the temporal muscle before the treatment in the males was 0.28 ± 0.04 sec., and after the treatment it was 0.35 ± 0.02 sec. The time of bioelectric rest (BER) in the temporal muscles in the males went up (0.25 ± 0.05 sec. to 0.41 ± 0.03 sec.), due to which the ratio of excitation and inhibition (K coefficient) went down from 1.12 ± 0.08 to 0.85 ± 0.05. There was a significant decrease in the number of the dynamic cycles

Table 4. *Temporal muscles tone*

	Temporal muscle tone indicator			
	Before treatment		After treatment	
	Males	Females	Males	Females
Resting tone (Rt)	65.9 ± 3.3	53.2 ± 2.6	54.3 ± 2.9	45.1 ± 2.2
Tension tone (Tt)	158.1 ± 4.2	133.9 ± 5.3	169.3 ± 3.8	152.2 ± 3.2

Table 5. *Tone of the masseter muscles*

Tone status	Masseter muscles tone indicators			
	Before treatment		After treatment	
	Males	Females	Males	Females
Resting tone (Rt)	63.6 ± 3.7	55.1 ± 2.9	53.9 ± 3.1	44.9 ± 2.5
Tension tone (Tt)	160.7 ± 4.8	140.5 ± 5.6	172.9 ± 4.1	157.5 ± 4.6

Table 6. *Temporal parameters of electromyograms (patients, 6 m after treatment)*

EMG parameters	Temporal indices for muscle EMG			
	Temporal muscle		Masseter muscle	
	Males	Females	Males	Females
BEA	0.35 ± 0.02	0.37 ± 0.07	0.38 ± 0.03	0.41 ± 0.03
BER	0.41 ± 0.03	0.42 ± 0.05	0.40 ± 0.02	0.39 ± 0.02
K	0.85 ± 0.05	0.88 ± 0.09	0.95 ± 0.09	1.05 ± 0.08
DC	0.79 ± 0.19	0.81 ± 0.06	0.75 ± 0.03	0.84 ± 0.03
DC No	18.1 ± 2.6	19.6 ± 1.12	18.2 ± 1.5	18.9 ± 1.5
FPM	14.1 ± 1.1	15.8 ± 1.1	13.9 ± 1.6	15.4 ± 1.6

(22.8 ± 1.11 to 18.1 ± 2.6) as well as in the time of the full period of mastication (FPM) – from 17.6 ± 1.9 to 14.1 ± 1.1 sec. A similar situation was observed in the females where the ratio of excitation and inhibition (K coefficient) went down from 1.33 ± 0.09 to 0.88 ± 0.09. A significant decrease was to be seen in the number of the dynamic cycles (23.4 ± 1.13 to 19.6 ± 1.12) and in the time of the full period of mastication (FPM) – from 18.7 ± 1.3 to 15.8 ± 1.1 sec.

There was also a change in the parameters of electromyograms in the masseter muscles (both the females and the males). The bioelectric activity phase (BEA) of the masseter muscle in the males was 0.33 ± 0.02 sec. prior to the treatment, while afterwards it was 0.38 ± 0.03 sec. The time of bioelectric rest (BER) in the masseter muscles in the males went up from 0.26 ± 0.03 sec. to 0.40 ± 0.02 sec., due to which the ratio of excitation and inhibition (K coefficient) reduced (1.27 ± 0.05 to 0.95 ± 0.09). There was a significant drop in the number of the dynamic cycles (21.7 ± 2.8 to 18.2 ± 1.5) as well as in the time of the full period of mastication (FPM) – from 16.9 ± 1.3 to 13.9 ± 1.6 sec. This was also the case with the female population where the ratio of excitation and inhibition (K coefficient) went down from 1.24 ± 0.09 to 0.84 ± 0.03. The number of the dynamic cycles reduced significantly as well as the time of the full period of mastication (FPM) — from 17.5 ± 1.7 to 15.4 ± 1.6 sec.

CONCLUSION

Comprehensive orthodontic and prosthetic treatment for patients with dentition defects in the lateral segments with a reduced gnathic region yields favorable results — normalization of the teeth position

and dentition on the whole, restoration of the gnathic region's height, recovered chewing function and aesthetic characteristics.

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MINERALIEN IM DIENSTE DER GESUNDHEIT
ÜBERSICHT ÜBER DIE NANOVIT-FAMILIE

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ABSTRACT

Hintergrund. Mit dem Stichwort Mineralien in der Nahrung verbinden Ärzte und zahlreiche gesundheitsbewusste Zeitgenossen in erster Linie Spurenelemente und Salze. Zu Recht, denn etliche Metalle, aber auch andere Elemente des Periodensystems bilden lösliche Ionen und Elektrolyte, ohne die die normale Lebenstätigkeit der Zellen, Gewebe, Organe und des Gesamtorganismus einfach nicht funktionieren könnte.
Neuheit. In den zurückliegenden Jahren hat aber eine weitere Klasse von Mineralien enorme Aufmerksamkeit auf sich gezogen: Naturstoffe, die auf den ersten Blick unlöslich und inert erscheinen. Es sind Feststoffe aus Kieselsäure und anderen Verbindungen, gekennzeichnet von schichten- und käfigförmigem Feinaufbau. In aufgemahlener Form nehmen die Oberflächen dieser Körnchen erstaunlich aktiven Anteil an den Stoffwechselprozessen in unserem Körper. Sie katalysieren bestimmte biochemische Reaktionen, balancieren Redoxgleichgewichte aus, instruieren das Immunsystem, normalisieren den Takt der Zellteilungen in entzündeten Arealen der Haut, um nur einige der positiven Wirkungen zu nennen.
Anwendung. Bei der Produktserie Nanovit® handelt es sich um diätetische Lebensmittel für besondere medizinische Zwecke. In ausgewählten Formulierungen haben sie sich im Ergebnis multizentrischer klinischer Studien und zahlreicher Fallbeobachtungen bei der adjuvanten Behandlung einer Reihe von Erkrankungen bewährt. In dieser Übersicht werden die Behandlungserfolge bei Metabolischem Syndrom, speziell Diabetes mellitus Typ 2, Immundepression und Infektionsanfälligkeit infolge viraler Infektionen, Psoriasis und Neurodermitis, sowie bei speziellen Alterserscheinungen referiert .

VORSTELLUNG DER UNTERSUCHTEN PRODUKTE

A) ***Nanovit® Metabolic*** wird zur Prävention und zur adjuvanten Behandlung des metabolischen Syndroms, insbesondere des Diabetes mellitus Typ 2 eingesetzt. Dabei kommt es zu einer Optimierung des gestörten Zucker- und Fettstoffwechsels. Des Weiteren ist eine Verbesserung des antioxidativen Status zu beobachten. Besonders sind diese Effekte in Verbindung mit der Individuellen Systemischen BioKorrektur nachweisbar (1, 4). Nanovit® Metabolic sorgt für die Umwandlung eines Teils der Nahrungs-Glukose in Fruchtzucker. Dadurch wird der Insulin-abhängige Stoffwechselweg der Energiegewinnung bei Personen mit Insulinresistenz weniger belastet. Typ II – Diabetiker profitieren davon (2).

B) ***Nanovit® Immuno*** wird zur diätetischen Begleitbehandlung von Immunschwächen und erhöhter Infektanfälligkeit bei Immundepression, HIV-Infektion und AIDS eingesetzt. Die enthaltenen Immunoglobuline mit breiten Wirkungsspektrum und die abwehrstärkenden Faktoren aus bovinem Colostrum ergänzen die körpereigenen Schutzmechanismen. Das Mineral bewirkt die Fragmentierung viraler Antigene und ihre Präsentation zur Fremd/Eigen Unterscheidung. Die Viruslast wird gesenkt. Immunschwächebedingte Ulcera verheilen und repigmentieren.

C) ***Nanovit® Derma*** in Kapselform und ***Nanovit® Derma Creme*** werden zur Begleitbehandlung der Schuppenflechte und der Neurodermitis eingesetzt. Die Hauteffloreszenzen verschwinden bei systemischer und topischer Behandlung und der Juckreiz auch. Das Proliferationsverhalten der Keratinozyten in den betroffenen Hautarealen gleicht sich wieder dem in gesunder Haut an.

D) ***Nanovit® vital*** wird als ***ergänzende bilanzierte Diät*** zur Verzögerung von Alterungsprozessen eingesetzt. Im alternden Organismus kommt es zu asynchron verlaufenden Rückbildungen und Funktionseinschränkungen. Die Anwendung

von Nanovit® vital kann diese Prozesse verzögern und korrigiert die Altersdefizite beim Zellschutz. Macht sich darüber hinaus Muskelabbau (Sarkopenie) bemerkbar, bspw. infolge erzwungener Liegezeiten im Bett, dann kann ***Nanovit® vital*** mit Aminotroph (siehe E) kombiniert werden, um weiterem körperlichem Verfall entgegenzuwirken.

E) ***Aminotroph*** (in der Russischen Föderation als ***Nanovit® amino*** vertrieben) wird als ergänzende bilanzierte Diät zur diätetischen Behandlung von Muskelabbau (Sarkopenie) im Alter eingesetzt. Es enthält die für die Proteinsynthese und den Muskelaufbau ganz besonders wichtigen essenziellen Aminosäuren in einer optimierten Kombination und spezielle Vitamine. Es hat sich erwiesen, dass die Gabe der essenziellen Aminosäuren auch die Bereitstellung der anderen Aminosäuren in den Zellen verbessert und die Biosynthese der körpereigenen Eiweiße stimuliert – eine Voraussetzung für die Stärkung der Muskelfunktionen. Die Muskeln werden auch dadurch leistungsfähiger, weil Aminotroph die Zahl der Mitochondrien in den Zellen erhöht und mehr ATP produziert wird.

PRAXISERFAHRUNGEN UND STUDIENERGEBNISSE IM EINZELNEN

Zu A) Mehrere klinische Studien haben ergeben, dass mit Nanovit® Metabolic — als alleinige adjuvante Maßnahme oder in Kombination mit anderen - verschiedene positive Effekte erreicht werden können (1).

- Die Insulinproduktion wird stabilisiert (Schwerin).
- Der oxidative Stress wird reduziert (Crivitz, Heidelberg, Ravensburg). Die Insulin-Resistenz wird dadurch gemildert.
- Der Körper lernt, bei moderater Bewegungstherapie Fettreserven für die Energiegewinnung zu utilisieren. (Berlin, Leipzig, Bernau, Pockau).
- Ein Teil der Nahrungs-Glukose wird in Fruktose umgewandelt. Das entlastet den Stoffwechsel des Diabetikers, weil Fruktose insulinunabhängig veratmet wird (s.u.).
- Die Mikrozirkulation in den Geweben und mit ihr die Nähr- und Sauerstoffversorgung verbessern sich. Sekundärkomplikationen (Neuroangiopathien) wird entgegengewirkt (Bernau, Berlin).

Zu B) In einer Fallkontrollstudie von 40 Patienten mit gesicherter HIV-Infektion bzw. voll entwickelter Immundefizienz — AIDS- in Uganda wurde die Wirkung von ***Nanovit® Immuno*** auf das Krankheitsgeschehen untersucht. (3)

Dabei wurden neben den typischen klinischen Parametern (Anamnese, Begleiterkrankungen, aktueller klinischer Untersuchungsbefund, subjektives Wohlbefinden) die relevanten Laborparameter bestimmt (Viruslast per qPCR, CD4) Von den 40 untersuchten HIV/AIDS-Patienten zeigten eingangs 37 Patienten eine positive Viruslast (> 50 Kopien/ml) in Blut auf, lediglich 3 Patienten wiesen eine negative Viruslast auf (< 50 Kopien/ml). Bereits nach 6 Wochen Therapie sank die Viruslast bei 22 Patienten unter die damals definierte Nachweisgrenze von 50 Kopien/ml und bei 14 Patienten trat ein signifikanter CD4-Anstieg ein.

Die Behandlung erfolgte mit täglicher Gabe von 500 mg in Nanovit® Immuno-Kapseln in einer Dosierung von 2 Kapseln pro Tag über einen Zeitraum von 90 Tagen.

Das subjektive Befinden war bei allen 40 Patienten verbessert und in einzelnen Fällen gab es spektakuläre Wundheilungen bei sekundären Ulcerationen.

Die Virologen Dr. W. Thierfelder und Dr. H. Schäfer vom Robert-Koch-Institut Berlin und Kollegen des Friedrich-Loeffler-Instituts Insel Riems, sowie die Chefärztin der Hautklinik des Helios-Klinikums Berlin-Buch, Frau Dr. K. Lommel , empfehlen Nanovit® Immuno als adjuvante Behandlungsmöglichkeit bei Immundefiziten viraler (HIV, HPV) und nichtviraler Ätiologie. Bei Immundepression infolge einer Tumorerkrankung und bei rezidivierenden chronischen Infekten ist eine adjuvante Behandlung mit Nanovit® Immuno angezeigt.

Zu C) In einer klinischen Studie wurden insgesamt 30 Patienten im Alter von 25 bis 77 Jahren mit gesicherter Psoriasis vulgaris evaluiert und einer 12-wöchigen Behandlung mit 3 x 2 Kapseln Nanovit® Derma unterzogen.

Vor und am Ende der Therapie erfolgte die visuelle Beurteilung der betroffenen Hautareale. Es wurde eine Fotodokumentation durchgeführt und laborchemisch wurden das CrP, das Differentialblutbild und die Lymphozytendifferenzierung (CD3, CD4, CD8, CD16, CD19, CD56) erfasst (5).

Bei 29 von 30 Patienten ließ sich klinisch eine deutliche Verbesserung der Hautbefunde nachweisen. Sowohl die visuelle subjektive Einschätzung durch Arzt und Patient, als auch die Fotodokumentation bestätigte diese Aussage. Eindrucksvoll waren die positiven Veränderungen der befallenen Hautareale nach dreimonatiger Behandlung.

In der beschriebenen klinischen Studie von 2006 hatten sich keine signifikanten Änderungen der Lymphozytenmarker im Blut ergeben. In Zellkulturmodel-

len psoriatisch gestresster Zellen hat sich das bestätigt (6): Nanovit® Derma nimmt nicht auf das entzündliche Ausgangsgeschehen bei Psoriasis Einfluss, sondern auf die infolge der Entzündung eintretende reaktive Hyperproliferation der gestressten Keratinozyten. THP-1 Zellen (ATCC® TIB-202TM) hingegen zeigten unter Einwirkung der Bestandteile von Nanovit® Derma keine Veränderungen des Wachstums und der Zellmorphologie. Die THP-1 Zellen waren zu diesem Zweck mit Phorbol-12-Myristat-13-Azetat (PMA) induziert worden, damit sie adhärent wachsen und monozytisch differenzieren [H. Schwende, J Leuk Biol 1996; M. Daigneault, PlosOne 2010] e THP-1 Zellen (ATCC® TIB-202TM). Weder lösliche, noch korpuskuläre Bestandteile des Nanovit® Derma beeinflussten diese lymphytischen Kontrollzellen.

Weltweit existieren zahlreiche Positiverfahrungen mit der Anwendung vulkanischer Mineralien im Haut- und Wundbereich. Die Synergien zwischen vulkanischen Mineral und Phytosterolen (hier: Brennnesselextrakt normiert auf ß-Sitosterolgehalt) hinsichtlich Wirkung und Wirkmechanismus auf Hauteffloreszenzen sind im obigen Zusammenhang erstmalig untersucht worden (Dr. S. Heymann, ICP HealthCare GmbH Berlin, Dr. med. H. Gulbin, niedergelassene Hautärztin, Dr. rer. nat. Chr. Regenbrecht, CPO GmbH und Charité Berlin).

Zu D und E) Nanovit® Vita und Nanovit® Vital unterscheiden sich aus rein rechtlichen Gründen in der Beimischung der jeweiligen nootropen Substanz (Rosmarin bzw. Ginkgo). Verabreicht man Nanovit® Vita/Vital zusammen mit Nanovit® Amino (in der Europäischen Union vertrieben als AMINOTROPH®), sind die deutlichsten vitalisierenden Effekte, kognitiven und physischen Verbesserungen zu beobachten. Insbesondere ist in zahlreichen klinischen Studien in Italien nachgewiesen worden(7–12):

Abb. 1. *Zeolithe wirken als Katalysatoren im Zucker-Stoffwechsel. Ursprünglich war der Ablauf dieser Reaktion unter unphysiologischen Bedingungen entdeckt und beschrieben worden (2)*

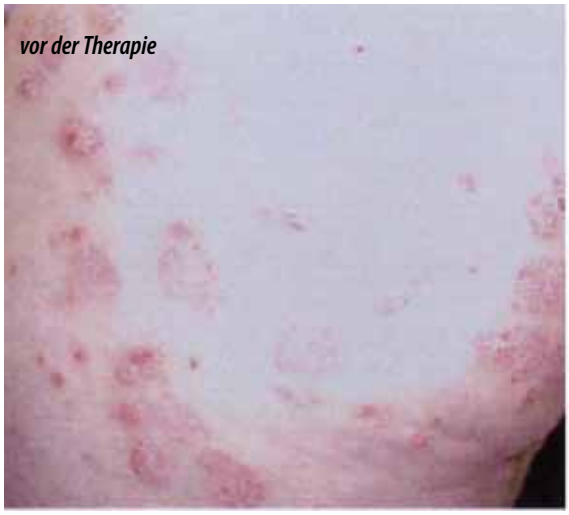
Reprinted with kind permission from S. Saravanamurugan, M. Paniagua, J. A. Melero and A. Riisager, Efficient Isomerization of Glucose to Fructose over Zeolites in Consecutive Reactions in Alcohol and Aqueous Media, J. Am. Chem. Soc., 2013, 135 (14), pp 5246–49 © (2013) American Chemical Society

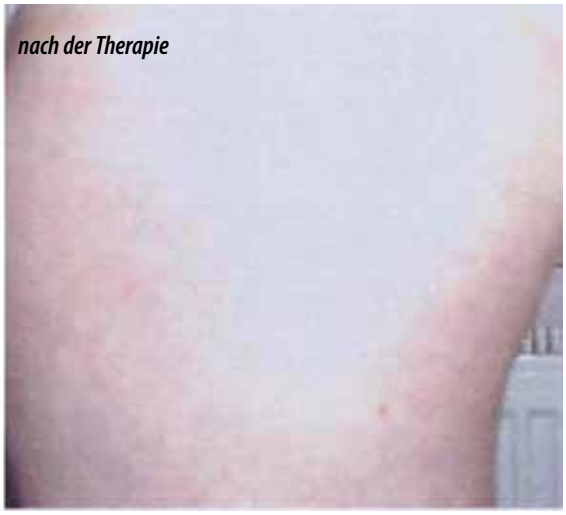
Tabelle 1. *Viruslast von 40 untersuchten Patienten und CD4-Verhalten vor und nach sechswöchiger Therapie*

	Anzahl der Patienten vor der Behandlung	Anzahl der Patienten nach der Behandlung
Positive Viruslast (> 50 Kopien/ml)	37	18
Negative Viruslast (<50 Kopien/ml)	3	22
Signifikanter CD4 Anstieg	Ø	14

— Vermeidung von Sarkopenie bei Immobilisation.
— Verbesserung der Muskelkraft.
— Verbesserung der Herzfunktion bei chronischer Herzinsuffizienz und Diabetes Typ 2.
— Verminderung des oxidativen Zellstress‘ bei älteren Personen.
— Verbesserung der körperlichen Leistungsfähigkeit bei COPD-Patienten.

Abb. 2. *Abheilung sekundärer Geschwüre bei AIDS Patienten (6 Wochen Einnahme von Nanovit® Immuno) Links: voll repigmentierter Zustand nach drei Monaten; unten: In Granulation befindlicher Wundrand*


vor der Therapie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GENE POLYMORPHISM OF GLUTATIONETRANSFERAZ SYSTEM AND EXPRESSIVENESS INTOXICATION SYNDROME IN PATIENTS WITH PULMONARY TUBERCULOSIS

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The work performed as a part of the grant of the President of Russian Federation with the state-term support of young Russian scientists doctors to perform research is-following "Development of algorithms personalized treatment and prevention of complications respiratory tuberculosis in the Astrakhan region." — MD-6325.2015.7.

ABSTRACT — The problem of tuberculosis spread is still topical throughout the world. There is no control epidemiological situation, so it is explained a number of problems, including forming serious adverse effects with long-term treatment with anti-TB medicines, the reduction of compliance and, as a consequence, refusal to the treatment with frequent formation of pharmacoresistant forms of tuberculosis. It is very important to improve efficiency and safety of a particular treatment in this situation. One of the tools of personality medicine is a pharmacogenetic study of the biotransformation is involved in the metabolism of anti-TB medicines. From these opinion, the definition of polymorphic gene genotypes of glutathione, can solve the problem of the formation of undesirable side effects and develop algo-rhythms are effective and safe treatment.

KEYWORDS — tuberculosis, unwanted side effects, pharmacogenetics, gene polymorphism of glutathione, personalized medicine.

INTRODUCTION

According to WHO, 9.4 million people in the world fall ill with TB and 1.3 million died each year [7, 11]. In 2014, TB killed more than 1.5 million people. In 2015, the world was found 9.6 million new TB cases, which exceeds the long-exponent of the previous year (http://www.postsovet.ru/blog/asia/622025.html). One of the strategically important issues related to the treatment of tuberculosis patients, is pro-continue to increase in the prevalence of medicine-resistant strains mikobakteries tuberculosis, reaching in Russia 30% of patients with newly diagnosed pulmonary tuberculosis and 60% in patients with relapses [5, 7, 8, 10, 12]. Formation of the resistance of the strains require the Office to strengthen modes of treatment for TB, which inevitably increases the number of unwanted side reactions anti-TB medicines [12, 13, 14]. The degree of clinical severity of the unwanted side reactions often requires discontinuation that contributes to the spread of disease, to attract additional economic cost and causes health medical and social and economic losses [4, 6, 9, 11, 13]. The most common adverse reactions of anti-TB medicines are hepatotoxic, the frequency of reaches 47% [11, 13].

In assessing the role of trigger factors in the emergence of the unwanted side reactions the value given to the study of metabolism of medicine [1, 2, 3, 4, 8, 14].

The enzymes of glutathione-S-transferase (GST), performing antioxidant and detoxifying role, provide cell resistance to lipid peroxidation, reactive metabolites of medicine involved in the formation of resistance to le medicament and preventing damage DNA [7, 13]. Multiplicity phi physiologically different system functions GST interindividual variability due to the presence of mutant alleles, reduce or block the expression of genes in many studies also associated with increased risk of disease [3, 7, 14].

In the liver of expressed isoenzymes GST potentially important are the GSTM1 and GSTT1, which describes a "null polymorphism" show full of-presence of proteins [2, 7], which is directly correlated with the severity of intoxication-foot syndrome and the incidence of the unwanted side reactions in the appointment anti-TB medicines. In this connection, it is relevant, of the present study and its practical feasibility of doubts does not cause-evaporated.

THE PURPOSE OF STUDY

to study gene polymorphism of glutathione in correlation with the severity of intoxication syndrome in patients with pulmonary tuberculosis of Astrakhan region (AR).

MATERIALS AND METHODS

The study involved 76 patients suffering from pulmonary tuberculosis treated in stationary-in GBUZ AO "Regional Clinical TB Dispensary" in Astrakhan in 2014. At the age of 18 to 65 years. Men — 56 (73.7%), women — 20 (26.3%). Patients unemployed working age were 54 (71.05%). City residents —

44.7%, rural — 55.3%. Contact with patients with tuberculosis was established in 20 (26.3%) patients. It is revealed by uptake of patients — 49 (64.47%), fluorography during medical examinations — 27 (35.53%). Annual fluorography were 10 (13.16%), were not surveyed for 2–3 years, a greater number of patients 38 (50%) and 28 (36.84%) — were not surveyed Fluorographic more than 3 years. In our study, newly diagnosed patients was — 56 (31.8%) and 20 (26.32%) were observed with a relapse of a specific process in the lungs. Distribution of patients according to clinical forms of tuberculosis were as follows: disseminated — tuberculosis, 27 (35.5%), infiltrative — 32 (42.1%), cavernous — 2 (2.6%), fibrocavernous — 15 (19.8%). Most common clinical forms were determined, with the collapse of lung tissue (r = 0,6). Determination of polymorphisms of genes GSTM1, GSTT1 was performed by polymerase chain reaction, pre-isolate DNA from the blood samples in the laboratory of D.O. Ott Research Institute of Obstetrics and Gynecology, Northwest Branch of RAMN, St. Petersburg.

All patients were divided into 5 groups: 1 — patients who develop enzyme GSTM1 performed (n = 27), 2 — patients with "zero" genotype, production of enzymes GSTM1 not performed (n = 49), 3 — patients who have expressed the GSTT1 enzyme-processing is performed (n = 63), 4 — patients with "zero" genotype, GSTT1 enzyme production is not carried out (n = 13) and 5 — patients with "zero" genotype on the development of both enzymes (n = 6). Intensity of intoxication syndrome was assessed using a scale proposed by Kibrik B.S., Tchelnokova O.G. [5]. The results were processed using a statistical software package for Windows 7. The level of reliability of statistical hypothesis was 0.05 ($p < 0.05$) by Student's test.

THE RESULTS OF THE STUDY

At admission to the hospital the symptoms of intoxication in different clinical forms of the five groups of patients had varying degrees of severity and duration (Table. 1).

Patients in group I on admission observed following symptoms: weight loss — 1 (3.7%); fever — 18 (66.7%); asthenia, marked weakness — 4 (14.8%); increased sweating — 3 (11.1%); hypotension — 0; signs lymphostasis as pastosity and swelling of the lower extremities — 0; changes in general blood test (ESR acceleration, leukocytosis shift formula to the left) — 12 (44.4%). The duration of symptoms of intoxication before admission amounted la 33 ± 6 days, amid ongoing detoxification therapy was 7 ± 3.

Group II on admission observed: weight loss — 38 (77.6%); fever — 44 (89.8%); asthenia, expressed ALS-Bost — 41 (83.7%); increased sweating — 36 (73.5%); hypotension — 21 (42.9%); DIGITS lymphostasis with a pastosion and edema of lower extremities — 24 (49%); changes in general blood test (ESR acceleration, leukocytosis shift formula to the left) — 46 (93.9%). The duration of symptoms of intoxication symptoms to admission was 39 ± 7 days, amid ongoing detoxification therapy was 18 ± 5.

Group III patients on admission to hospital noted: weight loss — 4 (6.3%); fever — 26 (41.3%); asthenia, marked weakness — 13 (20.6%); increased sweating — 2 (3.2%); hypotension — 1 (1.6%); signs lymphostasis as pastosity and swelling of the lower extremities — 0; changes in general blood test (ESR acceleration, leukocytosis shift formula to the left) — 8 (12.7%). The duration of symptoms of intoxication before admission was 18 ± 2 days, amid ongoing detoxification therapy was 7 ± 3.

Table. 1. *The duration of the clinical manifestations of the symptoms of intoxication in patients with TB patients, carriers of different alleles of polymorphic GSTM1 and GSTT1*

Monitoring Groups	Polymorphic genotypes	Number(n)	Duration / night (before admission and during therapy)	Significant differences
№ 1	polymorphic genotype GSTM1 (+/+; +/0)	n = 27	33 ± 6; 7 ± 3;	P1=0,001
№ 2	polymorphic genotype GSTM1 (0/0)	n = 49	39 ± 7; 18 ± 5;	P2=0,001
№ 3	polymorphic genotype GSTT1 (+/+; +/0)	n = 63	18 ± 2; 7 ± 3;	P3=0,001
№ 4	polymorphic genotype GSTT1 (0/0)	n = 13	45 ± 5; 24 ± 4;	P4=0,001
№ 5	polymorphic genotypes GSTM1 (0/0) + GSTT1 (0/0)	n = 6	65 ± 5; 29 ± 7.	P5=0,001

Note: *P1 — significant differences between the duration of intoxication syndrome on therapy in patients with genotype GSTM1 (+/+; +/0) VScGSTM1 (0/0); P2 — significant differences between the duration of intoxication syndrome on therapy in patients with genotype GSTT1 (+/+ +/0) VScGSTT1 (0/0); P3 — significant differences between the duration of intoxication syndrome on therapy in patients with genotype GSTM1 (+/+; +/0) VSGSTM1 (0/0) + GSTT1 (0/0); P4 — significant differences between the duration of intoxication syndrome on therapy in patients with genotype GSTT1 (+/+ +/0) VSGSTM1 (0/0) + GSTT1 (0/0) and P5 — significant differences between the duration of in-syndrome to toxic therapy in patients with genotype GSTM1 (+/+; +/0) VSGSTM1 (0/0) + GSTT1 (0/0).*

Patients of group IV at admission noted: weight loss — 5 (38.5%); fever — 13 (100%); asthenia, marked weakness — 10 (76.9%); increased sweating — 8 (61.5%); hypotension — 8 (61.5%); lymphostasis signs of pastiness and edema of the lower extremities — 6 (46.2%); changes in general blood test (ESR acceleration, leukocytosis shift formula to the left) — 12 (92.3%). The duration of symptoms of intoxication before admission was 45 ± 5 days, amid ongoing detoxification therapy was 24 ± 4.

Patients Group V on admission was observed in the following symptoms: weight loss — 6 (100%); fever — 6 (100%); Al-shadowing, marked weakness — 6 (100%); increased sweating — 5 (83.3%); hypotension — 5 (83.3%); lymphostasis signs of pastiness and edema of the lower extremities — 4 (66.7%); changes in general blood test (ESR acceleration, leukocytosis shift formula to the left) - 6 (100%). The duration of symptoms of intoxication before admission was 65 ± 5 days, amid ongoing detoxification therapy was 29 ± 7.

In this regard, we consider promising further research intended inductors and / or donatorovglutationa TB patients, to increase detoxification and antioxidant function of glutathione.

CONCLUSIONS

1. Analysis of the clinical manifestations of intoxication syndrome in patients with pulmonary tuberculosis showed that in patients with "zero" genotype to develop enzymes GSTM1, GSTT1 (II, IV, V group) intoxication symptoms significantly (r = 0,8 p = 0,001) are more pronounced and durable, even against the detoxification therapy, which will require the combined purpose of TB medicines, thus contributing to increased risk of PND.

2. detoxification therapy, the appointment of inductors and donators of glutathione in patients with tuberculosis "zero" genotypes GSTM1, GSTT1, should personalized implemented throughout the specific chemotherapy because accumulating xenobiotics and endogenous metabolites of TAP will contribute to the lengthening of the period of intoxication, formation of the NDP, reduction of compliance, the possibility of refusing specific chemotherapy and as a consequence, an increase in the prevalence of tuberculosis infection.

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ERNÄHRUNG IM ALTER

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Eine zweckmäßige Ernährung fördert nicht nur die Gesundheit, sondern beeinflusst das gesamte Wohlbefinden, die Lebensqualität und die Lebensfreude. Deshalb sollten die Qualitätsansprüche an die tägliche Kost bestimmten Grundsätzen genügen:

— ausgewogener Energie — und Nährstoffgehalt
— hoher Genusswert
— kulturvolle Speiseneinnahme.

Die täglich zugeführte Ernährung soll den Energiebedarf des Organismus decken, verbrauchte Körpersubstanzen ersetzen und ein Regenerationspotenzial aufbauen. Der ältere Mensch hat gleiche Bedürfnisse hinsichtlich des Genusswertes wie Jüngere.

Das leckere Aussehen, der appetitanregende Duft, der arteigene Geschmack und die Konsistenz der Speisen bestimmen den Genusswert. In dieser Hinsicht spielt auch der Abwechslungsreichtum der Kostgestaltung eine wichtige Rolle. Auserlesene, üppige Gerichte, ständig angeboten, bekommen wir über. Der Organismus verlangt naturgemäß eine stetige Vielfalt beim Speisenangebot. Die passende Verzehrtemperatur ist ebenfalls entscheidend für den Genusswert der Speisen.

In der heutigen Gesellschaft hat sich infolge von Stress, Zeitmangel und Hektik eine mangelnde Esskultur verbreitet. Diese negativen Einflüsse sind nicht zuletzt unter der immer knapper werdenden personellen Situation auch bei der Nahrungsreichung und -aufnahme in medizinischen- und Pflegeeinrichtungen zu beobachten. Gerade ältere Menschen benötigen mehr Zeit und Zuwendung, d. h. sorgfältig zubereitete Speisen sollten auch mit Bedacht gegessen werden.

Es kommt also nicht allein auf die Zusammenstellung der Speisen an, sondern gleichermaßen auf die Art, wie sie verzehrt werden. Dazu gehören die sorgfältig oder sogar liebevoll gedeckte Tafel, das gepflegte Aussehen der Essenteilnehmer oder auch die pünktliche Speiseneinnahme.

Es gibt nun ernährungsrelevante physiologische Veränderungen im Alter, die die Nahrungsaufnahme ungünstig beeinflussen. Dazu gehören beispielsweise:

— Abnahme des Seh-, Geschmacks- und Geruchsvermögens
— Zahnverlust oder Kaubeschwerden
— Mundtrockenheit und Schluckbeschwerden
— Reduzierung des Appetits
— Früher Eintritt von Sättigung während der Nahrungsaufnahme durch erhöhte Aktivität vom Sättigungshormon
— Verminderung des Durstempfindens
— Abnahme der Magensäureproduktion
— Abnahme der Muskelmasse
— Allgemeine Verminderung der Stoffwechselrate
— Abnahme der Fähigkeit, Zucker zu verstoffwechseln.

Des Weiteren ist der Energiebedarf im höheren Lebensalter geringer, so dass auch ein geringeres Kalorienangebot notwendig wird. Nicht selten sind auch andere Faktoren präsent, die eine gestörte Nahrungsaufnahme im Alter nach sich ziehen, wie beispielsweise:

— Psychische Probleme (z. B. einschneidende Lebensereignisse)
— Geistige Beeinträchtigungen (z.B. Vergesslichkeit)
— Eingeübte Ernährungsgewohnheiten
— Soziale Probleme (z.B. Einsamkeit)
— Krankheit (z.B. der Verdauungsorgane)
— Multiple Medikamenteneinnahme.

Der normale Nährstoffbedarf ist altersabhängig und beträgt bei älter als 75-jährigen Menschen ca. 1500–1700 kcal pro Tag (s. Tabelle 1).

Tab. 1.

Nährstoffbedarf des gesunden alten Menschen:		
bis 30 Jahre	ca.	2200 kcal/Tag
33–55 Jahre	ca.	2000 kcal/Tag
55–75 Jahre	ca.	1800 kcal/Tag
> 75 Jahre	ca.	1600 kcal/Tag

Dabei ist der Grundsatz zu beachten, dass im Nahrungsangebot ausreichend Kohlenhydrate und Eiweiß sowie sparsame Fett beinhaltet sind. Als allgemeine Faustregel für die tägliche Ernährungszusammensetzung gilt 50 % Kohlenhydrate, 20 % Eiweiß und 30 % Fett. Empfehlenswert sind dabei:

Kohlenhydrate:	Getreideprodukte, Kartoffeln, Obst, Gemüse, Zuckerprodukt
Eiweiß (ca. 50–70g/Tag):	mageres Fleisch, Fisch, Milch und Milchprodukte, Eier, Wurst
Fette:	Pflanzenöle, Butter, Pflanzenmargarine (Achtung: scharf gebratenes Fleisch, versteckte Fette)

Soll man allgemeine Grundsätze für eine bekömmliche Alterskost definieren, so gelten folgende Regeln: Altersentsprechende Ernährung sollte:

— verträglich sein
— gut schmecken
— eingeschränkte Funktionen berücksichtigen
— Verdauungsvorgänge fördern
— Organfunktionen unterstützen
— auf den geringeren Energiebedarf abgestimmt sein
— alle für den Körper notwendigen Nährstoffe in ausreichender Menge enthalten
— die Widerstandskräfte stärken
— die körperliche und geistige Leistungskraft stärken
— von höchstmöglicher Qualität sein „Qualität statt Quantität"

Dabei ist besonders empfehlenswert:

— Einschränkung tierischer Fette, mehr pflanzliche Fette und Öle
— Vollkornprodukte bevorzugen (Reis, Teigwaren, Brot)
— täglich Obst und Gemüse
— täglich Milchprodukte
— pro Woche 2–3 × Fleisch, 2 × Fisch und sonst vegetarisch
— 1,5–2 Liter Flüssigkeit am Tag

Tab. 2. Lebensmittelauswahl bei der Ernährung im Alter

Lebensmittelauswahl	+ empfehlenswert	– nicht empfehlenswert
Brot, Backwaren	weiche Brotsorten und Brötchen, Vollkornprodukte aus feingemahlenem Korn, Brot ohne Rinde, Kuchen, Kekse	fettreiche Backwaren, dicke Zuckerglasuren
Kartoffeln	Kartoffelbrei, Salz- und Pellkartoffeln, Kartoffelklöße, Kartoffelsuppe	fettreiche Zubereitungen z. B. Pommes frites
Reis, Teigwaren	Reisgerichte, Vollkornreis, Teigwaren aller Art besonders auch Tortellini, Lasagne, Nudelgerichte mit verschiedenen Soßen als Hauptgericht	Scharf gewürzte Reisgerichte, fettreiche Zubereitungen
Gemüse, Salate	weiche Gemüse und daraus hergestellte Suppen, Eintöpfe und Salate	keine blähenden Gemüse wie Kohl, Rettich, grobe Rohkostsalate, große Mengen Zwiebeln Lauch, Paprika
Obst, Säfte, Nüsse	Kompotte, weiches Obst wie Bananen, Melonen etc.	große Mengen Trockenobst, Fruchtsaftgetränke, Nüsse
Fleisch	alle Zubereitungen aus Brät und Hackfleisch aus verschiedenen Fleischsorten, zarte saftige Fleischteile	fettreiche Fleischarten und Zubereitungen, mit Speck gebratene und stark gewürzte Speisen
Wurst	streichfähige Wurstsorten, Wurst ohne grobe Fleischanteile, Schinken und Braten dünn geschnitten	fettreiche Wurstsorten, scharf gewürzte Wurstarten
Fisch	alle, fettere Fische in kleinen Mengen (günstige Fettsäuremuster), Fischklößchen	fettreiche Fischzubereitungen, fette Fischsalate
Eier, vegetarische Gerichte	Eierspeisen, Mehlspeisen, Soufflé, Gemüseterrinen,	fettreiche Zubereitungsarten
Milch und Milchprodukte	alle, Kräuterquark auch als Hauptmahlzeit	in großen Mengen fettreiche Käsesorten und Sahneprodukte, Käse mit Nüssen
Getränke	Kaffee, Malzkaffee, Tee aller Art, verdünnte Obst- und Gemüsesäfte, Wasser, Gemüsebrühe	zuckerhaltige Getränke, Alkohol
Brotaufstriche	Butter und Margarine in kleinen Mengen, Marmelade, Gelee, Honig, vegetarische Pasteten	./.
Sonstiges	Haferflocken mit Milch Breikost mit Kompott auch als Hauptmahlzeit	grobes Körner- und Früchtemüsli

Tab. 3. Ernährung im Alter — Tagesbeispiel

Frühstück		kcal	kj	EW/g	F/g	KH	Bst (g)
7,5 g	Kondensmilch	9,13	38,34	0,23	0,75	0,30	
200 ml	Kaffee, Tee		0,00				
10 g	Zucker	40,92	171,86	0,00	0,00	9,98	
60 g	Vollkornbrot	130,70	548,93	4,80	0,96	24,90	5
60 g	Weizenbrötchen	167,30	702,68	5,22	1,14	33,00	1,8
40 g	Wurst/ Käse	71,86	301,83	6,60	4,80	0,04	
25 g	Marmelade	70,21	294,89	0,13	0,00	17,00	0,1
15 g	Butter (Joghurtbutter)	98,57	414,00	0,23	10,50	0,00	
Zwischenmahlzeit							
150 g	Obst	70,11	294,46	0,00	0,00	17,10	
Mittagessen							
120 g	Rindfleisch, mager	134,04	562,97	26,16	2,88	0,00	
100 g	Braune Rahmsoße	88,60	372,12	1,00	6,00	7,00	
160 g	Kartoffeln	115,63	485,65	3,20	0,16	24,64	2,7
150 g	Gemüse	40,31	169,28	4,95	0,30	4,20	3
150 g	Dessert,fettarm	72,14	302,97	5,40	2,40	6,75	
Zwischenmahlzeit							
100 g	Obstkuchen	179,74	754,91	3,90	3,50	32,00	3
Abendessen							
200 ml	Tee		0,00				
10 g	Zucker	40,92	171,86	0,00	0,00	9,98	
60 g	Vollkornbrot	130,70	548,93	4,80	0,96	24,90	5
60 g	Mischbrot	140,39	589,63	4,68	0,60	28,20	2,8
90 g	Wurst/Käse	161,69	679,11	14,85	10,80	0,09	
15 g	Butter (Joghurtbutter)	98,57	414,00	0,23	10,50	0,00	
150 g	Salatgemüse	40,31	169,28	4,95	0,30	4,20	3
Zwischenmahlzeit							
150 g	Milchprodukt,fettarm	72,14	302,97	5,40	2,40	6,75	
Gesamtsumme		**1.974**	**8.291**	**97**	**59**	**251**	**26**

Eiweiß	93,8g	20%
Fett	55,5g	28%
Kohlenhydrate	236,1 g	52%

— Normalgewicht anstreben (altersabhängiger BMI)
— zusätzliche Nahrungsergänzungsmittel (z.B. Vitamin- und Mineralstoffe, Hefeprodukte, Eiweißkonzentrate, Weizenkleie, Leinsamen)

Zusätzlich sollten kleine Zwischenmahlzeiten zwischen Frühstück und Mittag sowie am Nachmittag eingenommen werden (z.B. Joghurt, Obst, Gebäck, Kuchen). Aus der Erfahrung heraus hat sich gezeigt, dass 5 Mahlzeiten besser für den älteren Menschen verträglich sind als nur 3 Hauptmahlzeiten.

Wird von den älteren Menschen eine sogenannte leichte Kost bevorzugt, so haben sich für die Speisezubereitungen einige Regeln bewährt, die eine gute Verträglichkeit garantieren, z.B.

— Weiche Speisen wie Omelette, Soufflé, Terrine bevorzugt anbieten
— Pürierte Speisen vermehrt in die Kost aufnehmen, ohne dass das Essen unappetitlich wirkt - Abwechslung durch Formen und Farben einbringen
— Passiertes Fleisch von verschiedenen Tierarten anbieten

— Gemüse weich kochen
— Fisch grätenfrei anbieten oder als Fischklößchen
— Fleisch als zart-saftige Mahlzeiten zubereite, Fleischteile mit Knochen meiden
— Soßen und Cremesuppen dürfen nicht zu dünnflüssig sein und keine groben Stückchen enthalten
— Bei Teigwaren darauf achten, dass sie leicht mit dem Löffel oder mit einer Gabel gegessen werden können, d. h., keine langen Spaghetti sondern kurze Gabelspaghetti und ähnliche Sorten auswählen
— Keine harten Salatsorten anbieten, Blattsalate klein gerupft servieren
— Keine sauren Speisen anbieten
— Keine spitzkantigen Speisen servieren, z.B., keine ganzen Körper auf Brötchen und Salaten, kein grobes Knäckebrot
— Keine Verpackungen wählen, die schwer zu öffnen sind
— Fingerfood als Buffetangebot zu allen Mahlzeiten bereitstellen

Ganz wichtig ist auch eine regelmäßige Trinkmenge von 1–2 Liter/Tag. Bei Erkrankungen können Abweichungen notwendig werden (z.B. Herzkrankheiten, Erkrankung der Nieren). Ansonsten sind keine bestimmten Getränkearten speziell für den älteren Menschen vorzugeben. Als Richtwerte kann man jedoch empfehlen:

Morgens:	1–2 Tassen Kaffee/Tee/Kakao
Vormittags:	1 Glas Saft / Buttermilch
Mittags:	1 Tasse Brühe / Suppe + 1 Glas Mineralwasser
Nachmittags:	1–2 Tassen Milchkaffee
Abends:	1–2 Tassen Frucht-/Kräutertee, 1 Glas Wein, Bier oder Saft

Oft herrscht die Meinung, dass die Speisen für ältere Menschen salzarm, gewürzarm oder sogar fade sein sollen. Das ist nicht richtig, denn diese Zutaten verbessern den Geschmack, fordern den Appetit und machen die Speisen bekömmlicher.

Für die tägliche Ernährungspraxis kann man letztlich noch folgendes zusammenfassen:

— je kleiner der Bissen, desto leichter sind die Speisen verdaulich, sie belasten kürzere Zeit den Magen-Darm-Trakt
— ein intaktes Gebiss begünstigt den Verdauungsprozess und letzten Endes die Gesundheit der Verdauungsorgane
— Aromastoffe tragen zur besseren Bekömmlichkeit der Speisen bei
— häufig kleinere Mahlzeiten verträgt der Organismus besser als wenige große, die Verdauungsorgane werden durch kleinere Mahlzeiten gleichmäßiger belastet und nicht überstrapaziert
— vor dem Essen sollten keine größeren Flüssigkeitsmengen aufgenommen werden, um die Verdauungssäfte nicht zu verdünnen
— Ballaststoffe sind unentbehrlich für die Darmperistaltik
— schwerverdauliche Speisen am Abend belasten den Organismus übermäßig
— mit übervollem, aber auch mit leerem Magen sind keine geistigen Höchstleistungen zu erwarten

TRINKEN IM HÖHEREN LEBENSALTER

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Das Trinkverhalten ist für jedes Lebensalter von entscheidender Bedeutung, da das Wasser lebensnotwendig ist und mehrere Funktionen für den Organismus übernimmt. So ist das Wasser Bestandteil aller Zellen und Körperflüssigkeiten, dient als Transport- und Lösungsmittel (z.B. Nährstoffe, Abbauprodukte) und erhält und regelt die Körpertemperatur (z.B. Schwitzen).

Da der Körper ständig Flüssigkeit über die Nieren, den Darm, die Haut oder beim Atmen über die Lungen ausscheidet, benötigt er regelmäßig Wasser. Normalerweise wird dies über ein entsprechendes Durstempfinden reguliert, das dann entsteht, wenn der Körper mehr als 0,5% seines Gewichtes in Form von Wasser verloren hat.

Bei älteren Menschen ist nun das Durstgefühl vermindert und es besteht die Gefahr einer Exsikkose (Dehydratation, Austrocknung).

Weshalb trinken gerade ältere Menschen zu wenig?

— reduziertes Durstgefühl
— Angst vor nächtlichen Toilettengängen
— Angst vor dem Trinken auf Grund von Inkontinenz bzw. Prostatabeschwerden
— Schluckstörungen
— Erziehung: „Beim Essen wird nicht getrunken!".

Die Folgen einer ungenügenden Flüssigkeitszufuhr sind Minderung der Leistungsfähigkeit, schlechtes Allgemeinbefinden, trockene Haut und Schleimhäute, Schwindel, Kopfschmerzen, Verstopfung, Verwirrtheitszustände, Kreislauf- und Nierenversagen (Tab. 1).

Untersuchungen in Krankenhäusern und Altenheimen haben gezeigt, dass zu wenig darauf geachtet wird, inwieweit die älteren Menschen regelmäßig und ausreichend trinken. Um einen ausgeglichenen Wasserhaushalt zu gewährleisten, sollte für den älteren Menschen täglich ca. 1,5 Liter Flüssigkeit angeboten werden. Es gibt auch relativ genaue Berechnungsvarianten für eine täglich notwendige Flüssigkeitsaufnahme:

— 30 ml pro kg Körpergewicht, bei der Berechnung ist jedoch das Soll-Gewicht zugrunde gelegt
— 1,500 ml + (15 ml × Ist–Gewicht–20) = Flüssigkeitsbedarf in ml.

Diese Orientierungsgrößen können jedoch vom tatsächlichen individuellen Bedarf abweichen, wenn etwa Grunderkrankungen, wie z.B. bei der Niereninsuffizienz oder Herzinsuffizienz, wo eine Flüssigkeitsrestriktion gefordert ist.

Bei starkem Schwitzen (im Sommer, bei Fieber, in überheizten Räumen, bei körperlicher Anstrengung) bei Durchfall, Erbrechen und Einnahme von Laxanzien oder Diuretika steigen die Wasserverluste an. Diese Verluste müssen durch vermehrte Flüssigkeitsaufnahme, d. h. über die o. g. Mengen hinaus, wieder ausgeglichen werden.

In diesen Fällen, aber auch bei chronischem Flüssigkeitsverlust sollten Trinkprotokolle geführt werden, um das Trinkverhalten zu kontrollieren und zu dokumentieren. Mit welchen Möglichkeiten ist nun ausreichende Flüssigkeitszufuhr zu erreichen:

— Zu allen Mahlzeiten Getränke anbieten und ggf. anreichen
— Morgens an häufig frequentierten Stellen der Wohnung bzw. des Zimmers die Getränke in Sicht- oder Reichweite bereitstellen
— In Senioreneinrichtungen Selbstbedienungsmöglichkeiten für Getränke (Trink-Oasen) einrichten oder Getränkeautomaten aufstellen

Tab. 1. *Folgen eines Wassermangels (Mann, 75 kg Körpergewicht):*

Wasserverlust in % des Körpergewichtes und in Litern	Symptome
ab 0,5	Durst, von älteren Menschen allerdings oft nicht wahrgenommen
bis 3 (2,5 l)	Durst, Gewichtsabnahme, Rückgang der Harnproduktion und Speichelsekretion, trockener Mund
ab 5 (4 l)	Nachlassende Gewebespannung der Haut, Anschwellen der Zunge, Schluckbeschwerden, beschleunigter Herzschlag, Temperaturanstieg, Bluteindickung
ab 10 (7 l)	Starke Abnahme der körperlichen und geistigen Leistungsfähigkeit, Verwirrtheit, Muskelkrämpfe, Kreislaufkollaps, ohne Flüssigkeitsersatz: Lebensgefahr!

— Leere Gläser und Becher immer wieder auffüllen bzw. gegen gefüllte austauschen
— Trinkrituale einführen, z. B. den Nachmittagskaffee oder den „5-Uhr-Tee“
— Auf die Flüssigkeitsversorgung von (vermeintlich) selbständigen Senioren achten
— Je weniger jemand isst, desto mehr muss er trinken
— Hilfs- und pflegebedürftige Senioren benötigen adäquate Hilfestellung und Unterstützung beim Trinken. Spezielle Trinkgefäße nutzen
— Viele Senioren greifen eher zu, wenn es sich dabei um ein buntes und/oder süßes Getränk handelt
— Die Senioren zum Austrinken ermuntern (... damit nichts umkommt).

Vorteilhaft ist auch ein individuell zusammengestellter Trinkplan, der eine ausreichende Flüssigkeitsmenge sicherstellen soll (Tab. 2).

Tab. 2. *Beispiel für einen Tages-Trinkplan für Senioren:*

Frühstück	2 Tassen Kaffee oder Tee	250 ml
Zwischenmahlzeit	1 Glas Fruchtsaftschorle oder Buttermilch	200 ml
Mittagessen	1 Glas Mineralwasser 1 Teller Suppe	200 ml 150 ml
Zwischenmahlzeit	1 große Tasse Tee oder Kaffee	200 ml
Abendessen	2 Tassen Kräutertee	300 ml
später Abend	1 Glas Saftschorle, Mineralwasser oder gelegentlich 1 Glas Bier bzw. Weinschorle	200 ml
Gesamtmenge		1500 ml

Sehr unterschiedlich wird auch die Frage von geeigneten bzw. ungeeigneten Getränken diskutiert.

Besonders geeignete Getränke sind Wasser, Kräuter- und Früchtetees, Säfte bzw. Saftschorlen. Auch Kaffee, schwarzer Tee sowie alkoholische Getränke werden entgegen häufig anderslautender aussagen zu den Getränken „dazugerechnet“. auf Grund ihrer anregenden Wirkung auf Herz und Kreislauf sind sie jedoch nicht zum Durstlöschen geeignet.

Gegen den täglichen Genuss von bis zu 4 Tassen Kaffee sowie gelegentlich einem Glas Bier oder Wein ist in aller Regel nichts einzuwenden. Gibt der gesundheitliche Zustand des Seniors Anlass zur Sorge, so sollte ein ärztlicher Rat eingeholt werden.

Immer wieder werden auch alkoholische Getränke z.B. täglich 1–2 Gläser Wein dem älteren Menschen verboten. Argumentativ kommen Suchtgefahr, Leberschädigung, Einschränkung der körperlichen und geistigen Leistungsfähigkeit zur Sprache. Deshalb einige Hinweise zu dem Problem „Wein und Gesundheit“.

Wein besteht zu 80–85% aus Wasser. Neben diesem Hauptbestandteil ist der Alkohol ein wesentlicher Inhaltsstoff. „Alkohol ist gefährlich“ — diese Aussage hat vor allem hinsichtlich der vielen Suchtkranken nach wie vor seine Berechtigung. Doch nach neuesten Erkenntnissen von Ernährungswissenschaftlern und Medizinern ist der im Wein enthaltene Alkohol nicht grundsätzlich ungesund. Im Gegenteil: Der Alkohol des Weines kann der Gesundheit durchaus förderlich sein. Dabei spielt allerdings die Mischung mit den anderen Inhaltsstoffen des Weines eine große Rolle.

Insgesamt hat Wein über eintausend verschiedene Inhaltsstoffe. neben Wasser und Äthylalkohol sind dies vor allem höhere Alkohole (z.B. Glycerin), Säuren, Zucker, Mineralstoffe, Spurenelemente, Aromastoffe und Vitamine. Vor allem die Spurenelemente Eisen, Magnesium und Kalium sowie die Vitamine des Weines tragen zu einer gesunden Ernährung bei. Doch die gesündesten Stoffe im Wein sind ohne Zweifel die „Polyphenole“. Dabei handelt es sich um vielfältige chemische Verbindungen, die vor allem in den Traubenstielen, -schalen und -kernen vorkommen.

Ihre Zusammensetzung ist je nach Rebsorte und Anbaugebiet sehr unterschiedlich. Die Polyphenole bilden das Immunsystem der Weinbeeren. Sie sorgen bei der Verletzung der Beerenhaut für eine schnelle Wundheilung und können Parasiten und Pilze abwehren.

Die Hauptbedeutung der Polyphenole liegt in ihrer Wirkung als Antioxidantien: Sie sind in der Lage, Reaktionen mit Sauerstoff (Oxidation) in den Körperzellen zu verhindern. Sauerstoff ist zwar lebensnotwendig, kann aber chemisch auch sehr aggressiv sein.

In den Körperzellen entstehen durch Oxidationsprozesse die gefürchteten „Freien Radikale", denen von Medizinern eine große Rolle bei der Entstehung von Krebs und Herzerkrankungen zugeschrieben wird. Mit ihrer zerstörerischen Kraft können sie sogar das Erbgut einer Zelle schädigen. Bis heute sind die Fähigkeiten, Freie Radikale zu neutralisieren, vor allem für vier Polyphenole wissenschaftlich nachgewiesen. Das wirkungsvollste Polyphenol ist ein Stoff mit dem Namen Resveratrol. Neben seiner antioxidativen Wirkung ist er auch in der Lage, den Cholesterinspiegel günstig zu beeinflussen. Am höchsten ist seine Konzentration in Cabernet-Sauvignon- und Spätburgunder-Trauben aus den kühleren Anbaugebieten.

Eine bahnbrechende Untersuchung zum Zusammenhang von Weinkonsum und Herzerkrankungen war die „Koppenhagen-Studie" von 1995. Danach verringert sich bei mäßigem Weinkonsum die Gefahr eines Herzinfarktes gegenüber entschiedenen Abstinenzlern um 60%, das allgemeine Sterblichkeitsrisiko immerhin noch um 50%. Und auch die Gefahren von Arteriosklerose und Angina pectoris bis hin zum Schlaganfall werden durch mäßigen Weinkonsum vermindert. Nach allgemeiner Überzeugung vieler Fachleute liegt die ideale Menge für Frauen bei 0,25 l, für Männer bei 0,4 l Wein täglich.

Bei höherer Dosierung des Alkohols verkehrt sich seine schützende Wirkung jedoch ins Gegenteil. Ab einem Liter Wein pro Tag wird die förderliche Wirkung des Alkohols auf Herz und Kreislauf aufgehoben. Nun treten wiederum andere Gefahren in den Vordergrund. Abgesehen von den Gefahren einer möglichen Alkoholabhängigkeit wird zunehmend die Leber belastet und bei dauerhaftem Alkoholmissbrauch auch geschädigt.

Bei der Betrachtung der Gesamtzufuhr von Flüssigkeit aus der täglichen Ernährung sind auch die Wassermengen aus den Lebensmitteln mit zu berücksichtigen. Das bedeutet, dass neben den notwendigen 1,5 l Flüssigkeitsangebot noch zusätzlich 750 ml Flüssigkeit aus den Lebensmitteln für einen ausgeglichenen Flüssigkeitshaushalt erforderlich sind, d. h. die Gesamtmenge an Flüssigkeitszufuhr pro Tag beträgt ca. 2,25 l (Tab. 3).

Bei konsequenter Einhaltung dieser Trinkregeln ist ein ausgeglichener Flüssigkeitshaushalt zu erreichen. Damit würden viele Krankenhauseinweisungen besonders bei sommerlichen Temperaturen vermeidbar sein und viele aufwendige Behandlung (z.B. Infusionen) reduziert werden.

Tab. 3. *Wassergehalt von Lebensmitteln:*

	Lebensmittel	Wassergehalt
Brot:	Graubrot, 1 Scheibe (40 g) ½ Vollkornbrötchen (30 g)	17 ml 11 ml
Milch und Milchprodukte:	Trinkmilch, 1,5 % Fett, 1 Glas (200 g) Joghurt, fettarm mit Früchten 1,5 % Fett, 1 Becher (150 g)	178 ml 119 ml
Gemüse:	Gemüse, gedünstet, 1 Portion (200 g) Gurke, 1 Stück (100 g)	175 ml 96 ml
Suppen und Eintöpfe:	Klare Suppe, 1 Teller (250 g)	224 ml
Salate:	Gemischter Salat mit Dressing, 1 Portion (150 g) Kartoffelsalat, 1 Portion (150 g) Tomatensalat mit Dressing, 1 Portion (130 g)	132 ml 121 ml 116 ml
Obst:	Apfel, 1 Stück (125 g) Apfelsine, 1 Stück (150 g) Banane, 1 Stück (140 g) Erdbeeren, Himbeeren, Stachelbeeren, 1 Portion (100 g)	106 ml 129 ml 103 ml 87 ml
Nachspeisen:	Pudding, 1 Portion (150 g) Kompott, Apfelmus, 1 Portion (125 g)	108 ml 99 ml
Fleisch- und Fischgerichte:	Putenschnitzel, 1 Stück (125 g) Gulasch, Ragout, 1 Portion (125 g) Fischkonserve, 1 Dose (180 g)	104 ml 92 ml 115 ml
Beilagen und Aufläufe:	Klöße, Knödel, 1 Portion (80 g) Kartoffelpüree, 1 Portion (150 g) Aufläufe (Kartoffelauflauf, Nudelauflauf...), 1 Port. (300 g) Spaghetti mit Tomatensoße, 1 Portion (250 g)	61 ml 119 ml 227 ml 178 ml

EFFECTS OF LONG-CHAIN POLYUNSATURATED FATTY ACIDS (LCPUFA) ON HUMAN HEALTH

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Human body is capable of producing various types of fatty acids from other fats as well as from other substances (raw materials). However in case of omega-3 fatty acids, it does not happen because they are not made in the body and are supplied with the food that is why they are essential fatty acids. Foods high in Omega-3 include fish, vegetable oils, nuts (especially walnuts), flax seeds, flaxseed oil, and leafy vegetables.

What makes omega-3 fats special? They are an integral part of cell membranes throughout the body and affect the function of cell receptors in the membranes. They provide the starting point for making hormones that regulate blood clotting, contraction and relaxation of artery walls, and inflammation. They also bind receptors in cells that regulate genetic function. Likely due to these effects, omega-3 fats have been shown to help prevent heart disease and stroke, may help control lupus, eczema, and rheumatoid arthritis, and may play protective roles in cancer and other conditions. (1)

WHAT ARE THE TYPES OF OMEGA-3 FATTY ACIDS?

There are three main omega-3s:

— Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA are found in fatty fishes such as herring, mackerel, salmon, tuna and trout.

— Alpha-linolenic acid (ALA), (the most common omega-3 fatty acid in most Western diets) the human body generally uses ALA for energy, and conversion into EPA and DHA is very limited. ALA is found in flaxseed, canola and soybean oils, and walnuts. (2)

All omega fatty acids play specific roles in overall health. Speaking about the effects of polyunsaturated n 3 fatty acids on different aspects of human health it is worth to note that there are a great deal of works dedicated to this theme from one hand and deviations and ambiguity of opinions on the other hand.

Nevertheless there are evidence that suggest that these LCPUFA can have health benefits, including:

— Prevent coronary heart disease;
— Prevent stroke;
— Prevent diabetes;
— Promote healthy nerve activity;
— Prevent cancer;
— Improve vitamin absorption;
— Maintain a healthy immune system;
— Promote cell development (3, 4, 5).

Supply of polyunsaturated omega-3 fatty acids into the body is associated with adequate consumption of fish, which also contains essential amino acids, vitamins and mineral substances a person needs to stay healthy. However in Germany the consumption of fish is much lower than consumption of meat. In 2012 the consumption of fish per person came to 14.4 kg (basing on the weight of the caught fish). (6). German Nutrition Society (DGE) recommends in this connection a weekly consumption of 80 – 150 gram of not oily fish (salmon, sea bass, cod) and 70 gr of oily fish (herring, mackerel). (7) It corresponds to 15 kg of white fish and 7,3 kg of oily fish per person per year. (8) Correspondingly, the consumption of an average German citizen is lower than recommended.

High blood pressure (HBP), hyperlipidaemia, inflammation and Diabetes Mellitus are serious risk factor for cardiovascular disease. Since numerous researches refer to a positive effect of omega-3 fatty acids DHA and EPA of sea origin on HBP, most researches have focused on investigation of the influence of fish oil on the progression of these very processes (9, 10, 11).

There are also works confirming the positive effect of omega-3 fatty acids DHA and EPA on frequency and clinical course of oncologic diseases (especially on the GI tumours) due to reduction of anti-inflammatory effect and the influence of eicosanoids and omega-3 on proliferation of cells. (12, 13, 14, 15, 16). However, number of authors indicate on a higher risk of incidence of prostate cancer due to consumption of omega-3 fatty acids DHA and EPA. (17, 18, 19, 20).

It is not always simple to differentiate the effect of omega-3, since fish contains as well fat-soluble vitamins and microelements possessing their own effects (e.g. vitamin D and selenium). In Germany there are people who do not eat fish or eat fish moderately (21). According to the consumption statistics about 16% of respondents do not eat fish. It might be accounted for ethical problems among vegans or vegetarians or the danger of contamination of sea products with compounds of mercury and dioxin, high concentrations of which might be found there in substantial qualities. Maximum permissible dose limits for mercury compounds in Germany is defined as 1,0 mg/kg (22). Highest concentrations of mercury compounds are found in tuna (0,9 mg/kg) and black halibut (1,03 mg/kg). This toxic compound is accumulated in the body and may cause Minamata disease. Thus, it is not recommended to eat fish in the amounts that exceed DGE recommendation, but not to give up eating fish due to high concentrations of omega-3 despite of relatively moderate concentrations of methylmercury (0,5 mg/kg) in some fish species, such as herring.

INFLUENCE OF POLYUNSATURATED OMEGA-3, 6 FATTY ACIDS (LCPUFA) ON DEVELOPMENT AND FUNCTIONING OF BRAIN, DEVELOPMENT OF VISUAL PERCEPTION AND COGNITIVE ABILITIES

There are practically no arguments among specialists regardiong prescription of omega-3, 6 fatty acids during pregnancy for optimal development of cognitive abilities and visual perception of an embryo (23, 24), as well as prescription in the long run for a positive effect on child's sleep and development of fine motor skills (25, 26, 27, 28). However, actual researches still question these effects and confirm so far only positive effect of omega-3, 6 fatty acids during infant's first moths and the influence later is evaluated as not significant. (29)

To what extent these results are true, will be testified by future researches but at present a daily intake of minimum 200 DHA is recommended to pregnant and breast feeding women for optimal development of the embryo and infant. If it is impossible to supply the required amount of DHA with fish intake, it might be consumed as dietary supplements. (26, 30)

Long-chain polyunsaturated omega-3 fatty acids DHA and EPA (LCPUFA) are essential elements for building, forming and physiological formation of nerve fibres (31). And this influence occurs long before the birth. Already in the third trimester of pregnancy the DHA begins to build up into the structures of embryo's brain and this process is going on during the first two years of life. (32, 33). Optimal development of the nervous system depends on adequate supply of long-chain polyunsaturated fatty acids (LCPUFA) (31). Most important role for development and formation of brain play DHA and Arachidonic acid (AA) (omega-6), which is supplied to exclusively breastfed infants together with other polyunsaturated omega-3, 6 fatty acids (34, 35, 36, 37). Especially high proportion of DHA, EPA and AA is revealed in phospholipids of cellular membrane of brain and retina (31). 10–15% of an adult brain consists of DHA.

Along with numerous integral functions polyunsaturated omega-3, 6 fatty acids play a crucial role in the functioning of the nervous system. Therefore, they affect formation and action of such neurotransmitters as serotonin, noradrenaline and dopamine. They also regulate intercellular (synaptic) signal reduction. Through this action modulation of basic processes such as memory, cognition, emotions, cycles of sleep, perception of pain, sexual behaviour takes place. (32, 38, 39, 40, 41, 42, 43).

Increase of DHA proportion in phospholipids membranes of nervous cells due to change of physical and chemical properties increases «fluidity» (penetration) of membranes. This, in its turn, activates receptors connected with the membrane and transport proteins, and finally induces transmission of a signal between nervous cells. (40, 41) Omega-3 fatty acids plays not a lesser role in complex processes in the nervous system as e.g. adaptation of the nervous system to external exposure (neuroplasticity) or regulation of neuronal gene expression. 38, 39, 40, 41, 42, 43, 44, 45).

Despite of the fact that data was collected from animal experimentation, the latest investigations confirm its relevancy for humans (23, 46)

The second place on DHA contents after the brain is occupied by the pigmented layer of retina and photoreceptor cells, where DHA possibly influences the projection of optical stimulation of subcortical centres (23).

Since recently the possibility of a protective role of DHA in pathophysiology of aged-related macular degeneration has been considered) (24).

The adequate consumption of polyunsaturated omega-3 fatty acids is necessary for correct formation of these structures during pregnancy. (23).

One more research question is the role of omega-3 fatty acids DHA and EPA in cognitive functions and occurrence of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and neuropsychiatric disorders (bipolar disorder, borderline personality disorder, schizophrenia, depressions).

Cerebral circulation is the most important factor affecting functioning of the brain. Due to a high energetic demand and relatively low storage capacity of energetic substrate the condition of cerebral vessels is decisive for its normal functioning. (46)

The quality of blood supply to the brain directly correlates with neurodegenerative and cerebrovascular diseases such as atherosclerosis, stroke and vascular dementia.

We have already mentioned numerous evidence on the impact of increased concentration of DHA on the condition of cerebral vessels and its result on cerebral circulation (46, 47), which is true both for animal and people. (48, 49)

A possible mechanism of effects on cerebral vessels is DHA interaction with acetylcholine receptors and induction of NO synthesis by means of which the increase of NO results in vasodilatation.

There is DHA dependant enhancing of cerebral circulation in the cerebral fissures and thalamus, which play a key role in general thought (cortex), as well as in development of personality and consciousness (50)

Latest researches (50) has shown that damages of blood circulation particularly in this areas of brain triggers incidence of Alzheimer's disease, dementia and decline of cognitive abilities in elderly people. Researchers revealed that increased DHA transportation in the body results in increased DHA concentration in the membranes of nervous cells which affects the fluidity and permeability and consequently changes the activity of membrane membrane-bound proteins. (40, 41).

Long chain omega-3 fatty acids, especially, DHA provides a marked influence on development, structure and physiology of the brain and evidently on blood circulation which is of key importance for neuropsychiatric and neurodegenerative diseases.

To demonstrate this correlation the model of Haast and Kiliaan was proposed (46), which comprise three compounds of brain health (structure, function and blood circulation). Basing on this model, LCPUFAs optimally impact all compounds of this model: quality of the structure, function and blood circulation meanwhile saturated fatty acids produce an opposite action.

Pathophysiological role of neuroprotection D1 (NPD 1) is well-documented. It is synthesised in the brain structures (24) and has a protective action on neurons.

This is manifested in antiapoptotic and anti-inflammatory properties and also in strengthening neural resistance against oxidative stress. (51, 52). Besides NPD 1 reduces production of the β-amyloid (51), which is the part of senile plaques, metabolism damage, which is along with other factors such as the phosphorylation of the microtubule-associated protein tau, weakening of antioxidative reserves and presynaptic cholinergic deficit constitute the main morphological peculiarity of Alzheimer and other dementia illnesses. Therefore, we can postulate that deficit of DHA due to reduction of NPD 1 production may contribute to the development of these illnesses. 53)

THE INFLUENCE OF POLYUNSATURATED FATTY ACIDS (PUFA) ON CARDIO-VASCULAR SYSTEM

Food ratio impacts health by means of a series of biological mechanisms. From one point it implies reduction of lipids and their subfractions in blood plasma. From the other point it is an important impact on blood pressure, thrombophilia, endothelial function and oxidative stress. (Thomas Stulnig, Ernährungsumschau (2015).

In the last years the attention of researchers was focused on the problem of subclinical inflammatory reaction, which is closely connected with the development of cardiovascular disease and its complications, Diabetes mellitus 2 and depends greatly on food. (54)

For better understanding the example of Mediterranean countries may be considered where relatively low level of cardiovascular illnesses is observed. This can be attributed to high consumption of vegetable oils (olive oil which contains simple unsaturated fatty acids) with relatively high consumption of fat. Complemented with a high level of carotenoids, secondary vegetative substances and water soluble dietary fibres, which signals adequate consumption of vegetables and fruits, meanwhile such a diet provides preventive impact on atherosclerotic illnesses.

Research PREDIMED conducted in 2013 (55) showed, that a diet may radically change the level of cardiovascular disease. In this research it was found out that relatively rich in fat Mediterranean diet containing olive oil and nuts reduces cardiovascular risk (myocardial infarction, stroke or death from cardiovascular illnesses) by 30% in comparison with a lower in calories and fat diet. On the other side low-fat diets often do not lead to reduction of cardiovascular

illnesses. (56). It allows to conclude that the quality and not the quantity of fat is decisive for development of cardiovascular illnesses.

Among polyunsaturated fatty acids (PUFA) the most biological impact is provided with omega-3 fatty acids DHA and EPA (C20 or C22), from which mediators (eicosanoids) with anti-inflammatory action are synthesised. Eicosanoids is a general group of physiologically and pharmacologically active compounds containing prostanoids (prostaglandins, prostacyclins, thromboxane) and leukotrienes. They have a very short life (are destructed within a few seconds), that is why they produce effects as "hormones of local action".(57). Most interesting from anti-Inflammatory point of view are derivates of omega-3 fatty acids DHA and EPA resolvin and protectin, two new families of bioactive mediators, termed resolvins and protectins, biosynthesized from omega-3 essential PUFAs.

Resolvins control inflammation at many levels, by reducing peritonitis and skin inflammation, protecting organs from reperfusion injury and neovascularization. Thus, D-series resolvins are of interest in the control of inflammation-resolution in host defence and in neural tissues (58).

DHA is converted in resolving exudates to another new family of mediators named protectins. Mediators of this family are distinguished by the presence of a conjugated triene double bond system and their potent bioactivity. They are biosynthesized via a lipoxygenase mechanism that converts DHA to a 17S-hydroperoxide-containing intermediate, which is rapidly converted by human leukocytes into a 16(17)-epoxide that is enzymatically opened in these cells into a 10,17-dihydroxy-containing anti-inflammatory molecule. This bioactive compound, initially coined 10,17-diHDHA or 10,17S-docosatriene, is now known as protectin D1 owing to its potent protective activity in inflammatory and neural systems documented in studies with N. Bazan and colleagues. It is termed neuroprotectin D170 when produced by neural tissues; the prefix neuro is added to signify its biosynthetic origin (59, 60, 61, 62).

Several 10, 17-dihydroxy-containing products are produced in vivo via different biosynthetic routes, the most potent being protectin D1. The other natural protectin D1 isomers have different double-bond configurations and are less potent in dampening neutrophil recruitment and inflammation. Protectin D1 is stereo-selective and log-orders of magnitude more potent in vivo than its precursor DHA. Protectin D1 is also produced by human peripheral blood mononuclear cells in T helper-2-type conditions in a lipoxygenase-dependent manner via a 16(17)-epoxide intermediate. Protectin D1 blocks T-cell migration in vivo, reduces TNF and interferon-γ secretion, and promotes T-cell apoptosis (63).

Protective attributes of long chain (more than C20) omega-3 essential PUFAs are probably connected with a number of molecular mechanisms including anti- inflammatory effects (64, 65, 66, 67). On the clinical level such effects due to intake of omega-3 essential PUFAs as anti-arrhythmic and hypotensive actions with relatively low dosages (from 1 gr per day) (66). On the opposite, such properties as reduction of triglycerides in the serum depends from the dose. Additional protective effects include neurovegetative changes, improvement of endothelial function and decrease of vascular resistance and in high doses changes in thrombocyte function is observed (68, 69, 70, 71, 72, 73).

It is interesting to note the difference in action between omega-3 fatty acids DHA and EPA and omega-6 fatty acids LA and AA.

Above described mechanisms of PUFA cardioprotective effect are characteristic of omega-3 fatty acids DHA and EPA but not of omega-6 fatty acids LA and AA. The review of all randomised investigations shows reduction by 19% in CHD risk reduction after increasing intake PUFA (74).

An increase of dosages of exclusively omega-6 fatty acids LA and AA shows on the opposite an increase of the risk. Clinical data give evidence on the benefits of omega-3 fatty acids DHA and EPA for prevention of illnesses. A low level of EPA in the serum correlates with a higher risk of atherosclerotic changes in the coronary vessels. Serum concentration of omega-6 fatty acids does not correlate with vascular changes in the heart vessels. A similar connection was revealed between the frequency of subclinical strokes, diagnosed by magnetic resonance imaging, and a high level of DHA and EPA (75). The finding of Thies et al. (76) in a randomised research showed significant qualitative reduction of macrophages after intake of omega-3 fatty acids (cod liver oil) unlike omega-6 fatty (sunflower oil) in comparison with the control group.

It is noteworthy to mention that α-Linolenic acid, which is often called «plant omega-3 unsaturated fatty acid» do not produce a protective effect on cardiovascular system (cc3). On the opposite, omega-3 fatty acids DHA and EPA from cod liver oil produce a protective effect, which can be reproduced in the researches (66).

In the GISSI-Prevenzione trial, with participation of 11000 post myocardial infarction patients, were administered to 1 gram of DHA and EPA as compared to placebo with intake of vitamin E (randomised). However, as after intake of vitamin E no positive effects were reported, after intake of omega-3 fatty

acids the reduction of mortality level, myocardial infarction without mortality and stroke by 15%, as well as mortality from cardiovascular diseases by 30% were observed. (77). This effect is especially manifested on cases of sudden deaths, the level of which reduced by 50%, which is of great importance for this vulnerable cohort. Similar effects were observed in Japan in the patients for whom statins are prescribed. (JELIS studio). (78) In this case EPA daily doses were 1800 mg and the study lasted 5 years. The data showed that levels of myocardial infarction, unstable angina pectoris, cardiac bypass, angioplasty and stenting was reduced by 19% (p = 0,011)

In other works (79) was noted that Alfa Omega Trial (223 mg EPA plus 149 DHA) has an anti-arrhythmic effect even in relatively low doses. This effect was confirmed in Meta-analysis too. (10, 13, 80)

Thus, we can make a conclusion that a decisive role in the efficacy of food fats belongs to their quality. Long chain omega-3 fatty acids DHA and EPA that are found in cod liver oil produce a protective effect in cardiovascular diseases (unlike shorter chain plant-based omega-3 fatty acids and omega-6 fatty acids LA and AA), which allows to recommend these preparations to patients for prevention of cardiovascular diseases. (81)

AGE RELATED COGNITIVE DECLINE

Aging facilitates reduction of neurons, synapses and brain volume (82), which in its turn leads to decline in cognitive abilities (83). Reduction in grey matter begins after twenties and in the white matter after forties. DHA concentration in the brain substance is also constantly decreasing. Therefore, it can be imagined that due to neurophysiological functions DHA acts as a neurotropic growth factor (84), which improves brain neuroplasticity and stimulates production of synapses (85, 86)

Despite of all mentioned above there are a very few studies that give evidence to the effect of LCPUFA supplementation on cognitive abilities in elderly people, (87), most of the studies were carried out on animals (88, 89). The available human data shows increase in grey matter and increase in brain volume as response to DHA supplementation.

However in these studies there are no clinically relevant endpoints and they are limited to radiological measurements of brain volume. Interesting that DHA supplement to the ratio especially significantly impacts the grey matter, so called cortico limbic system, the area of the brain which presents a functional unity of brain structures responsible for emotionally motivated behaviour, such as nutritional, sexual, defensive instincts. This system is involved in sleep-wake cycle. Impairment in functioning of this area may probably lead to various psychic pathologies. Studies showed that increase of the doses of trans-unsaturated fatty acids in healthy adults may cause reduction in brain atrophy (90).

A few human studies, we have at our disposal, which demonstrate the impact of either DHA or DHA+ EPA on cognitive abilities of elderly people contain contradictory findings (91, 92, 93, 94, 95, 96).

In the work Abubakari et al. (97) are given data on memory improvement due to a low dose supplementation of DHA+ EPA (<1,7 g/d), at the same a higher dose (> 1,7 g/d) was not associated with the effect. (97)

Nevertheless, Cochrane Metaanalyse (2012) reveals no influence of supplementation on improvement of cognitive abilities and reduction of dementia incidence in healthy people after 60 (98).

It is difficult to evaluate reliability of the conclusions because certain factors were not accounted: such as the differences between different omega 3 fatty acids, cod liver oil (mono and combined preparations), between Alzheimer's and other dementia forms. Authors of the actual meta-analysis (2015) basing on more than 15 intervention studies indicate that DHA supplementation of 500–1000 mg/d (50,2) may improve episodic memory in healthy people. This conclusion is valid only in regard to healthy respondents with mild memory complains but by no means in regard to respondents without subjective memory problems and particularly to the respondents diagnosed with dementia.

ALZHEIMER DISEASE

The brain of Alzheimer's patients differs not only with a higher concentration of the β-amyloid but a lower concentrations of DHA and NPD 1 (24, 82). This accounts for the areas responsible for learning abilities and memory. (99) Despite of the fact that most studies confirming the influence of DHA on pathogenesis of Alzheimer's disease were conducted on animals (100, 101), the studies allow to make a conclusion on possible interaction between a daily dose of DHA in ratio and the prevalence of Alzheimer disease (102, 103). In particular there are data that Mediterranean diet can reduce the prevalence of this disease. 104, 105). Anyway these conclusions can be objected. (106, 107, 108) Summing up, it is impossible to state with 100% probability that «the more n 3 FS, the less Alzheimer disease», too many factors should be taken into account while conducting such researches, which makes it to date impossible to single out only the impact of n 3 FS.

The results of intervention studies are more transparent and give evidence that there is no connec-

tion between supplementation of n 3 FS and levels of Alzheimer incidence rate (98) and Alzheimer dementia (109, 103, 110, 111)

Similar situation is observed with Parkinson's disease: there are numerous experiments on mice, which showed that DHA acts neuroptotectively and anti-inflammatory on dopaminergic neurons (112, 113, 114, 115, 116, 117, 118) and in animal experiments with Parkinson's models DHA reduce dopamine-dependent movement disorders. (119,120). However, there is no data confirming protective and therapeutic influence of n3 FS supplementation on the condition of Parkinson's patient. Scientists in general doubt that the result of experiment on mice can be extrapolated on humans and thus explain why most of animal-tested medications do not pass the tests in clinical trials.

Despite the divergence of the regulatory landscape between mouse and human, the pattern of chromatin states (defined by histone modifications) and the large-scale chromatin domains are highly similar between the two species. Half of the genome is well conserved in replication timing (and by proxy, chromatin interaction compartment) with the other half highly plastic both between cell types and between species. It will be interesting to investigate the significance of these conserved and divergent classes of DNA elements at different scales, both with regard to the forces driving evolution and for implications of the use of the laboratory mouse as a model for human disease. (2014) (121)

Most optimistic data on n3 FS influence on neuropsychiatric diseases is provided in regard to EPA supplementation of depression. This is confirmed by large meta-analyses, placebo controlled intervention studies, which report that a daily consumption EPA (200 -2200 mg/d), but not DHA significantly reduce depressive symptoms. (121, 122). At combined administration it is necessary to account that correlation of EPA/ DHA > 60% (121)

Nevertheless, unfortunately there is no evidence of the equally effective impact of LCPUFA supplementation for bipolar disorders (123), borderline disorders, (124), schizophrenia (125), autism (126), children with specific learning disorders (127), or attention deficits and hyperactivity in children (128) (children with ADHS).

Therefore, obviously that the quality of fats is decisive on the possibility of prevention of cardiovascular diseases. On the other hand it refers only to the impact of cod liver oil containing EPA and DHA. There are reliable and available data of prospective and randomised studies as well as meta-analyses, confirming this. Probably it does not spread on other fatty acids, such as shorter chain plant based n-3 PUFAs или n-6 PUFAs. So far accordingly to the latest data Long-chain polyunsaturated fatty acids (LCPUFA) produce important positive effects on a number of most essential functions of the human body but in the first line on the prevention of cardiovascular diseases.

In this connection nutritional supplementation of long-chain polyunsaturated fatty acids (LCPUFA) is recommended or 1-2 portion of fish which according to recommendation of German Nutrition Society should be 80 – 150 grams of low fat fish (salmon, sea perch, cod) and 70 grams of fat fish (herring, mackerels) per week (2,3).

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PECULIARITIES OF OSTEOPOROSIS IN COPD PATIENTS

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ABSTRACT — The high incidence of osteoporosis in patients with chronic obstructive pulmonary disease (COPD) explains relevance of our study. 79 women (overage age 66,9 ± 1,7 years) with postmenopausal osteoporosis without steroid treatment have been examined in order to identify peculiarities of osteoporosis in female population with COPD. Our Results showed that COPD patients demonstrate significantly lower values of FEV1, forearm BMD, forearm T-score and significantly more frequent forearm fractures to be compared with patients without obstructive lung disease and with bronchial asthma. Conclusions: Patients with COPD demonstrate more severe course of postmenopausal osteoporosis.

KEYWORDS — COPD, Osteoporosis, FRAX, fractures, T-score.

INTRODUCTION

The Chronic Obstructive Pulmonary Disease (COPD) is socially significant pathology and according to WHO data takes the 4th place in structure of mortality [1]. According to the BOLD study prevalence of GOLD II and more severe stages (GOLD III, IV) of COPD among persons senior than 40 years is approximately 10,1±4,8% in whole groop; 11,8±7,9% — for men and 8,5±5,8% — for women [3]. According to the GARD study [4, 5] conducted in Russia high prevalence of chronic respiratory diseases was revealed. The spirometric research data showed that 21,8% of respondents corresponded to COPD criteria. The extrapolation of these data on the general population showed that expected amount of patients with spirometric criteria of COPD must be approximately 15,3% of the Russian population, or 21 986 100 people, more than 9,3 times higher than official statistical data (2 355 275,6 people) [6]. The definition of COPD in the GOLD 2015 document tells that "COPD is a common preventable and treatable disease, which is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients"[2]. In addition to respiratory tract pathology, systemic effects of COPD due to systemic inflammation [9] with great

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role of cytokines (such as FNO-α, IL-1β and IL-6) [10, 11, 12] are described. Cachexia with loss of fat mass, hypotrophy and atrophy of skeletal muscles, depression, anemia, the increased risk of development of cardiovascular diseases, and osteoporosis are among the large number of comorbidities due to systemic inflamation [7, 8]. The World Health Organization in 1994 recognized osteoporosis (OP) "as general metabolic disease for which decrease in density of bone, the disturbance of its microarchitecture leading to increase of risk of fractures" [1]. The Russian epidemiological researches have shown that in age of 50 years and more osteoporosis is observed in 30–33% women and 22–24% men that makes more than 10 million people [14]. Frequency of osteoporosis (OP) in COPD patients in 2014 is 28–34%, according to official data of the Russian Respiratory Society [13]. Spontaneous, and also low-traumatic fractures define the medical social importance of OP. The femoral neck fractures have the greatest medical and social importance due to high invalidisation and mortality of patients. Frequency of femoral neck fractures in Russia in persons over 50 years and more has averaged 105,9 on 100 000 population, and is more often in women — 122,5, then in men — 78,8. The frequency of forearm fractures is observed more often in women population (563 on 100 000 people), than at men (426 on 100 000 population) too. Average values of mortality in Russia is 30–35%. 78% of the survived patients in year after fracture and 65,5% patients in two years after fracture needs permanent third-party assistance [15, 16]. There is increase of new cases of OP and osteopenia in process of pulmonary diseases progression [19, 20]. OP frequency was especially high at patients with end-stage of different chronic pulmonary diseases, including COPD, to be the candidates for lung transplantation [21]. Some authors speak about natural to "age comorbidity" of COPD and OP [17, 18].

THE MAIN AIM

of our work was to determine the osteoporosis peculiarities in elder women with obstructive lung diseases.

MATERIALS AND METHODS

We have examined 79 women with post-menopausal osteoporosis with middle age of 66,9±1,7 years. All women did not use oral glucocorticoid therapy. All patients under examination have been divided into 3 groups. 31 non-smoking women with the bronchial asthma (BA) with middle age of 65,9 ±2 years formed the first group. The second group included 23 smoking patients with COPD with middle age of 67,7±2,3 years. The average experience of smoking was approximately 14±2,2 packs/years. All patients of the first and second groups received inhaled glucocorticoids in daily dose of 1000 mkg (beclomethasone). The third group included 25 women without lung disease and smoking experience. The complex lung function examination including spirometry (MasterScreen spirograph) with the reversibility test, osteodensitometry(DXA) on the densitometer Lunar Prodigy General Electric (GE Healthcare) with assessment of bone mineral density(BMD) and T-score in femoral neck, lumbar spine and forearm, risks of law-traumatic fractures during 10 years with use of FRAX®, the tool to assessment risk of fractures developed by WHO (https://www.shef.ac.uk/FRAX/index.aspx), has been defined to all patients.

STATISTICAL ANALYSES

was carried out with IBM SPSS V.19.0 program (USA). Comparison of groups was done by means of the nonparametric Mann-Whitney test for quantitative variables and the Chi-square — for categorial signs. Pearson coefficient was used for carrying out the correlation analysis. Statistically significant we considered distinctions at $p < 0,05$.

RESULTS

The main characteristics of the studied parameters are provided in Table 1. Patients with COPD had a significantly lower value of FEV1, forearm BMI, T-score in forearm ($p \leq 0,05$) then patients with bronchial asthma and without lung disease. Fractures have been met more often in COPD patient to be compared with patients with BA. No significant distinctions in bone density indicators were found between patients with BA and subjects without lung diseases. However tendency for more frequent cases of fractures in BA patients was found due to values of BMD.

Table 1 and figure 1 show that FEV1, forearm BMD, T-score of forearm were significant lower in COPD patients to be compared with bronchial asthma patients and women without lung disease ($p \leq 0,05$). The greatest frequency of forearm and vertebral fractures were also observed in COPD patients.

The major osteoporotic and hip fractures risk assessment during 10 years in investigate group of patients are provided in table 2 and diagram 2.

As can be seen from table 2 and diagram 2 hip the major osteoporotic and hip fractures risk assessment during 10 years were higher in patients with obstructive lung diseases. The 10 years hip fractures risk was statistically significantly higher in COPD patients.

Results of the correlation analysis using Pearson's criteria between spirometry (pre-FEV1 and post-FEV1) and densitometry indexes in patients with obstructive lung diseases and in control group are provided in table 3.

Table 1. *The main indicators of BMD, T-score and obstruction level in patients of the different groups. (n± standard deviation)*

Group/ title	n	the average age	FEV1 %	Forearm BMD	Forearm T-score	Forearm fractures frequency (%)	Vertebral fractures frequency (%)
1 (Bronchial Asthma)	31	65,9±2,0	76,8±3,9	0,63±0,02	-2,80±0,17	51,6	19,3
2 (COPD)	23	67,7±2,3	57,1±3,6[1]	0,57±0,02[1]	-3,37±0,18[1]	65,2	34,8
3 (Without lung disease)	25	67,5±2,0	92,9±1,5[2,3]	0,63±0,02[2]	-2,67±0,2[2]	44,0	16,0

1 — p<0,05 in comparison of group 1 and 2
2 — p<0,05 in comparison of group 2 and 3
3 — p<0,05 in comparison of group 1 and 3

Table 2. *FRAX indicators in groups, n± standard deviation*

Group/title	n	10-year probability of a major osteoporotic fracture (FRAX)®	10-year probability of hip fracture(FRAX)®
1 (Bronchial Asthma)	31	20,47± 1,102	5, 216± 0,7271
2 (COPD)	23	21,74± 1,1582	7,909± 0,73134
3 (Without lung disease)	25	16, 47± 1,0763	4, 264± 0,7159

1 — p≤0,05 in comparison of group 1 and 2
2 — p≤0,05 in comparison of group 2 and 3
3 — p≤0,05 in comparison of group 1 and 3
4 — p≤0,05 in comparison of group 2 and 3

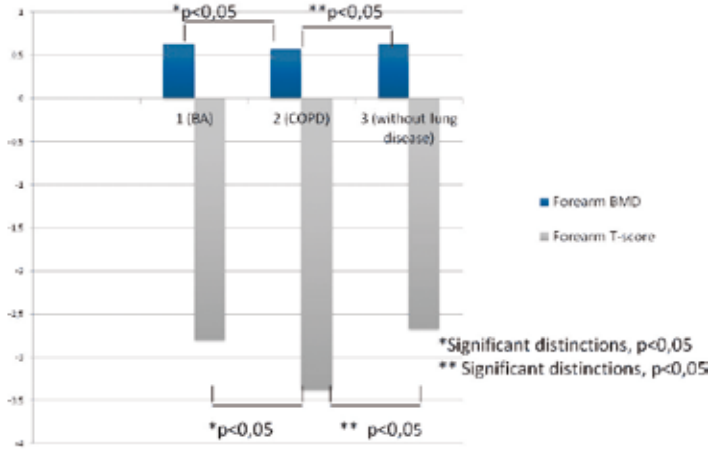

Figure 1. The mean value of BMD, T-score in patients with COPD and BA compared with control group without obstructive pathology.

Fig. 1. *The mean value of BMD, T-score in patients with COPD and BA compared with control group without obstructive pathology.*

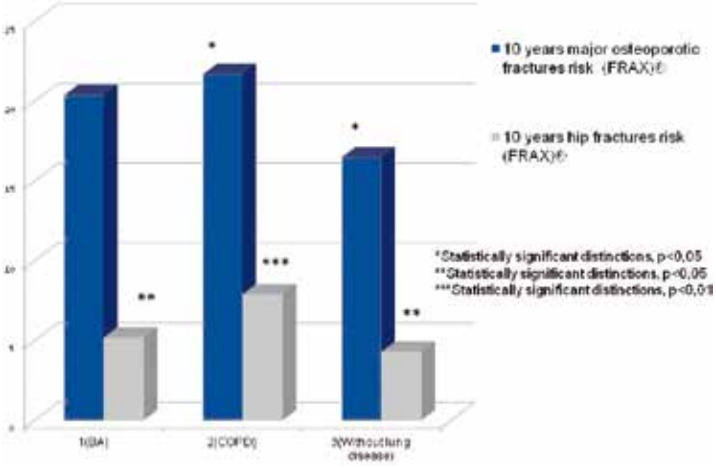

Figure 2. *10 years fractures risk in different groups (n± standard deviation)*

As can be seen from table 3, statistically reliable positive correlation between FEV1 values and densitometry data in patients with obstructive lung diseases (both BA and COPD) were revealed. Patients with COPD has greater number of this correlations. Statistically reliable correlations between FEV1 values and densitometry data in patients without lung diseases has not been revealed.

DISCUSSION AND CONCLUSIONS

The course of OP in COPD patients has certain peculiarities. OP proceeds with higher loss of bone mass compared to patients without COPD, often complicated with bones fractures. Our data demonstrate more severe duration of osteoporosis

Table 3. *The results of correlation analyses of spirometry and of densitometry indexes in different groups of patients.*

	Group/Title	1(Bronchial Asthma)	2(COPD)	3(Without lung disease)
Pre-FEV1 %	Femoral neck BMD	p>0,05	p<0,01 R= 0,611**	p>0,05
	Femoral neck T-score	p>0,05	p<0,01 R= 0,643**	p>0,05
	Forearm T-score	p<0,05 R= 0,413*	p<0,01 R= 0,546**	p>0,05
	Forearm BMD	p<0,01 R=0,457**	p<0,05 R= 0,418*	p>0,05
Post-FEV1 %	Femoral neck BMD	p>0,05	p<0,05 R= 0,452*	p>0,05
	Femoral neck T-score	p>0,05	p<0,05 R=0,489*	p>0,05
	Forearm T-score	p>0,05	p<0,05 R=0,389*	p>0,05
	Forearm BMD	p<0,01 R= 0,427**	p>0,05	p>0,05

** statistically reliable with p <0,05*
*** statistically reliable with p <0,01*

in COPD patients in comparison to BA patients and patients without lung diseases. It is confirmed by authentically significant decrease in values of BMI and T-score of forearm, statistically reliable increase in 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) and hip fractures (FRAX) at these patients. The main role of disturbances in bone metabolism in COPD patients is most probably related with smoking status and systemic inflammation. No differences in course of OP between BA and control group suggests minimal impact of allergic inflammation and inhaled glucocorticosteroid therapy on bone metabolism.

The conflicts of interests are absent.

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TREATMENT OF GONARTHROSIS USING OZONE THERAPY IN A REHABILITATION DEPARTMENT

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We used ozone therapy to treat patients with gonarthrosis. We used the introduction of ozone-oxygen mixture, parenteral (layer-by-layer maintenance: subcutaneous, tendon, injection), the soft tissue around the knee joint (anterior and posterior surfaces). The ozone-oxygen mixture we injected in both knee joints (even if clinical changes were only in one joint). On one session, we used up to 20 ml of the mixture, which was injected at a depth of 1–3 cm ozone Concentration of 5 mg/l. the Treatment was performed daily for 7 days. After the introduction of ozone was carried out by light relaxing massage of the joint area for 3–5 minutes (to evenly distribute the gas under the skin). The course of treatment consisted of 7 sessions. With this method of treatment mechanism of action of ozone was mainly anti-inflammatory, antihypoxic (Russia patent of invention № 2413548, Authors: A.G. Remnev and A.A. Oleynikov, 2009).

Our research involves the study of 253 patients with deforming osteoarthritis. Stage of remission or partial remission. Group 1 patients — 137 persons (age between 55 and 68 years) received complex ozone therapy. Group 2 patients — 116 people (age between 56 and 63 years) received nonsteroidal anti-inflammatory drugs (Voltaren®, Diclofenac®, Ortofen®) and massage. Subjective treatment outcomes (the nature and intensity of pain) we were evaluated on 3 point scale and, by definition, limits movement in the joint (due to pain due to bone changes), pain in joints (palpation and when moving). Objective of instrumental diagnostic methods we applied x-rays of the knee and ultrasonography of the knee. The effectiveness of the treatment we evaluated on three levels: significant improvement, moderate improvement, no improvement.

THE RESULTS OF TREATMENT

In group 1 all patients reported positive results. Of these, 98 patients (72%) improved, confirmed by instrumental methods of research (primarily, the reduction or disappearance of the signs of bursitis, synoviitis, and effusion in the upper volvulus front). Increased range of motion, decreased pain in the joint. Laboratory data did not change significantly during the treatment. In group 2, 45 patients (39%) reported positive results, not confirmed by instrumental methods. Long-term results after 6 months. In group 1 in 71 patients remained a positive effect. In group 2 the positive effect was preserved in 9 patients.

Thus, the use of ozone therapy allows to achieve lasting positive effect in the treatment of gonarthrosis deforming in the Department of rehabilitation.

APPLICATION OF A NEW METHOD OF DIAGNOSIS OF VARICOSE VEINS ANTERIOR RADICULAR LUMBAR SPINE

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Varicose epidural veins in the lumbar spine – a pathological condition in which there is an expansion of the epidural venous plexus, increased pressure in the veins, depositing a large amount of blood. Because of this, the extension veins is compression of the dural area and spinal nerve roots. Diagnosis of this pathological condition is complicated, often interpreted incorrectly. At the sanatorium Barnaul we have developed a new method for the diagnosis of varicose anterior radicular veins of the lumbar spine (invention Patent of Russia № 2372849, Authors: A. G. Remnyov, A. A. Oleynikov, 2008).

The essence of this invention lies in the fact that for the visualization of the anterior radicular veins change the scanning plane with the lateral edge e of the convex probe is rotated cranially at an angle of 20 degrees, estimate the diameter of the anterior radicular veins and increasing the diameter to 3.01±0.43 mm or more are diagnosed with varicose veins of the anterior root in the direction of increasing diameter. The technical result is providing an objective visual determination of blood flow in the anterior radicular veins of the lumbar spine, the determination of the exact localization of the pathological process in the form of varicose anterior radicular veins of the lumbar spine, improving the quality of studies and enabling control of the results of treatment in the presence of varicose anterior radicular veins of the lumbar spine. In accordance with the claimed method the studied group of healthy patients (39) aged from 19 to 26 years old. In the study of the inventive method a group of healthy patients radicular veins on the monitor of the ultrasound scanner was defined as colored red stripe. Form the strip straight, smooth edge. When measuring diameters of the anterior radicular veins of the right and left values did not exceed 1 mm in all patients. In the study group of patients (84 patients aged 25–49 years) with signs of impaired venous blood flow at the level of the lumbar spine was determined signs of varicose veins of the anterior root at various levels of the lumbar spine, right and left. These features were expressed as an increase in diameter of the anterior root veins from 2.4 mm to 5.0 mm (average of 3.07±0,42).

Thus, the use of this method allows for an objective visual determination of blood flow in the anterior radicular veins of the lumbar spine, to establish exact localization of pathological process in the form of varicose anterior radicular veins of the lumbar spine, as well as to ensure the possibility of controlling the results of treatment in the presence of varicose anterior radicular veins of the lumbar spine.

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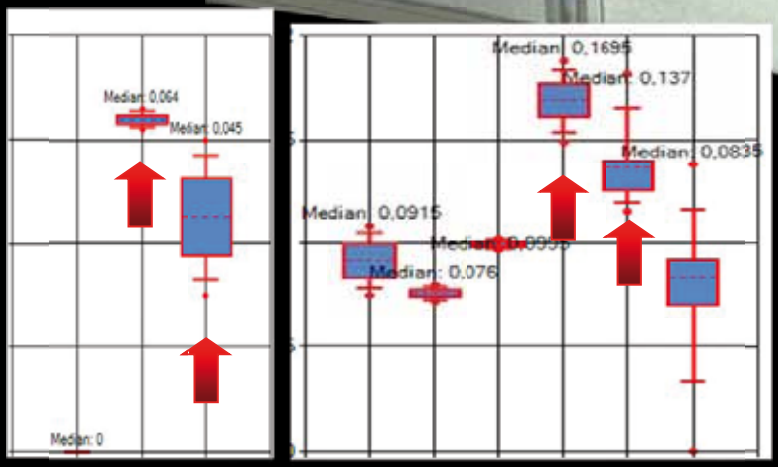

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