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# CONTENTS

<p><i>I.P. Artyukhov, O.S. Shilkina, N.A. Shnayder, D.V. Dmitrenko E.N. Bochanova, I.S. Babina</i></p> <p><b>PARADIGMS IN MANAGEMENT OF JUVENILE MYOCLONIC EPILEPSY .....2</b></p>	<p><i>C. K. B. Ferrari, A. L. Vieira dos Santos, G. S. L. Ferrari, S. R. B. Cavalcante</i></p> <p><b>QUALITY OF LIFE AND SLEEPINESS AMONG GRADUATE STUDENTS OF NURSING AND PHARMACY FROM A FEDERAL UNIVERSITY IN MATO GROSSO, BRAZIL .....30</b></p>
<p><i>G. Becher, S. Heymann, O. Marksteder, R. Purkhart, J. Schulz</i></p> <p><b>EVALUATION OF THERAPEUTIC BIOCORRECTION BY EXHALED MARKERS OF METABOLISM A PILOT STUDY .....8</b></p>	<p><i>O.A. Ovsyannikova, A.A. Zhidovinov, D.V. Karpeeva, M.D. Osipenko, A.V. Naumov, D.A. Shikunov, T.A. Shishkina</i></p> <p><b>FEATURES OF CHANGES OF THE ERYTHROBLASTIC ISLANDS ON THE STAGES OF POSTNATAL ONTOGENESIS UNDER TOXIC STRESS AND PHARMACOLOGICAL CORRECTION .....34</b></p>
<p><i>E. Bespalova, M. Gordeeva, O. Pitirimova, M. Bartagova, R. Gasanova, A. Tuymeneva, O. Kosticova</i></p> <p><b>ULTRASOUND DIAGNOSTIC CRITERIA OF TAUSSIG-BING ANOMALY IN FETUS .....15</b></p>	<p><i>K.I. Sergatskiy, V.I. Nikolsky, S.A. Budachev</i></p> <p><b>TREATMENT OF PATIENTS WITH ACUTE PARAPROCTITIS AGAINST THE BACKGROUND OF THE INOPERABLE MALIGNANT TUMORS OF THE RECTUM .....38</b></p>
<p><i>D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko</i></p> <p><b>CORRELATION OF DENTAL ARCH MAJOR LINEAR PARAMETERS AND ODONTOMETRIC INDICES GIVEN PHYSIOLOGICAL OCCLUSION OF PERMANENT TEETH IN VARIOUS FACE TYPES .....18</b></p>	<p><i>M.G. Sokolova, S.V. Lobzin, I.V. Litvinenko, V.A. Penniyaynen, M.V. Rezvantsev</i></p> <p><b>SEARCH FOR NEW APPROACHES TO TREATING PATIENTS WITH SPINAL MUSCULAR ATROPHY, 2 TYPE AS PART OF CLINICAL-EXPERIMENTAL STUDY .....41</b></p>
<p><i>D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko</i></p> <p><b>MISTAKES IN PONT (LINDER-HARTH) METHOD USED FOR DIAGNOSING ABNORMAL DENTAL ARCHES IN TRANSVERSAL PLANE .....23</b></p>	
<p><i>T.N. Doronina, N.S. Cherkasov, A.A. Zhidovinov</i></p> <p><b>THE PECULIARITIES OF MYOCARDIAL CONDITION ESTIMATION IN INTERATRIAL SEPTAL DEFECTS IN CHILDREN OF EARLY AGE .....27</b></p>	

# PARADIGMS IN MANAGEMENT OF JUVENILE MYOCLONIC EPILEPSY

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**ABSTRACT** — Juvenile myoclonic epilepsy (JME) is one of the most common forms of idiopathic generalized epilepsy. In this article we describe the results of a clinical study into JME management in patients living in the Siberian Federal District. We show that late diagnosis, misdiagnosis and inadequate treatment of JME most often arise due to incompetent management of primary care, rather than as a result of the complexity of clinical symptoms. The outcomes from this study give a deeper insight into the diagnosis and prognosis of this form of idiopathic generalized epilepsy.

**KEYWORDS** — Idiopathic Generalized Epilepsy, Juvenile Myoclonic Epilepsy, Clinic, Management, Delayed Diagnosis, Prognosis

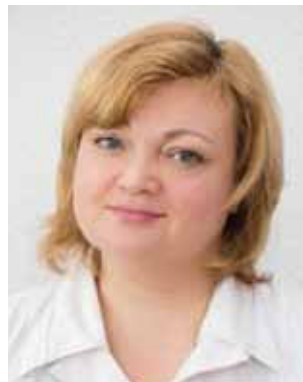
## INTRODUCTION

Juvenile myoclonic epilepsy (JME) is one of the most common forms of idiopathic generalized epilepsy debuting in adolescence, and it is characterized by the

appearance of massive myoclonic seizures arising in the period after awakening. Debut age for JME varies from 7 to 21 years, with a peak in the age range 11–15 years. In some cases, the disease can begin at an earlier



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age with absence seizures or generalized seizures, with subsequent gain of myoclonic seizures in adolescence. Consciousness is maintained at the time of myoclonic seizures; they arise or become more frequent in the first minutes and hours after awakening. In 90% of diagnosed cases these coincide with generalized seizures and in 40% of patients these are additionally accompanied by short absences of juvenile kind [1, 2].

Usually establishing JME diagnosis is not difficult because of the "bright" clinical picture. However clinical practice shows that the correct diagnosis of the disease is frequently delayed [3, 4, 5].

Special statistical study of diagnostic errors in JME diagnosis in London, UK, conducted by Panayiotopoulos S.P. et al. (1992), showed that from 180 epilepsy patients examined, 15 were diagnosed with JME. Yet upon admission to hospital, diagnosis was correctly identified only in one patient. The average time of JME diagnosis was 14.5 years after the debut of epilepsy. Furthermore, seven patients were prescribed inappropriate anticonvulsants [6].

In a study by P. Genton et al. (2000), the authors found that diagnosis of JME was not made correctly in any of the cases prior to the admission of patients to a specialized epilepsy center in Marseille (France) [7].

Similarly to the aforementioned studies, our own clinical observations suggest repeated errors in the diagnosis of JME [8].

Nevertheless, the timely diagnosis of JME is crucial for the correct management of symptoms and prevention of disease development [9].

In general, excellent seizure control can be achieved in JME patients with relatively low doses of appropriate anticonvulsants [10].

Traditionally, treatment of JME in the XX–XXI centuries was carried out via administration of valproic acid (VA). High efficacy of VA in relieving all types of seizures was demonstrated in patients with JME (myoclonus, generalized seizures, absence seizures), and this drug type was firmly established as the gold standard in the treatment of this form of epilepsy.

Where effectiveness of valproate was suboptimal, they always featured in combination therapy with succinimides (in resistant absences), PB (in resistant GSP), and with clonazepam (in expressed myoclonus and photosensitivity). However, new broad-spectrum antiepileptic drugs (AEDs) have been developed in recent years (LTD, TPM, LEV) and several publications demonstrated their efficacy in JME.

Literature strongly suggests that levetiracetam may be used as a first-line drug in the treatment of JME. Levetiracetam was demonstrated to be as effective as valproate, with significant advantages over it safety criteria. Despite having favorable tolerability

profile, Lamotrigine was not sufficiently effective in a monotherapy in JME patients. In addition, in some cases it led to an aggravation of seizures (in particular, myoclonus). Topiramate was shown to be highly effective for GSP, but demonstrated reduced efficacy with absences and myoclonus [11].

It is important to keep in mind that seizures may aggravate and side effects could be detrimental with ineffective treatment, which could reduce the quality of life of JME patients. When managing patients with JME, administration of diuretics and vascular drugs that increase blood flow and perfusion to the area of epileptogenesis, should be avoided, as there is no liquorodynamic dysfunction in JME.

Despite a relatively easy control of the seizures on appropriate treatment, JME is considered to be a chronic disease with a life-long duration. The issue of remission upon termination of AEDs in JME patients is currently under debate. According to Martinez-Juarez et al. (2006), only 5% of JME patients who stopped AEDs demonstrated no recurrence of seizures [12]. Yet according to the observations of B. Baykan et al., this figure is about 10% [13].

Similarly, favorable prognosis in patients with JME was not confirmed by Russian groups [14]. However long-term remission with AEDs cancellation was reported in some patients [15]. According to C. Camfield & P. Camfield (2009), cessation of all types of seizures was observed in 17% of patients with JME, with only myoclonus remaining in 13% after the completion of AEDs [16]. Nonetheless, often JME is diagnosed late due to disease progression or inadequate therapy, with significant reduction in the patients' quality of life [17]. Previously, we proposed a variety of enhancements for the accurate diagnosis of JME [8, 18, 19]. In this study, we evaluated the quality of care for patients with JME in the Siberian Federal District.

#### *Aim:*

to identify and analyze problems of management and repeated diagnostic errors in JME diagnosis.

## MATERIALS AND METHODS

### *Study Design*

This study was conducted in the Neurological Center of Epileptology, Neurogenetics and Brain Research (hereinafter — NC UH) of the Voino-Yasensky Krasnoyarsk State Medical University Hospital, Krasnoyarsk-city, Siberia, Russia. It was performed as part of a complex research project No. 210-16 "Epidemiological, genetic and neurophysiological aspects of nervous system disorders (central, peripheral, autonomic) and preventive medicine" (state registration No 0120.0807480).

### Participants

We randomly selected 124 patients with JME, who were diagnosed between 2006 and 2016. All patients were Siberian Federal District's residents and underwent preliminary anamnestic and clinical selection using stratified randomization. In accordance with the Declaration of Helsinki, all of the participants signed informed consent. The study was approved by the local ethics committee of the Voyno-Yasenetsky Krasnoyarsk State Medical University.

### Procedures

JME diagnosis was verified in all patients enrolled in this study using video-EEG monitoring with carrying out stress tests. The latter included rhythmic photostimulation (RPS); trigger photo-stimulation (TPS), hyperventilation (HV) and according to preliminary findings, sleep deprivation. Female participants were monitored during peri-menstrual cycle, taking into account fluctuations in estrogen levels, which have the potential to promote convulsions. Additionally we tested the level of consciousness during the functional tests (RPS, TPS and HV), with serial counting aloud while standing with outstretched arms (all necessary precautions were taken to ensure patients' safety in the event of loss of balance or consciousness). All patients underwent brain MRI (1.5 Tesla or higher). Detailed analysis of disease history for each patient included debut age, the type of epileptic seizures at debut and the dynamics of the disease progression.

### Statistical Analysis

All statistical analyses were carried out using licensed software package SPSS, version 20.0 (USA). Data with nonparametric distribution were presented as median and quartile (Me [P25; P75]); otherwise, average mean and standard error were used. For a comparative analysis of quality indicators in two groups of patients, chi-squared test and Fisher's exact test (for small sample sizes) were used. Values were considered statistically-significant when  $p < 0.05$ .

## RESULTS

We enrolled 123 patients with JME for this study, with the following geographical distribution: 50.4% were residents of Krasnoyarsk (62 cases), 38.2% — of Krasnoyarsk Territory regions (47 cases) and 11.4% were from the neighboring regions of the Siberian Federal District (14 cases). Age debut of the disease varied between 2 and 29 years, with average of  $13.28 \pm 0.42$  years, and median of 14 (11:16) years.

Age of original diagnosis varied between 7 and 54 years old, with average age of  $22.46 \pm 0.73$  years old, and a median of 20 (17:26) years old. The time be-

tween onset of the disease and diagnosis of JME varied between 0 and 41 years of age, with average time of  $9.5 \pm 0.78$  years and median of 7 (2:16) years.

In 68 of 123 cases (55.3%) there were mistakes in the appropriate management of JME before enrolling to the NC UH: in Krasnoyarsk there were 34 cases from 62 (54.8%), which was the same in comparison with the cities of Krasnoyarsk Territory and other regions of the Siberian Federal District that were 27 from 47 cases (57.4%) and 7 cases from 14 (50%), respectively ( $p > 0.05$ ). Upon review of medical errors, mistakes in the original diagnosis were identified in 40 out of 68 cases (58.8%); inadequate therapy for the disease onset was prescribed in 45 out of 68 cases (66.2%), incorrect dose of AEDs was prescribed in 14 out of 68 cases (13.6%) and irrational combination of drugs — in 14 out of 68 cases (13.6%).

In all cases, before referral to the NC UH there were no registered reports of any side effects from AEDs in the medical records, even if they had it in the past, or at the time of referral. In addition, no pharmacogenetic profile was specified in any of the cases, including those with side effects from AEDs. It should be noted that therapeutic drug monitoring and pharmacogenetic studies of liver cytochrome P450 isozyme genes (CYP1A1, CYP2C9, CYP2D6, CYP2E2) are readily available in Krasnoyarsk and are inexpensive.

All the patients with confirmed JME were recommended therapeutic drug monitoring (TDM) and in 54 (43.9%) of 123 cases, a blood test to study polymorphisms of cytochrome P450 isozymes genes had been advised. In 36 out of 54 cases, the analysis was performed, with compliance for a molecular-genetic study of 66.7%. In 19 cases of 36 (52.8%), adverse pharmacogenetic profile was identified (so-called "slow metabolizers") which required dose corrections, regular TDM (at least once every 3 months), or a change in AEDs, in case of serious side effects.

All identified AED side effects in patient's medical history and at the time of referral were included in the Register of the Side Effects from AEDs, which was compiled by the NC UH in conjunction with clinical pharmacologists. The Register's main aim is to analyze and provide solutions for any difficulties associated with therapeutic management of epilepsy, including JME, in the Siberian population. In accordance with the current Russian legislation (Federal Law of December 22, 2014 N 429-FL, Article 64-66), all current side effects from AEDs are recorded and sent to the National Health Control Authority.

## DISCUSSION

Typical electroencephalographic abnormalities are highly supportive of the clinical diagnosis of JME.

However the clinical scenario might not be as clear as the classical description would suggest. Delayed diagnosis (and/or misdiagnosis) of JME directly impacts development of the disease. Inadequate treatment allows aggravation of seizures and worsening of the condition, alongside undesired side effects and emotional stress, all of which significantly reduce patients' quality of life.

It is essential that a patient's anamnesis is thorough and detailed. This can be facilitated by active questioning about presence of myoclonic seizures in patients, who may be ignoring (or not remembering) these episodes, especially at first presence. In addition, family members, friends, classmates and teachers could be quizzed to get a more complete picture of the disease. Awareness should be raised among GPs to flag such conditions and thoroughly investigate causes of seizures.

It is important to keep in mind the possibility of childhood or juvenile absence epilepsy transformation into JME in young patients to maximize a timely and correct diagnosis [18]. Catching JME early will enable correct management of the disease and subsequent long-term improvement in quality of life.

The selection of antiepileptic drugs for the treatment of JME depends on several factors, including the patient's comorbidities, preferences, previous history of adverse events, gender and pharmaco-genetics [20]. In most patients with JME, seizures are well controlled with monotherapy. Valproic acid has been considered the treatment of choice for JME for many years, but epileptologists are increasingly using other choices as first-line therapies. Approximately 80% of patients with JME become seizure-free with valproate monotherapy. A low-dose requirement is not unusual; in fact, the great majority of patients with JME need relatively low levels of anticonvulsants to achieve adequate seizure control (as long as it is an appropriate medication for the syndrome). A great majority of children born to women taking anticonvulsant monotherapy are healthy [22]. Valproic acid and divalproex sodium clearly pose a recognized risk of neural-tube defects (category D) that is higher than the risk associated with older anticonvulsants. Evidence suggests that supplementation with folic acid may decrease this risk.

In general, low doses of appropriate anticonvulsants are needed to successfully treat JME. Although treatment with phenytoin, carbamazepine, or phenobarbital may control some seizure components of JME (typically at high doses), these drugs may increase seizure frequency (eg, myoclonic exacerbation with carbamazepine) and occasionally precipitate new seizure types, such as absence seizures [21, 22, 23].

As this study demonstrates, JME diagnosis was established at an average of 9.5 years of age in the Siberian Federal District, which is comparable with the

results of the Panayiotopoulos S.P. et al. (1992) study [6].

Errors in the management of JME, including inadequate treatment and incorrect dosage of drugs, were more common in remote regions of the Krasnoyarsk region, Siberian Federal District, compared with the city of Krasnoyarsk. At the same time, errors of the diagnostic management, including errors in diagnosis and irrational drug combinations, did not vary significantly between the regions. In all cases, modern approaches to personalized treatment of JME, including the study of pharmaco-genetic profile, were not used as a primary method. All identified errors were eliminated after the treatment of patients in a specialized neurological center of epileptology, NC UH, which improved both, the quality and the safety of treatment.

Repeat cases of prescription of sub-optimal drugs for this form of epilepsy, which could aggravate the seizures and contribute to progression of the disease, even with the correct original JME diagnosis, remain a stereotypical mistake of the neurologists around the world. [5, 7]. These mistakes are systemic, witnessed in over 50% of diagnosed cases, both in Russia and abroad. They continue to register in the XXI century and in comparison with the XX century, did not tend to decrease, despite rapid developments in the field of neurophysiology, neurogenetics, neuroimaging. Thus we can conclude that there is an imminent need to change the paradigm of JME management, with introduction of a new disease management model that will be based on years of experience and modern achievements in science and practice. Numerous domestic and foreign studies report the aforementioned issues, yet no feasible ways to resolve it have been suggested to date. We propose that to solve the problem of JME management will only be possible via combined efforts of clinicians and health managers, with organization of regular local, regional and specialized conferences aimed at review of individual cases and system errors in JME management. In addition, it is important to develop new paradigm of JME management which based on modern achievements of science and practice.

## CONCLUSION

Thus, repeated mistakes in diagnosis and treatment of JME are a problem of management and continuity of patient management among physicians in primary health care. It is important to resolve this problem, both at clinical and institutional level, including medical practitioners, health administrators and clinical pharmacologists.

Specialized epilepsy centers play a key role in the identification and correction of diagnostic and therapeutic management errors of JME and organizing educational programs for primary care physicians.

**Table 1.** Diagnostic and therapeutic mistakes in JME management.

Management problem	Total (N=123)	Krasnoyarsk (n1=62)	Krasnoyarsk territory (n2=47)	Siberia district (n3=14)	P value
1	2	3	4	5	6
Mistakes in JME management	68 (55.3%)	34 (54.8%)	27 (57.4%)	7 (50%)	$p_{3,4}=0.0003$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$
Mistakes in JME diagnosis	40 (58.8%)	23 (37%)	12 (25.5%)	6 (42.9%)	$p_{3,4}=0.0001$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$
Inadequate therapy of JME	45 (66.2%)	22 (13.2%)	18 (38.3%)	5 (35.7%)	$p_{3,4}=0.0001$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$
Incorrect dose of AEDs	14 (13.6%)	4 (6.5%)	9 (19.1%)	1 (7.1%)	# $p_{3,4}=0.0678$ # $p_{4,5}=0.3232$ # $p_{3,5}=0.6512$
Irrational combination of drugs	14 (13.6%)	10 (16.1%)	4 (8.5%)	1 (7.1%)	# $p_{3,4}=0.2284$ # $p_{4,5}=0.6823$ # $p_{3,5}=0.3951$
Lack of therapeutic drug monitoring	123 (100%)	62 (100%)	47 (100%)	14 (100%)	$p_{3,4}=0.0001$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$
Lack of side effects of AEDs monitoring	123 (100%)	62 (100%)	47 (100%)	14 (100%)	$p_{3,4}=0.0001$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$
Lack of pharmacogenetic monitoring	123 (100%)	62 (100%)	47 (100%)	14 (100%)	$p_{3,4}=0.0001$ $p_{4,5}=0.0001$ $p_{3,5}=0.0001$

$p$  = chi-square test; # $p$  = Fisher's test.

## REFERENCES

1. **MUKHIN K.Y., PETRUHIN A.S.** Idiopathic forms of epilepsy: systematics, diagnosis, therapy. Moscow: Art-Business-Center. 2000: 319. (In Russian)
2. **SHNAYDER N.A., SHAPOVALOVA E.A., DIMITRENKO D.V., ET AL.** The epidemiology of childhood epilepsy. Siberian Medical Review. 2012; 74(2): 44–50. (In Russian)
3. **KARLOV V.A.** Epilepsy in children and adults, women and men. Guide for physicians. Moscow: Medicine, 2010: 244–248. (In Russian)
4. **JANZ D.** Epilepsy with impulsive petit mal (juvenile myoclonic epilepsy). Acta Neurol Scand. 1985; 72(5): 339–359.
5. **PANAYIOTOPOULOS C.P., TAHAN R., OBEID T.** Juvenile myoclonic epilepsy: factors of errors involved in the diagnosis and treatment. Epilepsia. 1991; 32(5): 672–676. doi: 10.1111/j.1528-1157.1991.tb04708.x
6. **GRÜNEWALD R.A., CHRONI E., PANAYIOTOPOULOS C.P.** Delayed diagnosis of juvenile myoclonic epilepsy. J Neurol Neurosurg Psychiatry. 1992; 55(6): 497–499. PMID: PMC1014908
7. **GENTON P., GELISSE P., THOMAS P.** Juvenile myoclonic epilepsy today: current definitions and limits. In: Schmitz B, Sander T, editors. Juvenile myoclonic epilepsy: the Janz syndrome. Petersfield: Wrightson Biomedical Publishing. 2000. p. 11–32.
8. **ARTYUKHOV I.P., SHILKINA O.S., SHNAYDER N.A., ET AL.** Case report of management problem of juvenile myoclonic epilepsy. Case Reports in Clinical Medicine. 2016; 5: 217–224. doi: 10.4236/crcm.2016.57040.
9. **PANAYIOTOPOULOS C.P., TAHAN R., OBEID T.** Juvenile myoclonic epilepsy: factors of errors Involved in the diagnosis and treatment. Epilepsia. 1991;32(5): 672–676. doi: 10.1111/j.1528-1157.1991.tb04708.x
10. **WHELESS J.W., CLARKE D.F., ARZIMANOGLU A., CARPENTER D.** Treatment of pediatric epilepsy: European Expert Opinion, 2007. Epileptic Disorders. 2007; 9 (4): 353–412.
11. **PETRUHIN A.S., MUKHIN K.Y., KALININA L.V., PILAEVA O.A.** Lamictal: poly- and monotherapy of epilepsy. Psychiatry and Psycho-pharmacotherapy. 2004 / Annex 1. – pp. 20–26. (In Russian)
12. **MARTINEZ-JUARES I.E., ALONSO M.E., MEDINA M.T. ET AL.** Juvenile myoclonic epilepsy subsyndromes: family studies and long-term follow-up. Brain. 2006; 129 (Pt 5): 1269–1280. http://dx.doi.org/10.1093/brain/awl048

13. **BAYKAN B., ALTINDAG E.A., BEBEK N. ET AL.** Myoclonic seizures subside in the fourth decade in juvenile myoclonic epilepsy. *Neurology*. 2008; 70 (22 Pt 2): 2123–2129.
14. **JARMUHAMETOVA M.R., BOGDANOV E.I.** The prognosis of juvenile myoclonic epilepsy. *Kazan Medical Journal*. 2011;6: 820–822. (In Russian)
15. **KLEVELAND G., ENGELSEN B.A.** Juvenile myoclonic epilepsy: clinical characteristics, treatment and prognosis in a Norwegian population of patients. *Seizure*. 1998; 7: 31–38. [http://dx.doi.org/10.1016/S1059-1311\(98\)90005-X](http://dx.doi.org/10.1016/S1059-1311(98)90005-X)
16. **CAMFIELD C.S., CAMFIELD P.R.** Juvenile myoclonic epilepsy 25 year after seizure onset. A population — based study. *Neurology*. 2009; 73(29): 1041–1045. doi: 10.1212/WNL.0b013e3181b9c86f
17. **SHILKINA O., PETROV K., DIUZHAKOVA A., MARUEVA N., SHNAYDER N.** Frequency of juvenile myoclonic epilepsy clinical phenotypes in Siberia. *World Journal of Neuroscience*. 2016; 6: 32–36. doi: 10.4236/wjns.2016.61004
18. **SHNAYDER N.A., BOCHANOVA E.N., ZYRYANOV S.K., ET AL.** Using the register of patients with epilepsy and epileptic syndromes for the analysis of adverse drug reactions of antiepileptic drugs. *Modern problems of science and education*. 2016; 2: 1–6. (In Russian) <http://www.science-education.ru/article/view?id=24254>
19. **SHNAYDER N.A., DMITRENKO D.V., SADYKOVA A.V., ET AL.** Epidemiological studies on epilepsy in Siberia. *Medical and Health Science Journal*. 2011; 6: 35–42. <http://dx.doi.org/10.15208/mhsj.2010.105>
20. **SHNAYDER N., PILUGINA M., DMITRENKO D., ET AL.** Pharmacogenetics of valproic acid as unmodified risk factor of adverse drug reactions. *Medical and Health Science Journal*. 2011; 7: 26–38. doi: 10.15208/mhsj.2011.129
21. **CARROLL E., CAVAZOS J.E.** Juvenile myoclonic epilepsy. *Medscape*. <http://emedicine.medscape.com/article/1185061-overview> Updated: Dec 23, 2015
22. **DMITRENKO D.V., SHNAYDER N.A., KISELEV I.A., ET AL.** Problems of rational therapy for epilepsy during pregnancy. *Open Journal of Obstetrics and Gynecology*. 2014; 4: 506–515. <http://dx.doi.org/10.4236/ojog.2014.49072>
23. **SHNAIDER N.A., SYCHEV D.A., PILYUGINA M.S., ET AL.** Importance of the pharmacokinetics of valproic acid in an individualized approach to the treatment of epileptic women of fertile age. *Neuroscience and Behavioral Physiology*. 2012; 42: 963–968. <http://dx.doi.org/10.1007/s11055-012-9663-2>



# EVALUATION OF THERAPEUTIC BIOCORRECTION BY EXHALED MARKERS OF METABOLISM A PILOT STUDY

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## INTRODUCTION

In daily clinical practice, it seems not suitable to get a blood sample for monitoring of metabolic parameters a couple of times a day or manifold during one patients test. Nevertheless, especially in elderlies and disabled patients effective monitoring of the disease is needed.

So, there is a great need to make a non-invasive assessment of the metabolism, for example by marker from the exhalate. Previous known publications [1] reported evidence in the breath condensate as a marker of oxidative stress or note on metabolism of more unsaturated fatty acids on MDA. EBC needs a long-lasting sampling of about 15 minutes, and highly complicated laboratory methods for analyses.

There is urgently need for evaluation of Individual Systemic Biocorrection is an adjuvant therapy for patients suffering from Metabolic Syndrome, especially from Diabetes mellitus type 2.

IMS seems to give a chance to detect volatile parameters in exhaled breath. IMS has a detection limit of around ppb and ppt. A pre-settled gas chromatographic column will enhance the sensitivity of the IMS as well as the possibility to differentiate ionized markers with different specific weight [2; 4; 8]

In a pilot study, it was checked whether MDA or MDA-related markers in breath using MCC-IMS as a single breath method is immersion.

## METHODS

A training procedure of moderate physical load in a controlled breathing atmosphere of 26 % oxygen (hyperoxia) [3; 5; 6] was performed in diabetic patients and healthy, but overweight, volunteers. The training parameters are adjusted individually by means



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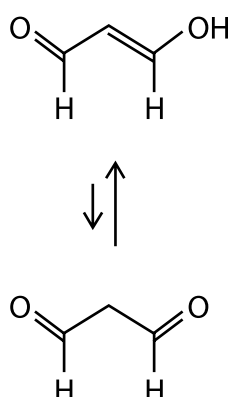
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of the Respiratory Quotient (RQ) to be kept in the range of 0,75–0,85. Under these conditions, the cellular energy balance is gradually shifted from sugar to fat utilization. After 10 training units, one hour each, the patient's metabolism normalizes noticeably: blood glucose and triglyceride concentration are improved, indicators of the oxidative-antioxidative equilibrium assume normal values, and the patient's subjective well-being improves significantly.

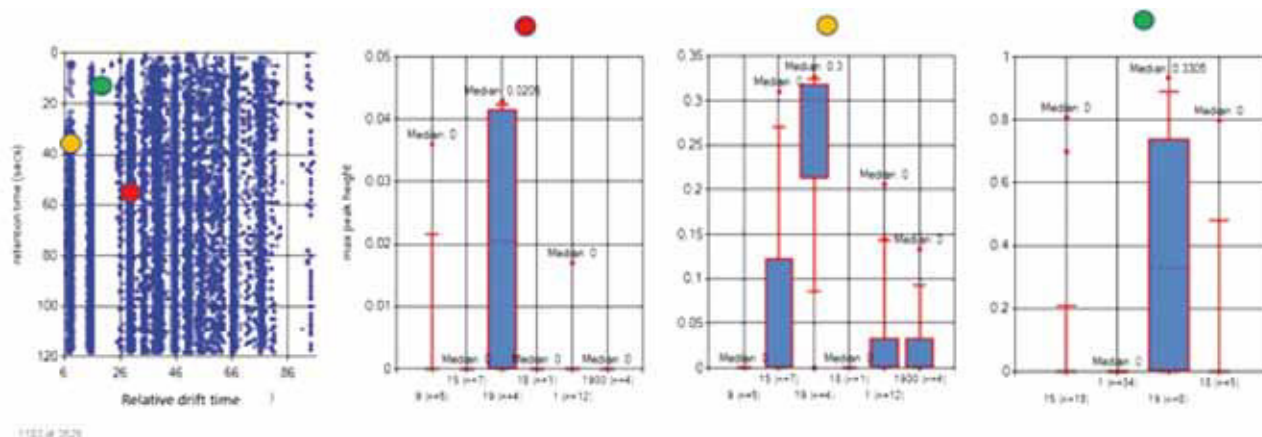
RQ and heart rate were checked during repetitive training sessions on treadmill every ten minutes.

A MCC-IMS from STEP Sensortechnik was used for the investigations. The system is a combination of a multi capillary column with an ion mobility spectrometer.

Spectra of the reference substance for MDA and breath samples from subjects with moderate physical exertion were measured. The comparable peaks of the



**Fig. 1a.** MDA (i.e. Malondialdehyde resp. Propandial) a major breakdown product in the oxidation of polyunsaturated fatty acids. MDA serves as biomarker of oxidative stress mostly elevated in plasma of diabetics



**Fig. 1b.** Experimental identification of clusters which represent MDA from related chemicals or controls spectrograms (MDA 19; mint oil 9; Barbituric acid 15; thio-barbituric acid 18; cooled MDA 1900; clean air 1)

reference and the air were determined by means of cluster analysis-based software. The classification has been carried out with a leave-one-out cross validation and support vector machine. The spectra were analyzed by a statistical program based on cluster analysis and non-parametric statistics (U-test).

Using cluster analysis by support vector machine based software the peaks of all measurements were detected and compared each other. Sensitivity and specificity of differentiation was evaluated by Leave-One-Out cross validation method [7; 8]

In comparison to previous experimental investigations a Cluster of acetone and three clusters representing MDA-related ions were analysed first (fig 1a).

Similar chemical structures with barbituric acids are the reason for comparative peaks of these agents, but can be differentiated by calculating the complementary peaks. The following figures show identical and different peaks of the substances, enabling the calculation of the specific peaks of one substance (fig 1b).

Clusters representing experimental investigated reference-substances were used for further investigations on exhaled breath for detection of VOC's of fatty acid metabolism.

Breath samples were taken as a single breath test. The volunteer has had to perform a slowly exhalation for at least 20 secs following a deep nearly complete inspiration. During the second half of expiration a 2.5 cc sample of breath was taken by IMS (fig. 2).

#### Volunteers:

The study included 6 volunteers, (3 female, 3 male) which performed overall 26 treadmill tests in hyperoxide conditions with a moderate effort. Each test last 60 minutes.

Mean age was  $69 \pm 3$  (Diabetes) and  $69,5 \pm 2$  (control), respectively. The body weight was  $82 \pm 29$  kg in Diabetics and  $99 \pm 8$  kg in healthies.

During each test at point zero and every ten minutes — up to 7 times the following parameters were measured: Heart rate, Respiratory quotient (RQ), and a single breath test for IMS was taken (fig. 3).

The initial values were taken at the onset of the test, for standardized conditions in all volunteers.

## RESULTS

All volunteers were able to perform the one hour treadmill tests without break or premature stops during a time-course of up to 4 weeks.

Fig 4 and 5 shows the tracings of Heart rate (HR) and RQ as mean of all tests + SD. There was a visible difference between diabetic patients and healthy controls. HR of diabetics was even at the beginning of a test higher than in healthy volunteers.

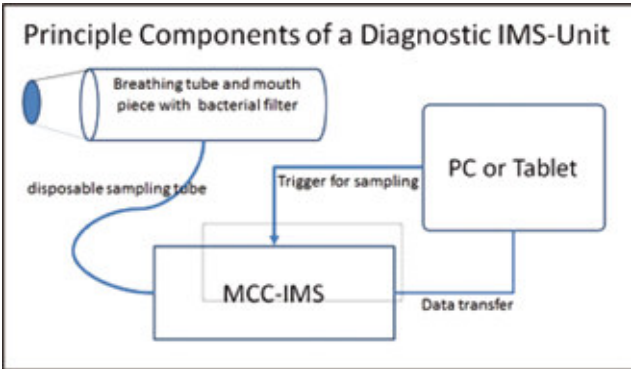


Fig. 2. Schematic diagram of setup for breath sampling

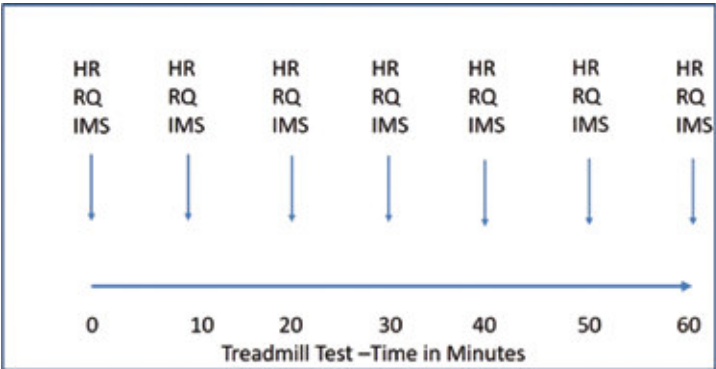


Fig. 3. Treadmill Test – time course and points of parameters sampling

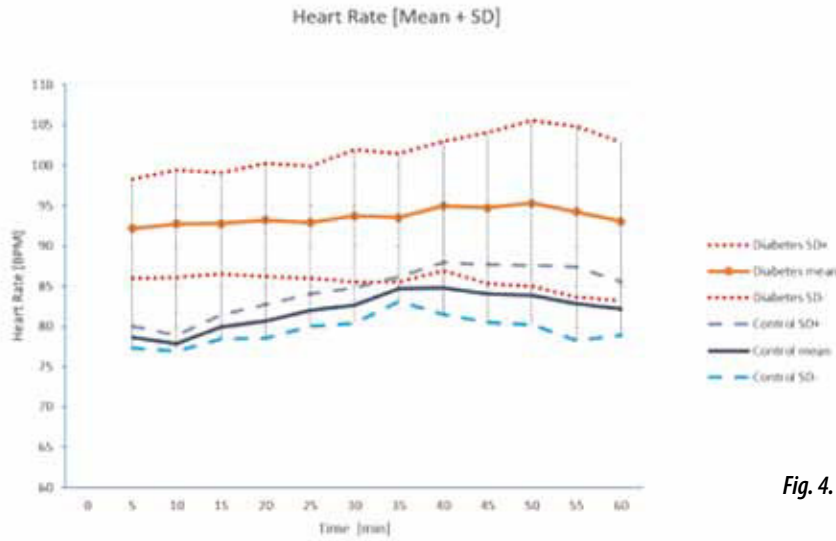


Fig. 4. Heart Rate [mean + SD] during the test

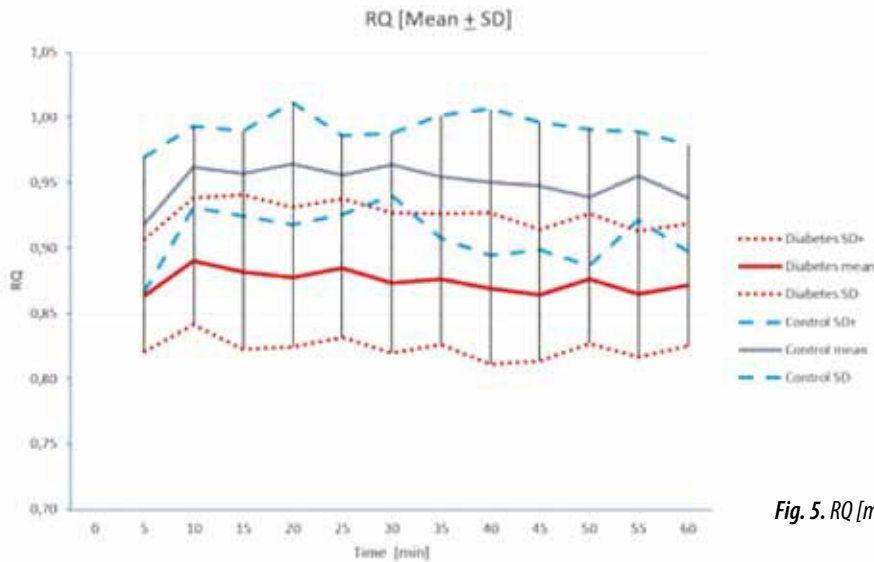
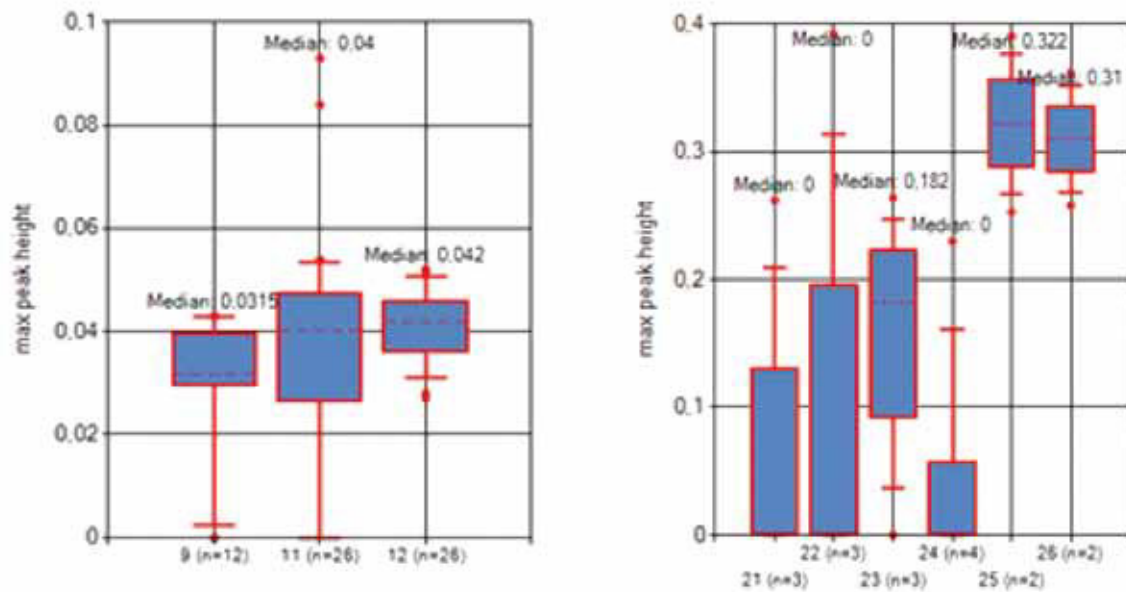


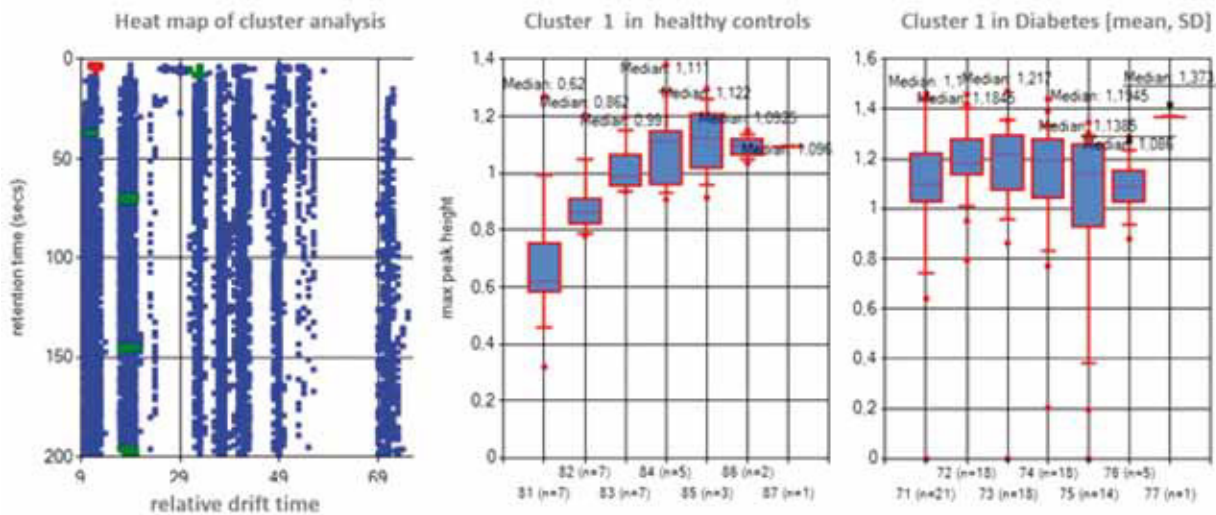
Fig. 5. RQ [mean + SD] during the test



**Fig. 6.** Specific clusters in experimental investigations and exhaled breath for detection of MDA related peaks, due to the yellow-indicated peak in Fig.1b.

**Left:** Cluster 49 of 391 compared the MDA reference (9) to air of patients before (11) or to moderate exercise stress (12) in diabetics.

**Right:** wDiabetes mell. - treadmill-training 3 times a week, (21, 22 and 23 first measurement at beginning of a test series, 24, 25 and 26 measurement during the last test of an individual series



**Fig. 7.** Time Course of Cluster 1 (acetone-related) during treadmill-tests in diabetics and healthy controls [mean + SD, median]

The differences represent the specific training effect of the volunteers.

Diabetic patients with overall higher heart rate showed a lower increase of HR during exercise tests at mean than the healthy controls (fig. 4, 5).

RQ showed a higher physical limit of healthy controls than in diabetics within the threshold under the hypoxic limit.

After initial increase by beginning of each treadmill test a slowly decrease during the test occurred, but remaining above the level at rest.

The physiological parameters demonstrated that the physical exercise in all tests was in a range below



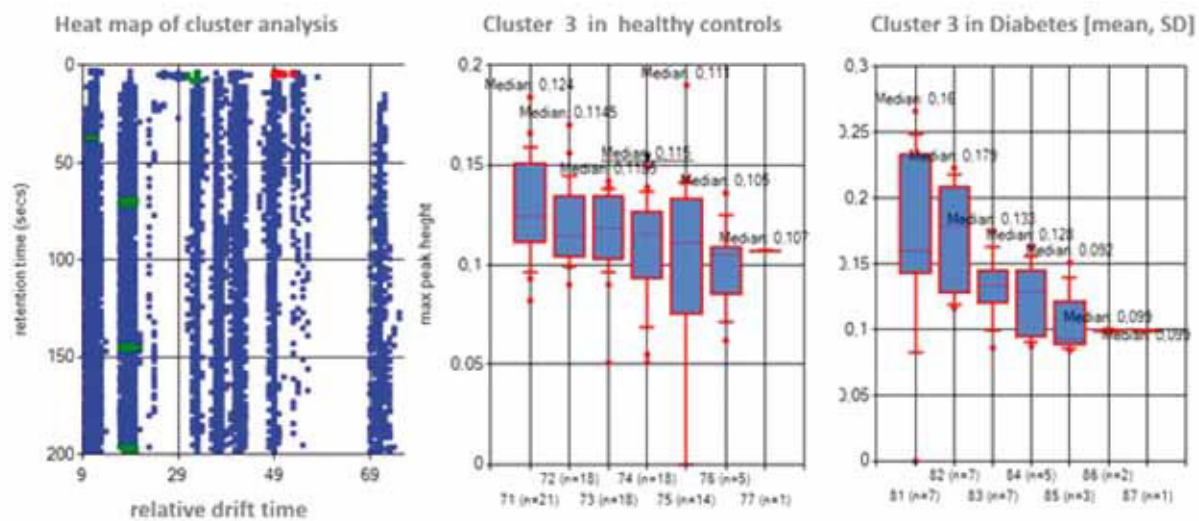


Fig. 8. Time Course of Cluster 3 during treadmill-tests in diabetics and healthy controls [mean + SD, median]

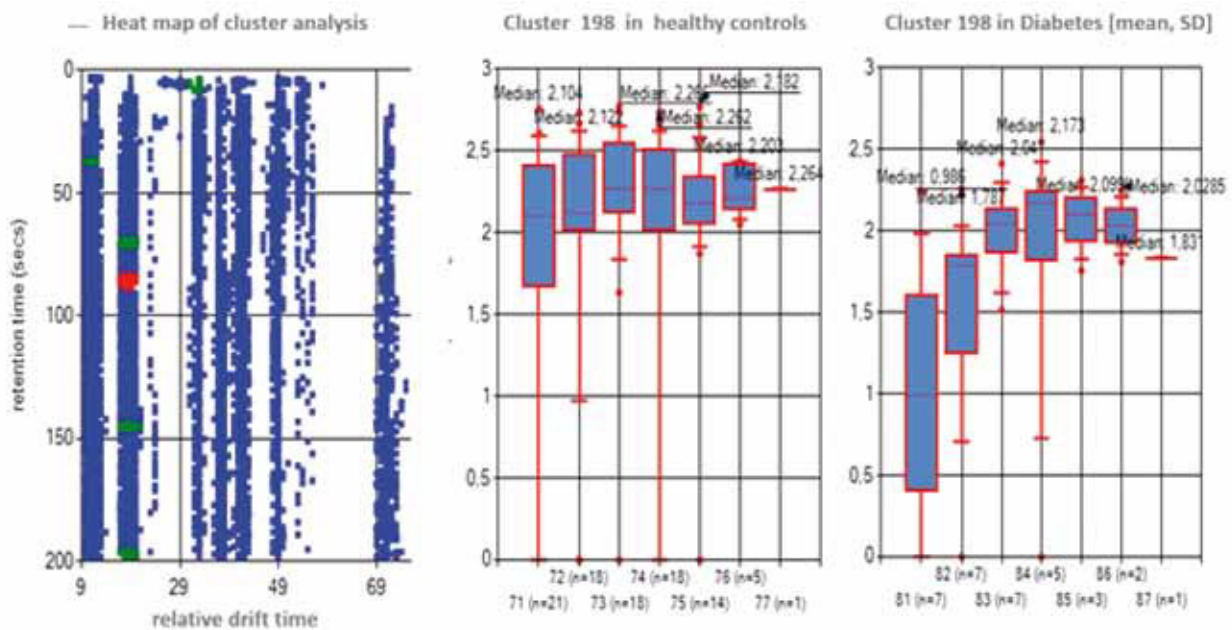


Fig. 9. Time Course of Cluster 198 during treadmill-tests in diabetics and healthy controls [mean + SD, median]

the individual hypoxic threshold which shows the correct test level due to the described target.

In IMS analyses could be shown that identical peaks such as for reference measurements even in exhaled air of subjects are identifiable. Different height of peaks represents the concentration in air (fig. 6).

The right part of figure 6 shows the difference of MDA related VOC-exhalation between first and fifth

exercise test. The results may serve as indicator for effective metabolic switching due to moderate exercise tests in diabetics within a few weeks of training.

The following figures indicate the occurrence and height of different clusters in IMS-tracings between diabetics and healthy controls. Each left diagram give the sum of all identified clusters in all measurements, the specific cluster is indicated red.

The middle and right diagrams give this cluster for healthies (middle) and diabetics (right) (fig. 7).

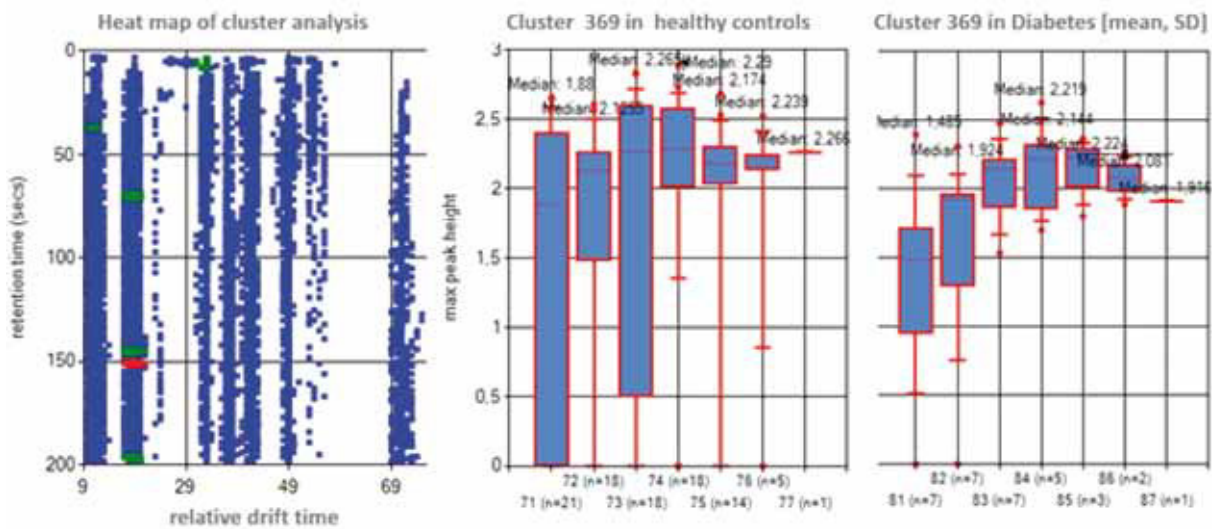


Fig. 10. Time Course of Cluster 369 during treadmill-tests in diabetics and healthy controls [mean + SD, median]

Cluster one is due to acetone and correlates with the glucose-concentration and degradation. Acetone is one volatile product of the “Krebs-Cycle” (fig. 8)

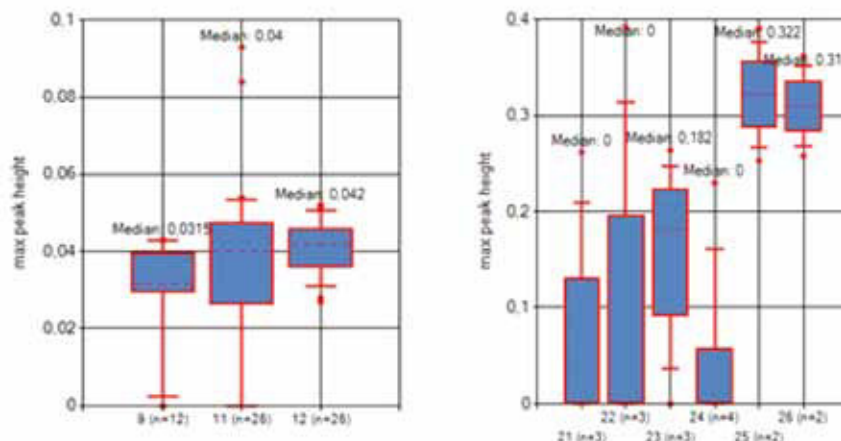
Cluster 3 represents a short chain Carbohydrate like two or three carbon-atoms. This marker is reduced in breath in diabetics more than in healthy volunteer during exercise (fig. 9, 10).

Cluster 198 and 369 represents longer chained VOC's which may be an indicator of degradation of fatty acids. Whereas in healthy controls there is no significant change of these markers in diabetics there was found in all patients an increase during the tests. This increase is a hint for a shift in metabolic processes due to the exercise.

## DISCUSSION

The results give some evidence that moderate exercise training in diabetic patients may induce a shift between carbohydrate and fatty acid metabolism. This is the effect which was expected by so-called Biocorrection Methods [9; 10].

It was demonstrated that MDA is measurable also bypassing the Breath condensate directly out of the exhaled air, using MCC-IMS. For detection was suitable a air-sample of 2.5 cc.



The data of increasing levels of acetone (Cluster 1), as well as cluster 198 and 369 in diabetics show significant changes in metabolic processes during the tests. The differences between healthy controls and diabetics are evident.

It became evident that there is a sufficient sensitivity for measuring in air at least for MDA with the MCC IMS. Further investigations must show if the found parameters of oxidative metabolism and the metabolism of unsaturated fatty acids can be used to track metabolic alterations during exercise non-invasive.

Unless not fully understood peaks in exhaled breath it was shown that between healthy volunteers and diabetic patients seems to be distinguished differences in metabolism of carbohydrates and fatty acids for cellular energy balance.

Healthy volunteers shift their energy metabolism during exercise tests by increased exhalation of acetone, indicating high glucose metabolism, while diabetics already at rest are in different metabolic status due to glucose metabolism.

In the opposite diabetics seems to induce more fatty-acid degradation during exercises (Cluster 198), approaching the levels of the controls.

Further investigations must show if the found parameters of oxidative metabolism and the metabolism of unsaturated fatty acids can be used to track metabolic alterations during exercise non-invasive.

## SUMMARY

There is a great need to make a non-invasive assessment of the metabolism, for example by marker from the exhalate. Previous known publications reported evidence in the breath condensate as a marker of oxidative stress or note on metabolism of more unsaturated fatty acids on MDA. In a pilot study, it should be checked whether MDA using GC-IMS as a single breath method is immersion.

A MCC-IMS was used for the investigations. The system is a combination of a multi capillary column with an ion mobility spectrometer. Spectra of the reference substance for MDA and breath samples from subjects with moderate physical exertion were measured. The comparable peaks of the reference and the air were determined by means of cluster analysis-based software. The classification has been carried out with a leave-one-out cross validation and support vector machine.

It could be shown that identical peaks such as for reference measurements even in exhaled air of subjects are identifiable. Different height of peaks represents the concentration in air.

Thus, it appears that MDA is measurable directly out of the exhaled air. Furthermore, differences in metabolism between glucose and fatty-acids seems to be detectable by VOC analyses in breath.

It became evident that there is a sufficient sensitivity for measuring in air at least for MDA with the GC-IMS.

Further investigations must clarify if the found parameters of oxidative metabolism and the metabolism of unsaturated fatty acids can be used to track metabolic alterations during exercise.

## ABBREVIATIONS

EBC	Exhaled Breath Condensate
IMS	Ion Mobility Spectrometry
MDA	Malone Dialdehyde
ppb	Parts per billion
ppt	Parts per trillion

RQ	respiratory quotient $RQ = V_{CO_2}/V_{O_2}$ (relationship between expired $CO_2$ and inspired $O_2$ )
SD	Standard deviation
VOC	volatile organic compounds

## REFERENCES

1. **BECHER, G.:** Atemkondensat-Diagnostik (Exhalat-Diagnostik); In: „Spezielle Lungenfunktionsprüfung“, Hrsg.: Prof. K.-H. Rühle, München: Dustri Verlag Dr. Karl Feistle, 2013, S. 105–124.
2. **BUSZEWSKI, B.; KESY, M.; LIGOR, T. AND AMANN, A.:** Human exhaled air analytics: biomarkers of diseases. Biomed. Chromatogr. 21: 553–566 (2007)
3. **S. HEYMANN, J. SCHULZ, O.G. NIKOLAEV, S.V. FOMCHENKOV,** Fortschritte in der adjuvanten therapie des Diabetes mellitus Typ 2 mit Mineralien, archiv euromedica 5 (2015), 58
4. **A. HILLMANN:** Differenzielle Ionenmobilitätsspektrometrie als Methode zur Messung spezifischer Cluster von volatilen Substanzen in der Ausatemluft des Menschen. Bachelor; Hochschule Mittweida 2010
5. **R. KLOPP, W. NIEMER, J. SCHULZ,** Änderungen des Funktionszustandes der Mikrozirkulation durch eine adjuvante BioKorrektur-Behandlung bei Patienten mit Diabetes mellitus Typ II, archiv euromedica 4 (2014), 36–44
6. **KLOPP R., J. SCHULZ, W. NIEMER, K.J. RUHNAU,** Wirkungen einer physikalischen Stimulierung der spontanen arteriellen Vasomotion auf die Mikrozirkulation und das Immunsystem bei Patienten mit Diabetes Typ II und Wundheilungsstörungen, Zeitschrift für Gerontologie und Geriatrie 47 (2014), 415–424.
7. **R. PURKHART:** Klassifikation von Ausatemluft anhand ihrer differenziellen Ionenbeweglichkeitsspektrogramme. Diplomarbeit, HUB 2010
8. **R. PURKHART, A. HILLMANN, R. GRAUPNER, G. BECHER:** Detection of characteristic clusters in IMS-Spectrograms of exhaled air polluted with environmental contaminants. IJIMS, Feb. 2012 (DOI 10.1007/s12127-012-0090-4)
9. **SCHULZ J., S. HEYMANN, U. FUCHS, M. STURM, R. KLOPP,** Individuelle systemische BioKorrektur – adjuvantes Behandlungsverfahren bei Diabetes mellitus Typ II, archiv euromedica 3 (2013), 40–44
10. **M. STURM,** Der Einfluss eines Ausdauertrainings unter hyperoxischen Trainingsbedingungen mittels der Steuerung der Herzfrequenz und des respiratorischen Quotienten auf die individuelle systemische Biokorrektur des metabolischen Syndroms, Masterarbeit im Studiengang M.Sc- Sportwissenschaft – Prävention und Rehabilitation, Universität Leipzig, 2012



# ULTRASOUND DIAGNOSTIC CRITERIA OF TAUSSIG-BING ANOMALY IN FETUS

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## INTRODUCTION

Diagnose Taussig-Bing anomaly it is a very important and difficult for prenatal ultrasound. We want to discuss some important aspects of this problem.

Lev and Anderson defined double outlet of right ventricle (DORV) as «all of one great artery and 50% or more of the other artery must arise from the RV» [1].

The basis for their hypothesis is that, during conus malrotation changes in position of anterior portion of the muscular interventricular septum and differential conus absorption lead to such malposition of the great artery relations [4].

The anatomical variations of DORV are classified on the basis of:

1. the relationship between the VSD and the great arteries.
  - a) DORV with sub-aortic VSD;
  - b) DORV with sub-pulmonary VSD;
  - c) DORV with doubly-committed VSD;
  - d) DORV with non-committed VSD.
2. The position of the great arteries in relation to each other at the valvular level [2, 3].

Taussig-Bing anomaly is one type of double outlet right ventricle and based congenital heart defects with a transposition of the great arteries (TGA) and a sub-pulmonary ventricular septal defect (VSD) [Fig. 1]. This cardiac disease has been first described by Helen Taussig and Richard J. Bing in 1949 [5].



Characteristic features of the first heart described by Taussig and Bing include:

1. origin of the aorta from right ventricle;
2. aorta to the right of the pulmonary artery (side by side);
3. pulmonary artery in its approximately normal position and overbidding a VSD;
4. muscule polle (defined as outlet septum) separating the origin of the two great vessels.

## MATERIAL

A total of 321 fetal echocardiograms were obtained during an period between 2015–2016 years from with a prenatal diagnosis of DORV. 104 of these cases were Taussig-Bing anomalies.

All cases usually were diagnosed during the first echocardiography from 14 to 34 weeks gestation. Our prenatal cohort was verified by postnatal ultrasound and autopsy.

Ultrasound criteria of T-B anomaly is a large sub-pulmonary anterior malalignment VSD and side-by-side position of the great arteries with an aortic valve on the right side of the pulmonary valve with both vessels predominantly arising from the right ventricle [Fig. 2].

In Taussig-Bing anomaly, the VSD and the sub-aortic region by an infundibular septum, which extends from the interventricular septum to the anterior wall of the RV. Hypertrophy of the septum and the posterior limbus of the trabeculae can lead to a significant sub-aortic obstruction.

This is important part of prenatal ultrasound of Taussig-Bing anomaly was diffdiagnosis with transposition of great arteries (TGA) and sub-pulmonary VSD [Fig. 1, 3].

TGA includes atria-ventricular concordant and ventriculo-arterial discordant.

The anatomical variations of TGA are classified on the basis of:

- e) Simple version;
- f) TGA with sub-aortic VSD;
- g) TGA with sub-pulmonary VSD;
- h) TGA with doubly-committed VSD.

We were interested TGA with sub-pulmonary VSD.

### *Ultrasound diffdiagnosis Taussig-Bing anomaly and TGA with sub-pulmonary VSD*

For T-B anomaly: 50% or more of the PA must arise from the right ventricle, the most frequently the great arteries were positioned side by side or rarely aorta is anterior and right sided, the overriding of the pulmonary valve in the trabecular region of the ventricular septum.

For TGA with sub-pulmonary VSD: 50% or more of the PA must arise from the left ventricle, the most frequently aorta is anterior and right sided and rarely the great arteries were positioned side by side.

According to autopsy the specific criterias of anomaly T-B versus TGA with subpulmonary VSD were:

1. distance between aorta and mitral valve more than 1,3;
2. conus septum in 1,5 less versus normal;
3. prevailing relationship aorta and pulmonary truncus is "side by side"
4. mitral-pulmonary discontinuity

Unfortunately, it was impossible to visualize mitral-pulmonary discontinuity in utero.

## DISCUSSION

DORV is a heterogeneous group of conus arteriosus malformations. "All of one great artery and 50% or more of the other artery must arise from the right ventricle".

The basis for their hypothesis of conus malrotation, changes in position of anterior portion of the muscular interventricular septum and differential conus absorption lead to such malposition of great artery relations.

The basic condition of DORV is the presence of mitral-similar contact.

The basis of fetal ultrasound diagnosis of T-B anomaly were:

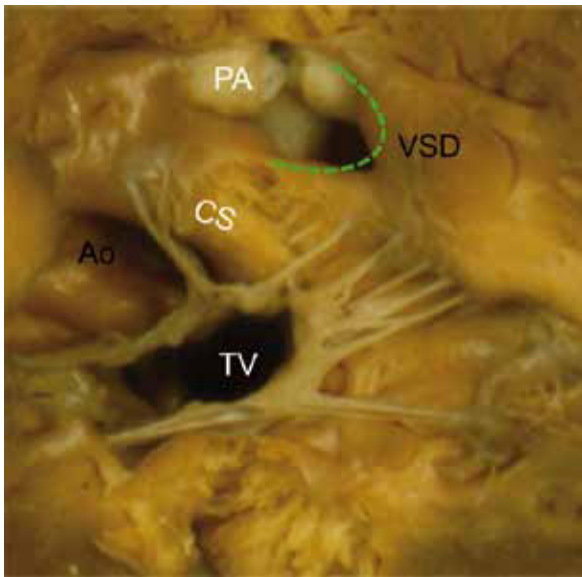
- the relationship aorta and pulmonary truncus;
- degree offset (overbidding) of great arteries, especial pulmonary truncus for time of gestation
- location and size of VSD.

The optimal transabdominal fetal ultrasound diagnosis of Taussig-Bing anomaly can be performed at 16 to 22 weeks of pregnancy.

Definition of fetal Taussig-Bing anomaly was attempted from multiple scan planes including four-chamber, long-axis of left ventricle and right ventricle, short axis of great arteries, aortic arch and ductal arch views.

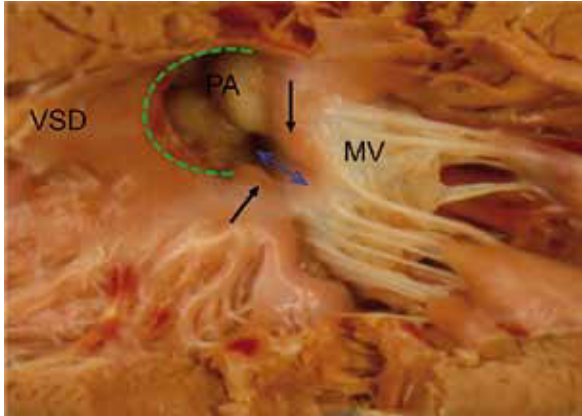
Doppler color flow mapping and pulsed Doppler interrogation were used to facilitate identification of great vessel relationship, location and size of VSD.

Postnatal examination of this CHD must be by postnatal echocardiography, angiography, surgery or autopsy.



**Fig. 1.** Taussig-Bing anomaly: double outlet right ventricle with a transposition of the great arteries and a sub-pulmonary ventricular septal defect.

VSD — ventricular septal defect, PA — pulmonary artery, TV — tricuspid valve, Ao — aorta, CS — conus septum.



**Fig. 3.** TGA and VSD type "malalignment". Right-side deviation of conus septum and a sub-pulmonary ventricular septal defect.

VSD — ventricular septal defect, PA — pulmonary artery, MV — mitral valve, Black arrows — segments of sub-pulmonary conus, blue arrow — fibrous mitral-aortic contact (MV-PA).



**Fig. 2.** Taussig-Bing anomaly: double outlet right ventricle with a transposition of the great arteries at fetus, 20 weeks of gestation.

PA — pulmonary artery, Ao — aorta, RV — right ventricle.

## REFERENCES

1. ANDERSON RH, WEBB S., BROWN NA., LAMERS W, MOORMAN A. AT AL. Development of intrapericardial arterial trunks. Heart;2003;89;1110–1118
2. BETIGERI A., DIVAKARAN J, GUHATHAKURTA S, CHERIAN K. Taussig-Bing complex- a morphologic diagnostic dilemma. ISPUB.COM/13/2/6469
3. HARTGE D.R., HOFFMANN U AT AL. Prenatal detection and perinatal management of Taussig-Bing anomaly with coarctation of the aorta and singular coronary artery: a case report.
4. SMITH RS. COMSTOCK CH, KIRK JS, LEE W AT AL. Double – outlet right ventricle an antenatal diagnostic dilemma. Ultrasound Obstet Gynecol 14:315–319,1999.
5. TAUSSIG H.B. AND BING R.J. Complete transposition of the aorta and a levorotation of the pulmonary artery. Am. Heart J;1949:551

# CORRELATION OF DENTAL ARCH MAJOR LINEAR PARAMETERS AND ODONTOMETRIC INDICES GIVEN PHYSIOLOGICAL OCCLUSION OF PERMANENT TEETH IN VARIOUS FACE TYPES

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**ABSTRACT** — Juvenile myoclonic epilepsy (JME) is one of the most comThe item offers a view on the outcomes of a study involving 192 persons aged 18–25 each possessing a full set of permanent teeth, with physiological occlusion and demonstrating various gnathic and dental face types and dental arches. The outcomes revealed a link between the size of the upper and lower dental arches. The ratio of the upper dental arch length taken against the similar parameters pertaining the lower jaw was  $1.065 \pm 0.005$  for all the types of dental arches. The index in question was employed to show the match between the teeth in the upper jaw and their lower counterparts. The ratio of the six front upper teeth to the crown width in the lower incisors and canine teeth was  $1.3 \pm 0.02$  and matched the findings obtained through Bolton's method. The ratio of half-sum of the 14 teeth to the frontal-distal diagonal was  $1.065 \pm 0.005$ , with the upper and the lower dental arch alike. The ratio of the upper arch's diagonal dimension to its lower counterpart averaged  $1.065 \pm 0.01$  for all types of dental arches.

**KEYWORDS** — physiological occlusion; mesognathic face type; brachygnathic face type; dolichognathic face type; normodontia; macrodontia; microdontia.

The ratio of the upper and lower jaw dental arches has always been of interest to various professionals [2,4,9]. The methods employed to evaluate the match in the teeth size within this current study involved Tonn's method, Bolton's method, etc. [26]. There is a view offered on the teeth and dental arch sizes in people with physiological occlusion depending on the respective gnathic and dental types [5,6,11,14,17]. Relation has been detected between the dental arch size in the sagittal and the transversal planes, as well as



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the indices shown to identify the type of a dental arch [10,12].

There are advanced classifications proposed for dental arch shapes along with their major linear parameters [3,13,22]. Methods have been developed to evaluate the teeth size based on the major parameters of the head and the face [21,24,29,30]. A detailed analysis has been offered for specific features of the shape and the size of incomplete dental arches, which is due to lack of premolars [18]. Notion is proposed that disturbed ratio of the dental arches is associated with abnormal occlusion resulting in malfunction [1,20,25,27,28].

The impact has been identified that pathological occlusion has on the oral cavity microecology, which, in turn, facilitates impairment development in the periodontal tissue and the mucosa [23].

There is a lot of data available currently offering analysis of odontometric features, as well as dental arches linear parameters in people with dolichognathic, brachygnathic, and mesognathic dental arches at their normodontia, macrodontia, and microdontia [15,16]. Such studies are of extreme importance for clinical Orthodontics where the said parameters serve to help determine the braces to be prescribed and the size of the metal arch in cases employing the edgewise technique [7,8,19].

However, special literature offers no sufficient data regarding the interrelation between the major linear parameters of the dental arches and the odontometric indices in people with different face types.

## AIM OF STUDY

To identify the relationship between the odontometric indices and the basic linear parameters for the upper and lower dental arches in cases of physiological occlusion with displaying various types of face.

## MATERIALS AND METHODS

The study involved 192 persons aged 18–25 each having a full set of permanent teeth, physiological occlusion and various gnathic and dental types of the face and the dental arches.

To determine the dental type of the face, its diagonal size was evaluated from the t spot (located on the tragus) to the subnasal sn spot. The measurements of t-sn within the range of 123 mm to 130 mm were typical of the normodontal face. Smaller diagonal measurements were specific for those with microdontia of permanent teeth while an increase in the diagonal indicated macrodontia.

The gnathic type of face was determined based on its gnathic index calculated as a ratio of the diagonal and the transversal measurements. Given that, the transversal dimensions included the width of the face as taken between the tragus points t-t. The mesognathic type of face had a gnathic index varying between 83% and 93%. A lower value was indicative of the brachygnathic, and a higher value – of the dolichognathic face type (Fig. 1).

Similar types were detected for dental arches, whereas the type of the arch was calculated as the sum of the mesio-distal sizes of the 14 teeth (the wisdoms were not taken into account due to variability in their size). The dental arch length of 112–118 mm indicated normodontal dental arches, while any values beyond the said values were accepted as indicative of macro- and microdontia arches, respectively. The dental arch width was measured between the spots located on the canine teeth cusp near the crown's occlusion profile. With the second molars, the spots were located on

the vestibular distal cusps. The arch diagonal was measured from the interincisal spot (on the vestibular side) to the second molars. The arch depth, too, was measured from the interincisal spot to the line joining the vestibular distal odontomeres of the second molars. The front-canine diagonal was measured from the interincisal spot to the canine cusp (Fig. 2a, 2b).

The interrelation was determined for the teeth size, the ratio of the transversal, sagittal and diagonal dimensions for the dental arches (both jaws) at all types of gnathic and dental types of face and dental arches.

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

## RESULTS AND DISCUSSION

The study showed that the major linear parameters and the odontometric indices for the upper dental arches correlated with similar parameters of the lower arches at all dental and gnathic types (Table 1).

The size of the teeth in people with macrodontal type of dental arches was reliably above that in people who revealed normodontia and all the more so in those who had microdontia, which appears something naturally expected. The length of the dental arch (the sum of the mesio-distal sizes of 14 teeth) was shorter in the lower jaw compared to the upper one. However, the mean ratio of the two values was  $1.065 \pm 0.005$  for all types of dental arches. The index in question revealed a match of the upper and the lower teeth, and was proven through Bolton's method.

The diagonal sizes of the dental arches typically correlated with the size of the teeth. The highest value for the frontal-molar diagonal was observed in people with macrodontal type of dental arches, while those with microdontia had the lowest value. The ratio of half-sum of the 14 teeth to the frontal-distal diagonal was  $1.065 \pm 0.005$  for both jaws.

The ratio of the diagonal dimension taken for the upper arch against its lower counterpart was an average of  $1.065 \pm 0.01$  for all types of dental arches.

The width of the upper dental arch between the second molars exceeded that if put against the lower



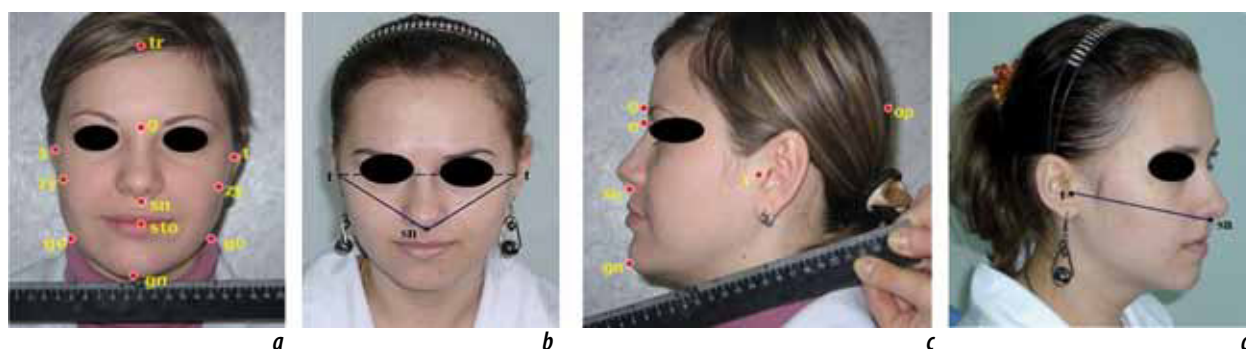


Fig. 1. Cephalometric points used to define gnathic type of person: a, b — frontal plane; c, d — sagittal plane

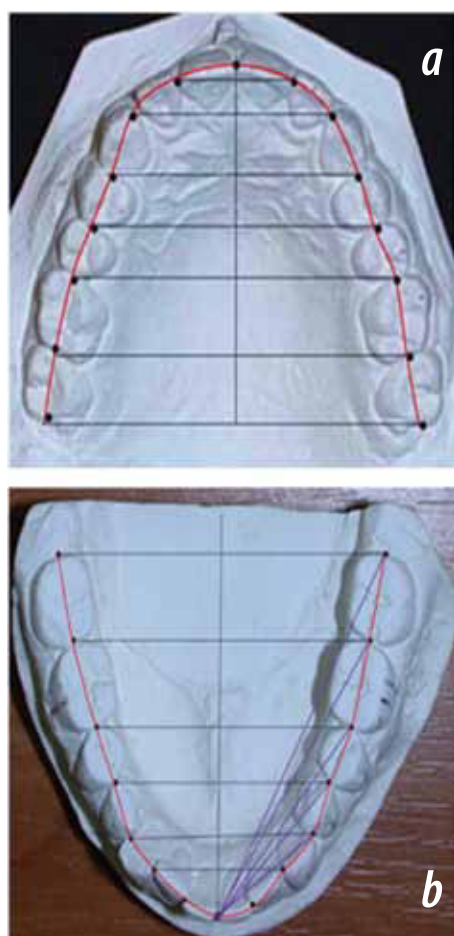


Fig. 2. Dental cast model, upper (a) and lower (b) jaws with the reference lines to measure the dental arch parameters (photograph)

arch width, regardless the type of the dental arch. The widest arches were found in those having brachygnathia, and in cases with brachygnathic macrodontia measured  $71.31 \pm 2.03$  mm on the upper

jaw and  $64.82 \pm 2.24$  mm on the lower one. The lowest value for the dental arch width on both jaws was detected in people with dolichognathic types. Regardless of the dental arch type, the ratio of the upper arch width at the molars to the similar lower jaw parameters was  $1.1 \pm 0.05$ .

The outcomes of the study obtained for the anterior part of the dental arches offer evidence to the fact that the major linear parameters and the odontometric indices on both jaws shared a correlation (Table 2).

The anterior part of the dental arch revealed patterns generally similar to those of the dental arches at large. For all types of dental arches, the anterior ratio (by Bolton's) was within the normal range ( $77.2 \pm 0.22$ ). The ratio of sum for the 6 front teeth mesio-distal sizes to similar sizes for the lower teeth was  $1.3 \pm 0.02$ , which might be used as an extra criterion to describe the front teeth sizes.

The ratio of the dental arch width between the upper canines to the intercanine space in the lower dental arch was an average of  $1.33 \pm 0.02$ . The size of the upper frontal-distal diagonal was above that of the lower dental arch at all types of the latter. During that, the ratio of the said parameters was  $1.32 \pm 0.01$ .

## CONCLUSION

The outcomes of the study reveal an interrelation between the size of the upper and the lower dental arches. The ratio of the upper dental arch length (the sum of the mesio-distal sizes of the 14 teeth) to the similar measurements of the lower jaw produced an average of  $1.065 \pm 0.005$  for all types of dental arches. The index in question points at a match in the size of the upper and the lower teeth. Meanwhile, the ratio of the 6 upper front teeth to the crown width in the lower incisors and canines  $1.3 \pm 0.02$ , which matched the values obtained via Bolton's method. The ratio of half-sum of the 14 teeth to the frontal-distal diagonal was  $1.065 \pm 0.005$  both for the upper and for the lower jaw. The ratio of the diagonal sizes of the upper arch to a similar measurement of the lower jaw was an average of  $1.065 \pm 0.01$  for all types of arches.

The results of the study may be used for offering description to physiological occlusion, for detecting a match between the major measurements for the upper and lower dental arches, as well as for developing treatment forecast regarding dental arch shape and size when dealing with patients displaying abnormal occlusion.

## REFERENCES

1. Deep premaxillary disocclusion: Scholarly monograph / D.A. Domenyuk, A.A. Korobkeev, E.G. Vedeshina [et all.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 191 p.
2. Diagnosis and treatment of patients' dental profile discrepancy between the size of permanent teeth and dental arch parameters: Scholarly monograph / D. A. Domenyuk, D. S. Dmitrienko, A. A. Korobkeev [et all.]. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 272 p.
3. **DMITRIENKO S.V., DOMENYUK D.A., DMITRIENKO D.S.** Modern classification of dental arches // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 14–16.
4. **DMITRIENKO S.V., DOMENYUK D.A., DMITRIENKO D.S.** Interrelation between sagittal and transversal sizes in form variations of maxillary dental arches // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 10–13.
5. **DMITRIENKO S.V., DOMENYUK D.A., VEDESHINA E.G.** Shape individualization in lower dental arches drawn on basic morphometric features // Archiv EuroMedica, 2015. – Vol. 5. – № 1. – P. 11.
6. **DOMENYUK, D.A.** Basic morphometric parameters of the dental arches in people with brachygnathic the form of a dental arch and the macro-, micro- and normodontia types of dental systems / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et all.] // Institute of dentistry, 2015. – Vol. 68. – № 3. – P. 44–48.
7. **DOMENYUK, D.A.** Biometric justification of main linear dimensions of the dental arches in orthodontic treatment tactics' development using edgewise orthodontic technique (part I) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et all.] // Institute of dentistry, 2016. – Vol. 70. – № 1. – P. 76–78.

**Table 1.** Major indices for dental arch parameters in people with physiological occlusion, (mm), ( $M \pm m$ ;  $p \leq 0.05$ )

Dental arch	Major indices for dental arch parameters					
	$\Sigma_{14}$ teeth on jaw		Molar width of arch		Arch diagonal	
	Upper	Lower	Upper	Lower	Upper	Lower
Meso-, Normo-	116.9 $\pm$ 2.87	108.7 $\pm$ 2.95	60.84 $\pm$ 1.14	55.16 $\pm$ 1.29	55.12 $\pm$ 1.29	51.34 $\pm$ 1.22
Meso-, Macro-	120.91 $\pm$ 2.92	112.42 $\pm$ 2.79	64.78 $\pm$ 1.84	58.89 $\pm$ 1.92	57.03 $\pm$ 1.32	53.04 $\pm$ 1.02
Meso-, Micro-	105.69 $\pm$ 2.31	99.26 $\pm$ 2.08	58.56 $\pm$ 1.57	53.31 $\pm$ 1.76	49.51 $\pm$ 1.15	46.37 $\pm$ 1.23
Brachy-, Normo-	115.5 $\pm$ 2.87	108.4 $\pm$ 2.95	67.34 $\pm$ 2.15	61.19 $\pm$ 2.12	54.23 $\pm$ 2.04	50.78 $\pm$ 1.33
Brachy-, Macro-	122.81 $\pm$ 2.98	114.69 $\pm$ 2.89	71.31 $\pm$ 2.03	64.82 $\pm$ 2.24	57.91 $\pm$ 2.18	54.08 $\pm$ 2.09
Brachy-, Micro-	107.32 $\pm$ 1.85	101.62 $\pm$ 1.92	61.74 $\pm$ 1.97	56.13 $\pm$ 1.43	50.63 $\pm$ 1.21	47.46 $\pm$ 1.11
Dolicho-, Normo-	115.4 $\pm$ 2.94	107.9 $\pm$ 2.93	56.49 $\pm$ 1.49	51.12 $\pm$ 1.41	53.92 $\pm$ 1.12	50.44 $\pm$ 1.42
Dolicho-, Macro-	121.01 $\pm$ 2.93	114.1 $\pm$ 2.87	60.87 $\pm$ 2.38	55.34 $\pm$ 1.97	56.55 $\pm$ 1.29	53.81 $\pm$ 1.83
Dolicho-, Micro-	109.01 $\pm$ 1.98	103.29 $\pm$ 1.89	56.52 $\pm$ 1.47	51.38 $\pm$ 1.12	51.74 $\pm$ 1.85	48.71 $\pm$ 1.98

**Table 2.** Major indices for anterior part of dental arches in people with physiological occlusion, (mm), ( $M \pm m$ ;  $p \leq 0.05$ )

Dental arch	Major indices for dental arch parameters					
	$\Sigma_6$ of anterior teeth		Canine width of arch		Canine diagonal	
	Upper	Lower	Upper	Lower	Upper	Lower
Meso-, Normo-	46.46 $\pm$ 1.03	35.92 $\pm$ 1.11	38.53 $\pm$ 1.28	28.96 $\pm$ 0.87	20.83 $\pm$ 1.32	15.76 $\pm$ 1.22
Meso-, Macro-	48.1 $\pm$ 1.19	37.16 $\pm$ 1.24	37.78 $\pm$ 1.21	28.15 $\pm$ 1.17	21.47 $\pm$ 0.44	16.44 $\pm$ 0.51
Meso-, Micro-	42.92 $\pm$ 1.17	33.22 $\pm$ 1.21	33.93 $\pm$ 1.26	25.19 $\pm$ 1.19	18.62 $\pm$ 0.59	14.19 $\pm$ 0.69
Brachy-, Normo-	47.92 $\pm$ 1.36	37.08 $\pm$ 1.62	40.95 $\pm$ 1.82	31.01 $\pm$ 0.89	21.42 $\pm$ 0.99	16.19 $\pm$ 1.49
Brachy-, Macro-	49.81 $\pm$ 1.43	38.38 $\pm$ 1.39	38.36 $\pm$ 1.36	28.66 $\pm$ 0.93	22.12 $\pm$ 0.76	16.87 $\pm$ 1.12
Brachy-, Micro-	43.56 $\pm$ 1.13	33.66 $\pm$ 1.45	33.54 $\pm$ 1.33	25.44 $\pm$ 0.97	19.29 $\pm$ 0.62	14.65 $\pm$ 1.26
Dolicho-, Normo-	48.54 $\pm$ 1.54	37.58 $\pm$ 1.55	35.71 $\pm$ 1.77	27.02 $\pm$ 0.93	20.95 $\pm$ 0.85	15.98 $\pm$ 1.24
Dolicho-, Macro-	57.32 $\pm$ 1.53	40.44 $\pm$ 1.59	37.31 $\pm$ 1.55	28.52 $\pm$ 0.98	20.88 $\pm$ 0.94	15.93 $\pm$ 1.28
Dolicho-, Micro-	45.92 $\pm$ 1.37	35.54 $\pm$ 1.42	34.58 $\pm$ 1.24	25.92 $\pm$ 1.09	20.03 $\pm$ 0.49	15.31 $\pm$ 1.07

8. **DOMENYUK, D.A.** Biometric justification of main linear dimensions of the dental arches in orthodontic treatment tactics' development using edgewise orthodontic technique (part II) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2016. – Vol. 71. – № 2. – P. 66–67.
9. **DOMENYUK, D.A.** Clinical anatomy of teeth and dentofacial segments: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 210 p.
10. **DOMENYUK, D.A.** Comparative analysis of morphometric parameters and dental arch in different variants of their shape / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko // Kuban scientific medical Herald, 2015. – Vol. 151. – № 2. – P. 59–65.
11. **DOMENYUK, D.A.** Dependence between size of permanent teeth and linear parameters of mesognathic dental arches / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2015. – Vol. 69. – № 4. – P. 78–80.
12. **DOMENYUK, D.A.** Interrelation between sagittal and transversal sizes in form variations of maxillary dental arches / D.A. Domenyuk, S.V. Dmitrienko // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 10–13.
13. **DOMENYUK, D.A.** Modern classification of dental arches / D.A. Domenyuk, S.V. Dmitrienko // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 14–16.
14. **DOMENYUK, D.A.** Morphometric analysis of dental arches in physiological occlusion of permanent teeth / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2015. – Vol. 69. – № 4. – P. 74–77.
15. **DOMENYUK, D.A.** Sagittal and transversal dimensions of dolichognathic dental arches in humans with macrodontia, microdontia, and normodontia / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2016. – Vol. 71. – № 2. – P. 60–63.
16. **DOMENYUK, D.A.** The main forms of individual microdontia formed in the mixed dentition of permanent teeth / D.A. Domenyuk, A.A. Korobkeev, E.G. Vedeshina [et al.] // Medical news of North Caucasus, 2016. – Vol. 11. – № 3. – P. 474–476.
17. **DOMENYUK, D.A.** Variability of odontometric parameters in patients with physiological occlusion of permanent teeth and mesognathic dental arches / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2015. – Vol. 68. – № 3. – P. 74–77.
18. **DOMENYUK D.A., VEDESHINA E., DMITRIENKO S.V.** Certain parameters of incomplete dental arches with missing premolars after orthodontic treatment // Socially Significant Human Diseases: Medical, Environmental and Technical Problems, and these Solutions III Japanese-Russian International Conference. – 2016. – P. 81–82.
19. **DOMENYUK D.A., VEDESHINA E., DMITRIENKO S.V.** Choice of metallic arches and braces prescription in view of individual shape of dental arches // Socially Significant Human Diseases: Medical, Environmental and Technical Problems, and these Solutions III Japanese-Russian International Conference. – 2016. – P. 83–84.
20. **DOMENYUK D.A., VEDESHINA E.G., DMITRIENKO S.V.** Efficiency evaluation for integrated approach to choice of orthodontic and prosthetic treatments in patients with reduced gnathic region // Archiv Euro-Medica. – 2015. – Vol. 5. – № 2. – P. 6–12.
21. Features of the maxillofacial region when macrodontia permanent teeth: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 159 p.
22. Methods for determining individual dimensions of the dental arches by morphometric parameters of the maxillofacial region: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 144 p.
23. Microecology of the oral cavity in children with congenital nonunion of the sky: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 160 p.
24. Optimization modern methods of diagnosis and treatment of patients with various forms to reduce the height of the lower portion of the face: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 260 p.
25. Pathogenesis, clinic and treatment muscular and articular dysfunction in patients dental profile with sagittal anomalies of occlusion: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 238 p.
26. **PROFFIT, W.R.** Contemporary orthodontics / U.R. Proffit; under the editorship of L.S. Persin. – M.: Med Press-Inform, 2008. – 560 c.
27. The morphology of dental tissues and periodontium in a metered loading: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 244 p.
28. Variant anatomy of the dentoalveolar segments: Scholarly monograph / D. A. Domenyuk, A. A. Korobkeev. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 200 p.
29. Variations of the structure and relative size of the facial skeleton and the dentition of metaflow: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2016. – 140 p.
30. X-ray morphometric techniques in the evaluation of the mullet dental status of patients with an established orthognathic occlusion of permanent teeth: Scholarly monograph / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko [et al.]. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 76 p.



# MISTAKES IN PONT (LINDER-HARTH) METHOD USED FOR DIAGNOSING ABNORMAL DENTAL ARCHES IN TRANSVERSAL PLANE

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**ABSTRACT** — This item is an analysis of the outcomes obtained through studying 362 cast models in patients (both females and males) revealing various gnathic and dental types of arches, which was done in order to identify the match of the estimates calculated via the Pont and Linder-Harth method, and the actual size of the dental arches between the premolars and the molars. The outcomes show that the transversal size of dental arches depend less on the teeth size and are determined by their gnathic type. For mesognathic dental arches, both methods are rather likely to be valid. When evaluating the parameter in question for brachygnathic arches, however, the methods based on Linder-Harth indices reveal significant faults. The index values based on Pont method are not recommended to be employed when working with people having dolichognathic dental arches with normo-, macro-, and microdontia.

**KEYWORDS** — physiological occlusion; mesognathic face type; brachygnathic parameters of dental arches; double arch technique; edgewise technique metal arches; precasted metal arches

Identification of specific features pertaining to teeth, dental arches, dentoalveolar and dentofacial areas is, in general, of both applied and clinical value, proof to that being various ideas from many experts [2,4,6,8,13,20,24,26,29,30].

There have been numerous approaches proposed to identify the size of dental arches as well as to diagnose transversal anomalies, while such approaches are based on various links between linear parameters and odontometric values [5,7,9,11,14,15,21,25,27].

The most common methods for detecting dental arch width are Pont method and Linder-Harth method, which employ the ratio of the total width



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of the four maxillary incisor crowns to the premolar index (80 and 85) and the molar index (64 and 65). These methods are used by orthodontists to diagnose abnormal size of dental arches in transversal planes. A difference between the estimated and the actual values is indicative of impaired dental arch shape and size at the premolar and the molar areas. Disturbing is the fact that the same estimated values are calculated through different indices, while interpreting the outcomes will often prove rather complex. Besides, there is no mention of the types of dental arches where such methods are recommended to be employed in clinical practice [10,12,16,28]. Nine major types were selected to describe dental arches even in cases of physiological occlusion, whereas each of the types reveals certain features of dental and gnathic nature [1,3,17,18,19]. There is data available stating that the gender and race



features do not affect the major dimensions as much as dentofacial and odontometric parameters do [22,23].

Special literature does contain no sufficient data on transversal sizes of dental arches for different dental and gnathic types, and there is no indication of the cases where the said measuring methods could be employed.

## AIM OF STUDY

To extend the role of transversal dimensions in diagnosing abnormal dental arch shapes in case of various dental and gnathic features.

## MATERIALS AND METHODS

In order to identify a match between the estimated values calculated via Pont and Linder-Harth methods, and the real size of dental arches between premolars and molars, we studied 362 cast jaw models obtained from people of both genders revealing different gnathic and dental types of arches. Subject to the methods above-mentioned, the mesio-distal sizes of four maxillary incisor crowns were measured. Transversal dimensions were taken between the Pont points located on premolars and molars (Fig. 1).

The types of the dental arches were identified following the dental index of the arch, taken as ratio of half-sum crown width of 14 teeth to the width between the second molars (Fig. 2).

The dental arches falling within the dental index range of  $0.94 \pm 0.03$  were taken as mesognathic. An index below 0.9 indicated the brachygnathic type while a value above 0.97 was considered to belong to dolichognathic type of dental arch (Fig. 3).

Normodontal dental arches had a length varying in between 112 mm and 118 mm. Any value beyond the range was taken as associated with macrodontal or microdontal arches respectively. The statistical processing was performed directly from the common data matrix of EXCEL 7.0 (Microsoft, USA) also involving certain features offered by the STATGRAPH 5.1 (Microsoft, USA) software, ARCADA (Dialog-MGU, Russia), and implied detecting the median values, its mean root square deviation, and the non-sampling error. Further on, following the patterns commonly employed for medical and biological studies (sample numbers; type of distribution; non-parametric criteria; reliability of the difference of 95%, etc.) the significance of the sampling difference was evaluated subject to the Student's criterion ( $t$ ) and the respective significance index ( $p$ ).

## RESULTS AND DISCUSSION

After odontometric evaluation, all the patients had the transversal size of their dental arches estimated based on Pont and Linder-Harth methods in view of

various dental and gnathic types of arches. Table 1 below offers a view on the outcomes.

It is obvious that the estimated transversal dimensions for macrodontia exceeded similar applicable values for other types of dental arches. Given that, the gnathic types of dental arches had no significant impact on the values. This is accounted for by the fact that in cases of macrodontia the sum of crown widths for the four upper incisors is larger compared with other types of arches.

The values calculated via Pont and Linder-Harth methods revealed significant differences in the area of premolars alone as the premolar index had major difference (80 and 85, respectively).

Measuring upper and lower dental arches demonstrated a mismatch between the estimated values and the actual ones (Table 2).

The study showed that the transversal dimensions of dental arches depend on the gnathic types of arches rather than on the teeth size.

Mention to be made that examination of mesognathic arches revealed no reliable difference between the estimated and the actual values. The data obtained serve evidence that Pont and Linder-Harth methods may be used to evaluate dental arch width in patients with mesognathic arches of all dental types (normo-, macro- and microdontia).

During that, the values obtained through studying brachygnathic arches with Linder-Harth method were reliably below the actual values. However, the estimated values used within Pont method revealed no significant difference when matched with the actual ones. This means that Linder-Harth method, if employed to analyze brachygnathic arches, is prone to significant errors.

In case of dolichognathic arches, the values were different from those obtained for brachygnathic arches. The estimated values obtained with Pont index were significantly above the actual values for normodontal as well as for microdontal and macrodontal dental arches. The estimated values taken within Linder-Harth method, however, demonstrated no difference from the actual values, which suggests that Linder-Harth method may be employed to detect the width of dolichognathic dental arches.

## CONCLUSION

1. Transversal sizes of dental arches depend less on the teeth size and are determined by the gnathic type of the arch.
2. Both methods are likely to appear valid when working with mesognathic type of dental arches.
3. When evaluating the said parameter of brachygnathic arches, the methods based on identifying

**Table 1.** Transversal size of dental arches evaluated following Pont and Linder-Harth method depending on the type of arches, (mm), ( $M \pm m$ ;  $p \leq 0.05$ )

Dental arch	Estimated size of dental arch by			
	Pont method, between:		Linder Harth method, between	
	premolars	molars	premolars	molars
Mesognathic normodontia	38.75 $\pm$ 0.54	48.44 $\pm$ 1.07	36.47 $\pm$ 0.97	47.69 $\pm$ 1.09
Mesognathic macrodontia	42.62 $\pm$ 0.69	53.03 $\pm$ 1.14	39.98 $\pm$ 0.82	52.23 $\pm$ 1.13
Mesognathic microdontia	36.15 $\pm$ 0.78	45.04 $\pm$ 0.96	34.16 $\pm$ 0.73	44.32 $\pm$ 1.15
Brachygnathic normodontia	39.37 $\pm$ 0.77	49.22 $\pm$ 1.03	37.06 $\pm$ 0.82	48.46 $\pm$ 1.26
Brachygnathic macrodontia	42.79 $\pm$ 0.75	53.51 $\pm$ 1.26	40.28 $\pm$ 0.79	52.68 $\pm$ 1.18
Brachygnathic microdontia	37.51 $\pm$ 0.74	46.87 $\pm$ 1.37	35.29 $\pm$ 0.84	46.15 $\pm$ 1.37
Dolichognathic normodontia	40.03 $\pm$ 0.59	50.03 $\pm$ 1.26	37.67 $\pm$ 0.87	49.26 $\pm$ 1.39
Dolichognathic macrodontia	42.33 $\pm$ 0.88	53.41 $\pm$ 1.13	40.21 $\pm$ 0.72	52.59 $\pm$ 1.08
Dolichognathic microdontia	36.27 $\pm$ 0.71	44.97 $\pm$ 1.21	33.92 $\pm$ 0.95	44.13 $\pm$ 1.19

**Table 2.** Transversal size of dental arches at molars and premolars depending on the type of arches, (mm), ( $M \pm m$ ;  $p \leq 0.05$ )

Dental arch	Size of dental arch (mm) on jaw			
	Upper, between		Lower, between	
	premolars	molars	premolars	molars
Mesognathic normodontia	37.14 $\pm$ 1.48	48.51 $\pm$ 1.86	36.97 $\pm$ 1.58	48.31 $\pm$ 1.58
Mesognathic macrodontia	40.89 $\pm$ 1.77	52.62 $\pm$ 2.03	41.11 $\pm$ 1.56	53.16 $\pm$ 1.58
Mesognathic microdontia	35.31 $\pm$ 1.73	45.69 $\pm$ 1.44	35.79 $\pm$ 1.64	45.61 $\pm$ 1.72
Brachygnathic normodontia	40.87 $\pm$ 1.34	52.77 $\pm$ 1.74	40.81 $\pm$ 1.28	52.69 $\pm$ 1.86
Brachygnathic macrodontia	43.97 $\pm$ 1.47	54.66 $\pm$ 1.85	44.01 $\pm$ 1.37	54.89 $\pm$ 1.79
Brachygnathic microdontia	37.89 $\pm$ 1.48	47.02 $\pm$ 1.52	38.17 $\pm$ 1.42	48.41 $\pm$ 1.44
Dolichognathic normodontia	36.4 $\pm$ 1.18	46.2 $\pm$ 1.29	35.18 $\pm$ 1.36	45.59 $\pm$ 1.46
Dolichognathic macrodontia	36.21 $\pm$ 1.53	46.59 $\pm$ 1.34	36.01 $\pm$ 1.75	46.89 $\pm$ 1.37
Dolichognathic microdontia	34.29 $\pm$ 1.17	42.11 $\pm$ 1.57	34.81 $\pm$ 1.66	42.05 $\pm$ 1.28

dental arch width based on Linder-Harth index, are prone to produce a significant error.

4. The index values based on Pont method cannot be considered reliable when working with dolichognathic arches with normodontia, macrodontia and microdontia.

## REFERENCES

1. **DMITRIENKO S.V., DOMENYUK D.A., DMITRIENKO D.S.** Modern classification of dental arches // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 14–16.
2. **DMITRIENKO S.V., DOMENYUK D.A., DMITRIENKO D.S.** Interrelation between sagittal and transversal sizes in form variations of maxillary dental arches // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 10–13.
3. **DMITRIENKO S.V., DOMENYUK D.A., VEDESHINA E.G.** Shape individualization in lower dental arches drawn on basic morphometric features // Archiv EuroMedica, 2015. – Vol. 5. – № 1. – P. 11.
4. **DOMENYUK, D.A.** Anatomic and topographic rationale for dental arch constructing and measuring methods / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko // Kuban scientific medical Herald, 2015. – Vol. 152. – № 3. – P. 31–37.
5. **DOMENYUK, D.A.** Basic morphometric parameters of the dental arches in people with brachygnathic the form of a dental arch and the macro-, micro- and normodontia types of dental systems / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2015. – Vol. 68. – № 3. – P. 44–48.
6. **DOMENYUK, D.A.** Biometric justification of main linear dimensions of the dental arches in orthodontic treatment tactics' development using edgewise orthodontic technique (part I) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2016. – Vol. 70. – № 1. – P. 76–78.
7. **DOMENYUK, D.A.** Biometric justification of main linear dimensions of the dental arches in orthodontic treatment tactics' development using edgewise orthodontic technique (part II) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // Institute of dentistry, 2016. – Vol. 71. – № 2. – P. 66–67.

8. **DOMENYUK, D.A.** Comparative analysis of morphometric parameters and dental arch in different variants of their shape / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2015. – Vol. 151. – № 2. – P. 59–65.
9. **DOMENYUK, D.A.** Dependence between size of permanent teeth and linear parameters of mesognathic dental arches / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2015. – Vol. 69. – № 4. – P. 78–80.
10. **DOMENYUK, D.A.** Factors determining choice of metal arches and braces specification in edgewise technique-based orthodontic treatment (part I) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2015. – Vol. 69. – № 4. – P. 92–93.
11. **DOMENYUK, D.A.** Factors determining choice of metal arches and braces specification in edgewise technique-based orthodontic treatment (part II) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2016. – Vol. 70. – № 1. – P. 54–57.
12. **DOMENYUK, D.A.** Geometrical and graphic reproduction of dentoalveolar arches in physiological occlusion of permanent teeth / D.A. Domenyuk, S.V. Dmitrienko, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2015. – Vol. 66. – № 1. – P. 62–64.
13. **DOMENYUK, D.A.** Impact of odontometric parameters on shape and size of mesognathic dental arches / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2015. – Vol. 153. – № 4. – P. 73–79.
14. **DOMENYUK, D.A.** Improved methods for diagnosing dentoalveolar abnormalities based on functional shifts in oral homeostasis (part I) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2016. – Vol. 71. – № 2. – P. 74–77.
15. **DOMENYUK, D.A.** Improved methods for diagnosing dentoalveolar abnormalities based on functional shifts in oral homeostasis (part II) / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2016. – Vol. 72. – № 3. – P. 58–61.
16. **DOMENYUK, D.A.** Interrelation between sagittal and transversal sizes in form variations of maxillary dental arches / D.A. Domenyuk, S.V. Dmitrienko // *Archiv euromedica*, 2014. – Vol. 4. – № 2. – P. 10–13.
17. **DOMENYUK, D.A.** Modern classification of dental arches / D.A. Domenyuk, S.V. Dmitrienko // *Archiv euromedica*, 2014. – Vol. 4. – № 2. – P. 14–16.
18. **DOMENYUK, D.A.** Morphometric analysis of dental arches in physiological occlusion of permanent teeth / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2015. – Vol. 69. – № 4. – P. 74–77.
19. **DOMENYUK, D.A.** Morphometric parameters of brachygnathic dental arches considering size of permanent teeth / D.A. Domenyuk, E.G. Vedeshina // *Kuban scientific medical Herald*, 2015. – Vol. 155. – № 6. – P. 47–53.
20. **DOMENYUK, D.A.** Optimization of treatment based on edgewise orthodontic technique in view of individual shape of dental arch / D.A. Domenyuk, E.G. Vedeshina // *Kuban scientific medical Herald*, 2015. – Vol. 154. – № 5. – P. 56–63.
21. **DOMENYUK, D.A.** Sagittal and transversal dimensions of dolichognathic dental arches in humans with macrodontia, microdontia, and normodontia / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2016. – Vol. 71. – № 2. – P. 60–63.
22. **DOMENYUK, D.A.** The main forms of individual microdontia formed in the mixed dentition of permanent teeth / D.A. Domenyuk, A.A. Korobkeev, E.G. Vedeshina [et al.] // *Medical news of North Caucasus*, 2016. – Vol. 11. – № 3. – P. 474–476.
23. **DOMENYUK, D.A.** Teeth sizes in their correlation with parameters of dentofacial arches and maxillofacial area based on native cranial preparations examination / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2016. – Vol. 157. – № 2. – P. 71–79.
24. **DOMENYUK, D.A.** Variability of odontometric parameters in patients with physiological occlusion of permanent teeth and mesognathic dental arches / D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina [et al.] // *Institute of dentistry*, 2015. – Vol. 68. – № 3. – P. 74–77.
25. **DOMENYUK D.A., VEDESHINA E., DMITRIENKO S.V.** Certain parameters of incomplete dental arches with missing premolars after orthodontic treatment // *Socially Significant Human Diseases: Medical, Environmental and Technical Problems, and these Solutions III Japanese-Russian International Conference*. – 2016. – C. 81–82.
26. **DOMENYUK D.A., VEDESHINA E., DMITRIENKO S.V.** Choice of metallic arches and braces press ription in view of individual shape of dental arche // *Socially Significant Human Diseases: Medical, Environmental and Technical Problems, and these Solutions III Japanese-Russian International Conference*. – 2016. – C. 83–84.
27. **DOMENYUK D.A., VEDESHINA E.G., DMITRIENKO S.V.** Efficiency evaluation for integrated approach to choice of orthodontic and prosthetic treatments in patients with reduced gnathic region // *Archiv Euro-Medica*. – 2015. – Vol. 5. – № 2. – P. 6–12.
28. **VEDESHINA, E.G.** Determining torque and angulation of permanent teeth in cases of brachygnathic dental arches depending on dentition type / E.G. Vedeshina, D.A. Domenyuk, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2015. – Vol. 155. – № 6. – P. 23–30.
29. **VEDESHINA, E.G.** Correlation between shapes and sizes of dentofacial arches and their stable parameters / E.G. Vedeshina, D.A. Domenyuk, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2016. – Vol. 158. – № 3. – P. 33–38.
30. **VEDESHINA, E.G.** Odontometric parameters in cases with mesognathic dental arches / E.G. Vedeshina, D.A. Domenyuk, S.V. Dmitrienko // *Kuban scientific medical Herald*, 2015. – Vol. 153. – № 4. – P. 44–48.

# THE PECULIARITIES OF MYOCARDIAL CONDITION ESTIMATION IN INTERATRIAL SEPTAL DEFECTS IN CHILDREN OF EARLY AGE

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**ABSTRACT** — 31 children of early age with interatrial septal defect (IASD) were observed concerning their laboratory – instrumental peculiarities of myocardial condition before and after surgical correction. There were 2 groups of patients in dependence of hemodynamics condition and levels of precordial sodiumuretic peptide (NT — proBNP) and myocardial fraction of creatinphosphokinaza (MB — CPhC) data. It was determined that the myocardial condition in children before cardiosurgical correction was exactly correlated with expressiveness of hemodynamic disturbances. After operation there may be the presence of changes in studied biochemical data witnessing the restructure of myocardium. In the late periods it may be connected with heart activity disturbances. It should be advisable to use the definition of levels of NP — proBNP and activity of MP — CPhC in combination with echocardiographic data for estimation of myocardial condition.

**KEYWORDS** — defect, interatrial septum, cardiosurgical correction, children, laboratory data (NP — proBNP, MB — CPhC), myocardium

The timely surgical correction of interatrial septal defect (IASD) leads to normalization of intracardial hemodynamics, positively influences on the condition and further fate of patients. But it is necessary to take into consideration that even qualified cardiosurgical correction may be complicated by different disturbances during postoperative period [1, 2, 3, 4, 7, 8].

It is known that in case of full closure of defect the lethal outcome is 1,5–2% after these operations.

The most frequent reasons are embolia, sepsis and progression of hemodynamic disturbances on the base of remodelling of myocardium [5, 6, 9, 10, 11, 12, 13.].

## *The aim of investigation:*

to find out laboratory – instrumental peculiarities of myocardium condition before and after surgical correction of interatrial septal defect in children of early age.

## THE CHARACTERISTIC OF CHILDREN AND METHODS OF INVESTIGATION

35 patients at the age of 1–3 years with congenital heart failure (CHF) – isolated by secondary non-restrictive interatrial septal defect (IASD) of mild size (5–12 mm) were under observation. 31 patients had operative treatment – closure of defect by endovascular (transcatheter) way using Amplatzer Septal Occluder or BioSTAR septalrepairimplant («NMT-Medical», Boston). The other (4) patients had no correction.

## *The methods of investigation included:*

anamnesic, clinical, biochemical, instrumental and statistic. The complex estimation of cardiovascular system condition in children was made in conditions of cardiorheumatological department of N.N. Silishcheva hospital in dynamics in 1 month before operation, in 2 weeks and 6 months after it. Laboratory investigations: there were defined the levels of sodiumuretic peptide (NT-pro-BNP) and activity of MB — creatinphosphokinaza (MB-CPhC) in blood serum using the method of immunoferment analysis (IFA).



### *The instrumental methods were:*

electrocardiography (ECG), echocardiography (EchoCG), dopplerechocardiography (Doppler-EchoCG), taking into attention the features of relocation, dystrophic and hypertrophic changes in myocardium, thickness of walls and size of heart cavities, features of diastolic dysfunction and disturbances of contractive capability.

## RESULTS AND DISCUSSION:

In 70,9% cases the diagnose of CHF was done antenatally, in other cases — 29,1 % — postnatally on the base of complex clinico-instrumental investigation. It was found out that in 19 (61,3%) patients the size of defect was not more than 7 mm, and in 12 (38,7%) — 8–12 mm. In detailed analysis of anamnestic data in 5 children (16,12%) there was determined negative dynamics of defect size (increase in 1–2 mm), but in 4 (12,9%) — positive (decrease in 2–3 mm) during observation, they were not included into further investigation. In 12 children (38,7%) the heart failure was in the stage of initial manifestation, in 9 (61,3%) there was marked clear clinical picture (IASD). It was defined that chronic heart failure (ChHF) manifested clinically in the I stage in 16 (51,61%), II A stage in 15 (48,39%) cases which had coincidence to 1–2 functional classes. There was marked the high frequency of respiratory diseases: recurrent acute respiratory infection in 17 (54,84 %), bronchitis in 8 (25,8%), pneumonia in 6 (19,3 %).

Clinically before operation in 5 patients (16,12%) there were found out the moderate backward in physical development, paleness of skin in 25 (80,65%), moderate dyspnea in 18 children (58,06%), moderate tachycardia in 15 cases (48,39%), widening of heart borders to the right in 16 patients (51,61 %), soft systolic sound in 2–3 intercostal part to the left from the sternum 15 (48,39 %).

In the ECG in 20 cases (64,52%) there were marked the rightgram, hypertrophic changes in myocardium in 21 children (67,74%), the features of relocation disturbances in 18 cases (58,06%), dystrophic changes in 10 children (32,26%). In EchoEG there were the significant increase of right parts of the heart in 16 (51,61%), moderate widening of pulmonary artery stem in 13 (45,14%). But the pressure in this vessel and in right ventricle was not higher than 30 mm Hg. According to dopplerEchoCG there was the significant outcome of blood in the left part to the right one in single cases 4 (12,9%). In 15 (48,3%) patients there were defined the disturbance of diastolic function, in other cases 16 (51,61%) — systolic dysfunction of myocardium.

So, clinic-instrumental data showed the presence of features of myocardium remodelling of different stage expressiveness in observed children before operation.

In laboratory investigation there were found out the real increase of levels of precordial sodiumuretic peptide (NT-pro-BNP) ( $p < 0,01$ ) and moderate increase of myocardial fraction activity of creatinphosphokinaza (MB-CPhC) ( $p < 0,05$ ) in comparison with normal one (Table 1).

The detailed analysis of biochemical data allowed to divide children into 2 groups: the first group had 14 patients with significant increase of levels NT-pro-BNP ( $p < 0,001$ ), the second one — 17 patients with moderate changes ( $p < 0,05$ ). Besides it, the children of the first group had the moderate increase of MB-CPhC ( $p < 0,05$ ) activity, and the second group had no such phenomena ( $p < 0,05$ ). It was marked that in the first group CHF was complicated by ChHD II A stage, in the second — mostly by I stage. All patients were operated because of heart failure.

In the early postoperative period in the first group in comparison with the second there were kept clinically moderate expressed features of disturbances in blood circulation: in 5 (35,71%) cases — insignificant dyspnea, moderate widening of heart borders to the right in 11 (78,57%) children. It was confirmed by ECG data, in 11 (78,57%) patients there were registered rightgram, hypertrophic changes in myocardium of right atrium was found in 6 children (42,85%). In EchoCG there were moderately increased the right parts of the heart in 7 (50%). In dopplerEchoCG in most cases 12 (85,71%) there were marked diastolic dysfunction, in half cases — systolic one. The received data witnessed that in children of this group in early postoperative period there may be kept the features of myocardium remodelling which had been before. In the second group clinic-instrumental data were differed greatly in comparison with the normal one. In biochemical data the patients of the first group had the following peculiarities increase of activity levels MB — CPhC in comparison with such ones before defect correction, it may be connected with undergone operation and presence of heart activity disturbances (Table 1). At the same time the levels of NT — pro- BNP decreased, it was the result of normalization of pathological processes in myocardium (Table 1). But in some cases — in 5 patients (35,7%) they remained moderately increased in spite of general tendency to normalization.

In other children there was made the comparison with clinico – instrumental data of remodelling. There was used non-parametric method of range correlation of Spirman, taking into account the coefficient of correlation and criteria of their statistic meaning. The coefficient of correlation was  $r = 0,85$  in  $p < 0,01$ . So, the condition of levels NT — proBNP may be considered as additional criterium for diagnostics of myocardial remodelling in children.

**Table 1.** The levels of biochemical data in children with IASD

Groups of children	Data	
	MB – CPhC (f/l)	NT – proBNP (pk/ml)
Before operation		
first	49,4±7,1	398±17,1
second	31,5±4,1##	285±17,1###
After operation: in 1–2 weeks:		
first	72,2±8,3**	332 ±15 **
second	39,5±7,2*###	243 ±16*###
In 6 months		
first	33,4±4,7*	260 ±15***
second	28,6±3,6*#	220 ±17*#

\* — meanings of reality in comparison of data before operation and in different periods after operation;

\* —  $p > 0,05$ ; \*\* —  $p < 0,01$ ; \*\*\* —  $p < 0,001$ .

# — meanings of reality in comparison of data of the first and second group;

# —  $p > 0,05$ ; ## —  $p < 0,05$ ; ### —  $p < 0,001$

In patients of the second group in comparison with preoperative period the changes of laboratory data were statistically not correct ( $p > 0,05$ ). In 6 months the patients of this group had the significant positive dynamics in comparison with the first one. It was marked the improvement of condition, disappearance of dyspnea, normalization of heart contractions frequency and respiratory movement.

At the same time the children of the first group had the presence of systolic sound in V point and in the second intercostal part in the left side from the sternum in 12 patients (85,71%). The expressed positive dynamics of changes in ECG in children of the first group there were marked more late periods after operation.

So, it was defined that the myocardial condition in children of the early age with ISAD before cardio-surgical correction clearly correlate with expressiveness of hemodynamic disturbances. In case of normalization of hemodynamics after heart operation there may be preserved the changes of biochemical data levels, which show the incompleteness of pathological processes and changes in myocardium. In late dates it may be the reason of complications and presence of heart activity disturbances. For estimation of myocardial condition it should be advisable to use the definition of levels NP — pro-BNP and activity of MB-CPhC in combination of echocardiographic data.

## REFERENCES

1. **BOKERIA L.A.** Modern ways to surgical treatment of congenital heart failure in the early children age (L.A. Bokeria, K.V. Shatalov, M.V. Arnautova et al // Abstracts of reports of All-Russian congress «Medicine to children» N.Novgorod, 2003. — P. 5.
2. **DORONINA T.N.** Congenital heart failure in newborns and children of breast nutrition age. / T.N. Doronina, N.S. Cherkasov: manuscript. — Astrakhan: ASMA, 2011. — 222 p.
3. **DORONINA T.N.** The peculiarities of epidemiology of congenital heart failure in children of early age. / T.N. Doronina, N.S. Cherkasov // Medical journal, 2012. № 3. — P. 175–176.
4. **KOMISSAROVA O. A.** Criteria of estimation of heart activity disturbance in children with congenital heart failure. / O.A. Komissarova, T.N. Doronina, N.S. Cherkasov, M.Ya. Ledyayev, L.K. Gavrikov // Bulletin of Volgograd state medical University. 2012. № 2. — P. 39–41.
5. **CHEKASOV N.S.** Diseases of heart in newborns and children of early age / N.S. Cherkasov. Rostov – on – Don: Fenix. — 2006. — 191 p.
6. **CHEKASOV N.S.** Diseases of heart in newborns and children of early age. N.S. Cherkasov, T. N. Doronina: manuscript – Astrakhan. Publishing house of ASMA, 2041. — 345 p.
7. **CHEKASOV N.S.** Child's heart. / N.S. Cherkasov, T. N. Doronina // manuscript – Astrakhan. Publishing house of ASMA, 2015. — 184 p.
8. **DORONINA T.N.** Clinico-biochemical criteria of cardio – adaptation of children // T.N. Doronina, N.S. Cherkasov / Archiv Euromedica. — Vol. 3. — №1 — 2013. — P. 61–63.
9. **GIAMBERTI A.** Combined atrial septal defect surgical closure and irrigated radiofrequency ablation in adult patients / A. Giamberti, M. Chessa, S. Foresti, et al. // Ann. Thorac Surg. — Vol.82.2006. — P. 1327–1331.
10. **PANOVA, T.N.** Algorithms of diagnostics and treatment in cardiology. Part 6. Heart diseases. An infectious endocarditis / T.N. Panova, A.T. Abdrashitov, A. A. Demidov // methodical grant, — Astrakhan, Public Educational Institution of Higher Professional Training AGMA. — 2013. — 99 p.
11. **PANOVA, T.N.** Chronic heart failure / T.N. Panova, L.A. Galtsev, A. A. Demidov // the Manual, - Astrakhan, Public Educational Institution of Higher Professional Training AGMA. 2013. — 88 p.
12. **SIGLER M.** Biocompatibility of septal defect closure devices / M. Sigler, C. Jux, et al. // Heart. — 2006. October 11. — Available at: <http://heart.bmjournals.com>. Accessed October 15, 2006.
13. **THOMASA L.** Atrial structural remodelling and restoration of atrial contraction after linear ablation for atrial fibrillation / L. Thomasa, A. Boyda, S.P. Thomasa et al. // Eur. Heart J. — Vol.24. — № 21. — 2003. P. 1942–1951.

# QUALITY OF LIFE AND SLEEPINESS AMONG GRADUATE STUDENTS OF NURSING AND PHARMACY FROM A FEDERAL UNIVERSITY IN MATO GROSSO, BRAZIL

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**ABSTRACT** — The aim of this study was to determine some important factors related to the quality of life and sleep among university students of nursing and pharmacy.

**KEYWORDS** — Sleep; leisure; sexual dissatisfaction.

## INTRODUCTION

Quality of life (QOL) has been defined as being a subjective perception of the person regarding his/her situation in social life according to cultural and value systems and also in relation to their concerns, standards, goals and expectations [1].

Also considered the subjective well-being, QOL is influenced by subjective values and expectations, age, social functioning, goal adjustment, self-efficacy, presence or absence of comorbidities, education, salary, employment status, and responsibilities [2–8].

The life of academic students, especially in developing nations, is not so easy. In fact, their transition to adult life is marked by excessive new responsibilities and greater physical and mental demands during each academic semester [9,10].

As a consequence of overload demands due to working and studying, university students, especially from the health sciences courses, had sleeping problems, physical fatigue, attention difficulties, anxiety, stress and depression as well as decreased perception of adequate QOL [10–12].

Considering that inadequate quality of life can compromise the whole life aspects of the future health professionals, the objective of the current study was to determine the QOL and sleepiness of nursing and

pharmacy students from a Federal University in Mato Grosso State, located in the Central-Western Brazil.

## MATERIALS AND METHODS

An observational transversal study was conducted with 196 university students of Nursing (83 subjects) and Pharmacy courses (113 subjects), both gender, from the Araguaia University Campus, located in Pontal do Araguaia, MT, Brazil. Family income (in Brazilian basic salaries, e.g., US\$200.00) of pharmacy students were higher than nursing students and is presented in Fig. 1.

Before answering the questionnaire students agree and signed an informed consent to engage the study. The instrument was the validated Brazilian version of the WHOQOL-bref plus two questions from the hole version [13] and the Epworth sleepiness scale [14]. Statistical analysis consisted of the z-test which compares the frequency of events in different two proportions (nursing students x pharmacy students) and the significance level was 5% ( $p < 0.05$ ).

## RESULTS

The presence of negative feelings tended to be increased among pharmacy than nursing students which, however, was not statistically different (5.88% versus 11.43%,  $p < 0.18$ ).

Considering the perception of QOL nursing students tended to had lower positive perception which was not confirmed by statistical analysis ( $p = 0.43$ ).

A higher frequency (90%) of university students

declared positive meaning attributed to life with no significant differences between groups ( $p=0.37$ ). Students also reported a higher satisfaction with received familial support during their courses (80%) with no differences between the groups ( $p=0.42$ ).

In respect of focusing capacity, learn and memory, 8.8% and 16.8% of nursing and pharmacy students had lowest values, whereas 32.6% and 43.4% of nursing and pharmacy academics had high focusing, leaning and memory capacity with no statistically significant difference between the two courses.

Self-satisfaction (67%) and self-image acceptance (60.85%) scores were higher among both student groups with no statistical differences.

A considerable proportion (23.35%) of both nursing and pharmacy students was not satisfied with their sleeping, whereas 54.5% were satisfied or very satisfied with their sleeping routines (Fig. 2).

Sexual satisfaction was different among nursing and pharmacy students (Fig. 3). More nursing students were dissatisfied with their sexual lifes comparing to pharmacy students (15.2% versus 6.3%,  $p=0.04$ ). However, in the other groups (neither satisfied nor dissatisfied and satisfied) there were no significant differences between pharmacy and nursing students.

As noted in figure 4, the proportion of nursing students that had lower leisure opportunities was higher than that found for pharmacy students (30.2% versus 16.7%, respectively,  $p=0.025$ ), whereas considering high leisure opportunities the proportion was greater among pharmacy than nursing students (43.5% versus 26.5%, respectively,  $p=0.015$ ).

The Epworth sleepiness scale indicates the probability of daytime sleeping and is an indirect method for measuring sleep quality and fatigue. In this respect, the mean Epworth scores of pharmacy students ( $\chi \pm \eta - 1 = 11 \pm 3.2$ ) classified them as mild excessive daytime sleepiness, whereas nursing students ( $\chi \pm \eta - 1 = 9 \pm 3.7$ ) were considered with normal daytime sleepiness.

## DISCUSSION

The presence of negative feelings (negative mood) was lower when compared to other studies. A study with nursing students in São Paulo, Brazil, reported prevalence of depression ranging from 15.4% to 28.6% [12].

Although using another method to verify the general satisfaction with QOL a study from Ribeirão Preto (SP), Brazil [15], found similar results compared to the present study.

However, a study from São Paulo (SP), Brazil, reported a 60.1% satisfaction with QOL [16], whereas nursing and pharmacy students, from the current work, reported 77.9% and 67.5% of QOL satisfaction,

respectively.

In another study conducted in Lorena, São Paulo state (SP) [17], the satisfaction with QOL was also lower (55%) when compared to the present study.

Focusing, learning and memory capacity in the current study was higher in both nursing (83.2%) and pharmacy (91.2%) students compared with data (62.18%) from a private nursing school in Curitiba, PR, Brazil [18]. A possible factor that explain this lower focusing, memory and learning score from nursing of Curitiba is that the majority of them had to work in order to pay for the course, whereas the majority of the students from the current work did not work. In the same study nursing students reported 66.91% had satisfaction with QOL which was lower than data from the current study.

Leisure opportunities among nursing students (45.35%) were higher in the study of Machado et al. [18] compared to nursing students of the current study (26.5%), but were similar to that found for pharmacy students (43.4%) of this study. In the same manner, satisfaction with leisure opportunities were similar to data from a study with nursing students in Lorena, SP, Brazil [17].

In the current study the proportion of nursing students dissatisfied with sexual life was higher than that found for pharmacy students. However, the sexual satisfaction among both nursing and pharmacy academics (64.5% and 61.3%, respectively) was similar to that found in Curitiba study [18].

The QOL of pharmacy students of the current work was similar to that reported by Belmiro et al. [10] studying pharmacy academics from University of Brasilia, Brazil.

A study of QOL with four health courses (medicine, nursing, pharmacy, and phonoaudiology) from a public state university in Campinas (SP), Brazil, revealed that nursing had lower QOL scores compared to pharmacy, whereas medicine had the lowest QOL values [19].

## CONCLUSIONS

The satisfaction with QOL of the academics was high, whereas the presence of negative mood was very lower. However, only 54.5% of students from both courses were satisfied with sleep. Pharmacy students had increased risk of excessive daytime sleepiness, whereas nursing students were more prone to have dissatisfaction with sexual life and leisure opportunities.

## REFERENCES

1. AMINI M, ARDEKANI GS, GOLKARA, JAFARI P, ALHASHEMI HRH, MOGHADAMI M, HOSSEINI MM, ZAHRAEE N. Quality of life of medical



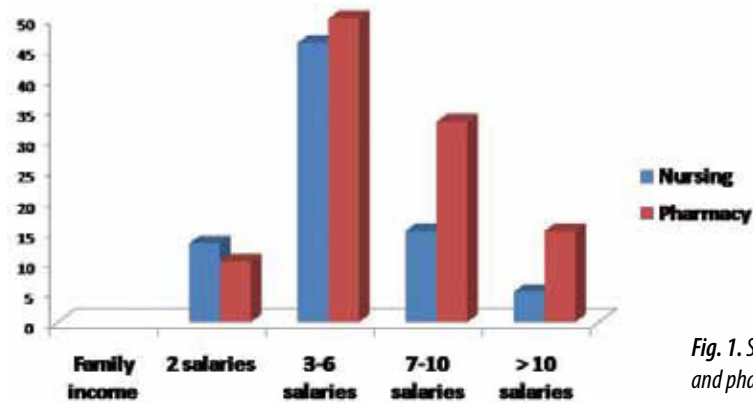


Fig. 1. Satisfaction with sleeping in nursing and pharmacy students

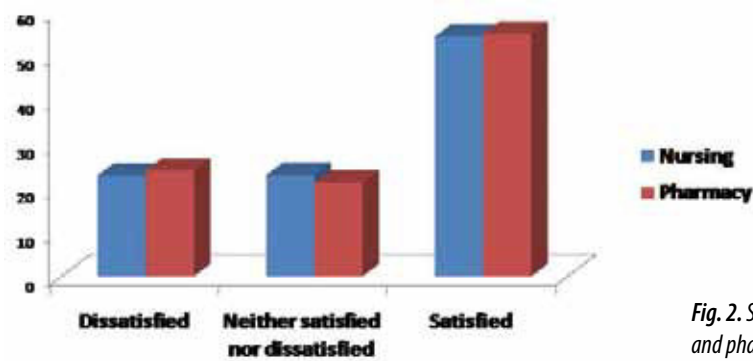


Fig. 2. Satisfaction with sleeping in nursing and pharmacy students

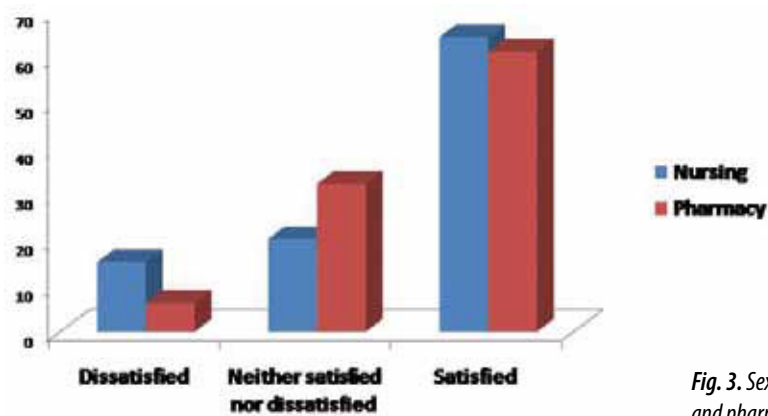


Fig. 3. Sexual satisfaction of nursing and pharmacy students

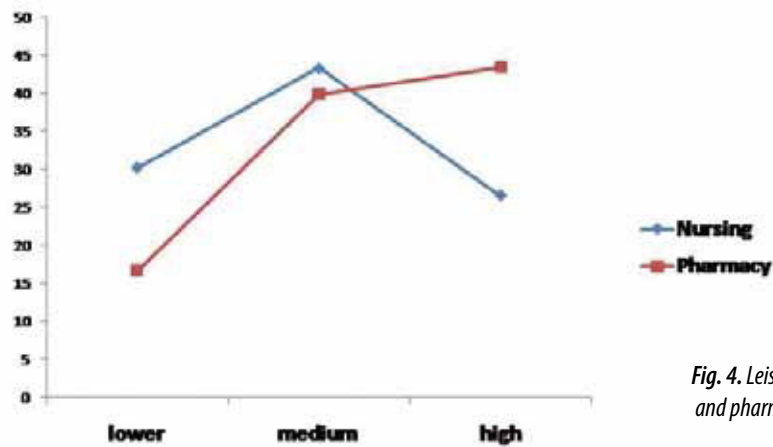


Fig. 4. Leisure opportunities among nursing and pharmacy students

- students in different stages – a multi center study. *Journal of Medical Education* 2007; 11(1/2):13-9.
2. **ARRONQUI GV, LACAVA RMVB, MAGALHÃES SMF, GOLDMAN RE.** Percepção de graduandos de enfermagem sobre sua qualidade de vida. *Acta Paul Enf* 2011; 24(6): 762-765.
3. **CARDOSO GM, VALOES LMA, ALMEIDA OAE, FERRARI CKB.** Qualidade de vida na percepção da gravidade da doença em portadores de diabetes mellitus. *Enf Foco* 2012; 3(3): 143-146.
4. **COFFEY L, GALLAGHER P, DESMOND D.** Goal pursuit and goal adjustment as predictors of disability and quality of life among individuals with a lower limb amputation: A prospective study. *Archives of Physical Medicine and Rehabilitation*, 2014; 95(2): 244–252.
5. **FERRARI CKB, FERREIRA RF.** Quality of life and exposition to unhealthy lifestyle risk factors of nocturnal university students from a greater metropolitan city. *J Biol Environm Sci* 2011;5(15):129-34.
6. **FERRARI CKB, GUIMARÃES CF, HONORIO-FRANÇA AC, FRANÇA EL.** Health and quality of life among workers from a great food supplier company in Sao Paulo (SP), Brazil. *Middle-East J Sci Res* 2011; 7(4): 543-549.
7. **FERRARI GSL, WADI JML, FERRARI CKB.** Qualidade de vida em profissionais da Estratégia de Saúde da Família (ESF) no Vale do Araguaia, Amazônia Legal, Brasil. *Scire Salutis* 2012/2013; 3(1): 78-85.
8. **FLECK MPA, LOUZADA S, XAVIER M, CHACHAMOVICH E, VIEIRA G, SANTOS L, PINZON V.** Application of the Portuguese version of the abbreviated instrument of quality of life WHOQOL-bref. *Rev Saúde Pública* 2000; 34(2): 178-183.
9. **FUREGATO ARE, SANTOS JLF, SILVA ED DA.** Depressão entre estudantes de dois cursos de enfermagem: autoavaliação da saúde e fatores associados. *Rev Bras Enf* 2010; 63(4): 509-516.
10. **JOHNS MW.** Daytime sleepiness, snoring, and obstructive sleep apnea: the Epworth sleepiness scale. *Chest* 1993; 103(1): 30-36.
11. **OLIVEIRA BM, MININEL VA, FELLI VEA.** Qualidade de vida de graduandos de enfermagem. *Rev Bras Enf* 2011;64(1): 130-135.
12. **MACHADO SA, OSELAME GB, NEVES EB.** Avaliação do perfil e qualidade de vida do acadêmico de enfermagem. *Rev Aten Saúde* 2016;14(47): 55-60.
13. **PANIAGO EN, FERRARI CKB.** Qualidade de vida e sono em mulheres de meia-idade e idosas do Vale do Médio Araguaia, Amazônia Legal. *Rev Lassalista de Investig* 2012; 9(1): 111-114.
14. **PEREIRA MO, PINHO PH, CORTES JM.** Qualidade de vida: percepção de discentes de graduação em enfermagem. *J Nurs Health* 2016; 6(2): 321-333.
15. **PARO CA, BITTENCOURT ZZLC.** Qualidade de vida de graduandos da área da saúde. *Rev Bras Educ Méd* 2013; 37(3): 365-375.
16. **SCHRIER E, SCHRIER I, GEERTZEN JHB, DIJKSTRA PU.** Quality of life in rehabilitation outpatients: normal values and a comparison with the general Dutch population and psychiatric patients. *Qual Life Res* 2016; 25(1): 135-142.
17. **UYSAL M, SIRGY MJ, WOO E, KIM HL.** Quality of life (QOL) and well-being research in tourism. *Tourism Management* 2016; 53: 244-261.
18. **VAN DELFT-SCHREURS CC, VAN BERGEN JJ, DE JONGH MA, VAN DE SANDE P, VERHOFSTAD MH, DE VRIES J.** Quality of life in severely injured patients depends on psychosocial factors rather than on severity or type of injury. *Injury* 2014; 45(1): 320–326.
19. **WHOQOL GROUP.** Study protocol for the World Health Organization project to develop a quality of life assessment instrument (WHOQOL). *Qual Life Res* 1993; 2(2): 153-159.

# FEATURES OF CHANGES OF THE ERYTHROBLASTIC ISLANDS ON THE STAGES OF POSTNATAL ONTOGENESIS UNDER TOXIC STRESS AND PHARMACOLOGICAL CORRECTION

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**ABSTRACT** — The study found that the process of erythropoiesis is dependent directly on the age group of experimental animals. The toxic effects of exogenous pollutants leads to a decrease of erythroid islands regeneration processes in the bone marrow dramatically reduces appear erythroid islands in involution. Especially vulnerable are the group of young and old animals during ontogeny. Against the background of the drug "etoksidol" with a strong antioxidant effect of the number of erythroid islands remodel increases in all study groups of experimental animals.

**KEYWORDS** — erythropoiesis, red bone marrow, a sulfur-containing gas, the experimental animals

Disturbance of the natural balance in a surrounding medium, connected with air pollution, water, soils, the emergence of emergency situations provoked by economic activity of the person by the beginning of our century essentially changed a natural xenobiotic profile of many territories that is especially shown in urbanized regions. From numerous technogenic toxic gases — the pollutants which are contained in the atmosphere and in the air of industrial production have the greatest value. Permanent release into the environment these pollutants leads to their accumulation, especially in the continuous production on oil and gas processing plants, which ultimately leads to chronic ecotoxicity of the environment [1, 2, 3, 5, 8].

The system of red blood is very sensitive to influences of production adverse factors of industrial environmental factors [4, 10, 12]. The modern research shows that the majority of xenobiotics has pro-oxidant properties. There is an activation of peroxide oxidation of lipids, balance upset between the formation and destruction of peroxides and excess accumula-

tion of toxiferous free radicals in a blood plasma and erythrocytes, which is an important component of the pathogenesis of negative conditions, in particular, of violations of erythropoiesis [7, 9; 13]. In this regard, the problem of protection of system of a hematopoiesis of the population living in the zone of influence of gas-chemical enterprises from influence of gaseous sulfur-containing pollutants, remains urgent now [14, 15].

The purpose of our research was the studying of feature of changes of the erythroblastic islands (EI) of red bone marrow at stages of a post-natal ontogenesis in the conditions of influence of sulfur-containing pollutants, and also at and pharmacological correction of antioxidant of a new generation — the medicine "ethoxydale". The properties, characteristic of this medicine, are: improvement of rheological behavior of blood, strengthening of cell metabolism, a high antioxidant activity, the ability to an inhibition of processes of peroxide oxidation of lipids, membrane-protective effect, speed of approach of effect, and also lack of negative consequences from its application [1].

The experiment is made on 72 white not purebred rats, who are contained in standard vivarium conditions in accordance with the "Rules of laboratory practice in the Russian Federation" (the order of MH of the Russian Federation № 708n from 23.08.2010). Group of three types were formed: I. — control; II. — exposed to sulfur pollutants; III. — treated as a protector domestic product "etoksidol" (JSC "Synthesis") intragastrically at a dose of 2.5 mg/kg, one time a day every day of the experiment.

As a toxic agent the natural drained gas of the Astrakhan gas condensate deposit was applied. In experiments the concentration of gas in steam-and-gas mixture making  $90 \pm 4$  mg/m<sup>3</sup> of hydrogen sulfide, which is 30 times more of threshold limit value of a hydrogen sulfide for working zones at simultaneous presence of hydrocarbons was used

The priming sour sulfur-containing gas was carried out 4 hours in autumn and winter seasons by a static method with simultaneous stay in the camera of 6 individuals daily within 30 days, except Sundays, strictly from 10 to 14 o'clock, temperature in the camera was  $+22 \pm 2^\circ\text{C}$ . The relative humidity during the experiment increased from  $53 \pm 4\%$  to  $66 \pm 6\%$ , fog-

ging of the walls was not noted. Concentration of gas and experimental conditions completely conform to the requirements stated in the edition of WHO [11] and the MH of the Russian Federation №267 from 19.06.2003. Control rats were of similar age experimental groups which 6 individuals in each group were also 4 hours in the air-locked inoculation camera in the same condations, as experieced, but in lack of sour gas were controled.

Bone marrow from the femurs was taken by means of the method developed by Yu.M.Zaharov, I.Yu.Melnikov and A.G.Rassohin [6]. Calculation of quantitative indicators characterizing a condition of an erythropoiesis in the EO was made by the method L.V. Vorgova Yu.M. Zaharov on the basis of the obtained data of the number of EO in the bone marrow of animals and their distribution by maturity classes. [6]

The quantitative data obtained in the course of the study, analyzed by methods of variation statistics and determine the significance of differences on Ulkokson-Mann-Whitney test. When carrying out statistical processing used OpenOffice Calc utility of free software OpenOffice (Ver. 3.0), running under Windows XP Home Edition (OEM X12-53766 certificate) operating system.

## RESULTS OF A RESEARCH

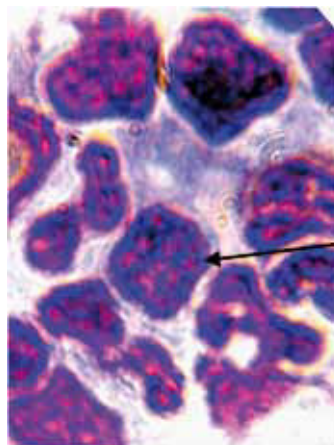
When analyzing the results of an experimental research with a protective action "etoksido" desire of age dynamics of content of all types of EO approach the level of the age norm is noteworthy that can be viewed as a relative normalization of erythropoiesis as a result of the process of improving its conditions. However, the severity of this process for various types of EO varies. In particular, EO maturity class can show a very significant and statistically highly significant increase in their number in response to the combined effects of pollutants and the tread in an immature age. In the following, an adult, a sharp drop in the number of islets of this species occurs under the tread that their number becomes scarce distinguishable from the age norm, ie, It is on the verge of statistical significance of differences.

In senile period of ontogenesis action tread leads to practical normalization of the structure and the amount of EO1, as the difference in their number and age control becomes statistically insignificant. As seen in Figure 1, the dynamics of the number of EO1 is almost completely determined by the involutive processes in the background of a slight effect of sulfur pollutants from the mature to old age in the conditions of the tread impact.

Age dynamics of the number of EO2 is similar in general terms to the same parameter EO1 under the

combined effects of pollutants and the tread. However, the effectiveness of the protective action is not as strongly dependent on the age, as in the previous case. It revealed that the protector reduces the amount of EO2 almost the exact same amount as a result of increased toxic effects, regardless of age. At the same time difference to the control remains reliable for all ages in the number using EO2 tread.

Deformed picnotic central macrophage determined statistically significantly less in comparison with the impact of sulfur-containing pollutants, namely  $21 \pm 8\%$  of the cases ( $P < 0,05$ ), while they themselves erythroblastic islands have a symmetrical structure. Age dynamics of content EO3 under the action of tread is very interesting. The desire to increase sharply reduced under the influence of this type of pollutant the number of the erythroblastic islands in the bone marrow is clearly expressed in an immature age. Content EO3 is virtually identical age control on the mature stage of ontogenesis.



*Fig. 1. EO 3rd class maturity rat elderly. Central macrophage is one large vacuole (arrow). Painting neutral red. Increase 90*



*Fig. 2. Remodel EO rats adulthood with several central vacuolated macrophages (arrows). Neutral red*



Further, in old age, there is a slight, but statistically significant excess of the amount EO3 over the age control, indicating, perhaps, the activation of the transformation in EO2 EO3 use as tread compounds and stimulation of erythropoiesis. Erythroblastic islands of this type under the tread actions look more organized compared to the experience without it. In the central macrophages pycnosis less pronounced. Vacuolation retained, however, in most cases, instead of multiple small observed 1–2 big vacuole. The protective effect on the content of erythroblastic islands in involution in terms of exogenous intoxication immature age is quite small.

This is confirmed by the lack of a statistically significant difference in the magnitude of this parameter in the case of the tread and without it. But in the mature period of ontogenesis the use of the tread gives a very noticeable effect, manifested in a high fidelity increasing number of EO in involution by 15% compared to only effect gas.

In old age the protective effect decreases, and does not ensure compliance with the age norm amounts erythroblastic islands in involution, although still statistically significant, because the number of EO of this type is significantly superior to the same amount without tread. Structurally EO in involution in the application of the tread differ slightly from similar, but only exposed to pollutants, as, indeed, and the last of the intact. In a small number of cases ( $9 \pm 3\%$ ) present picnotic central macrophages. At the same time, the number of central vacuolated macrophages, particularly those with large vacuoles statistically significant ( $P < 0.05$ ) reduced to  $42 \pm 8\%$  as compared with the experiment without the protector.

Using the tread under the impact of pollutants it is accompanied by the desire to remodel the dynamics EO content closer to the age norm. It turns out quite confident in immature and mature age of the experimental animals, as evidenced by highly significant difference ( $P < 0.01$ ) between the respective values.

In old age the tread less effective, since the difference between the amount of EO is reconstructed with the use of the tread and dramatically reduced without him, but still remained statistically significant ( $P < 0.05$ ). This fact indicates a significant slowing of the formation of this type of EO at this age, despite the use of the tread. Morphological studies show one of the mechanisms of this phenomenon. Since the total number of EO reconstructed in this case about 37% are composed of more than one of the macrophage and, frequently, 3–5 (Fig. 2), the latter apparently insufficient to produce the required amounts of EO type. Vacuolization central macrophages retained similar to that observed in the experiment, only the

influence of the sulfur-containing pollutants. More fully characterize the process of erythropoiesis by using the tread and its difference from a similar process in the conditions of exposure to sulfur pollutants only allow functional parameters are calculated based on the number of different types of EO.

The general tendency of the age dynamics of functional parameters using erythropoiesis tread, with rare exception, is the desire to return to the age norm.

Especially clear desire to return to normal with the help of the tread, despite the effect of the sulfur-containing gaseous pollutants, expressed in immature and mature stages of ontogeny of experimental animals. However, in old age is not so clear. These facts show a slight positive effect on the inhibited protective effects of intoxication intensity of involvement of dividing cells in the erythroid differentiation of macrophages and re participation in erythropoiesis. Despite the use of the tread, erythropoiesis continues to experience the negative impact of sulfur-containing gaseous pollutants, which is reflected in the decrease in the number of dividing cells of erythroid family, entered into differentiation. So, in response to the toxic effects of increasing the number of proliferating EO ( $EO_1$ ,  $EO_2$ ,  $EO_{rek}$ ) and drops EO, in which there is the maturation of red blood cells ( $EO_3$ ,  $EO_{inv}$ ). These processes are most intense in the immature age, their severity diminishes in adulthood and in old dies. The greatest environmental sensitivity erythrone system has in immature age, it is relatively stable in the mature and exhibits imbalance of self-regulation processes in the senile. This, in particular, is confirmed by the lack of effectiveness of protective effects.

## REFERENCES

1. **BLINOV, D. S.** Membrane mechanisms of antiarrhythmic action of a domestic cytoprotector of an ethoxydale // Messenger of arrhythmology. - 2011. - No. 66. - Page 42–45.
2. **GELASHVILI, O. A.** Variant of a periodization of biologically similar stages of ontogenesis of the person and rat / Saratov scientific and medical magazine. - 2008. - v.22. - No. 4. - Page 125–126.
3. **DUSHKIN V. A.** Laboratory livestock production [Text] / V. A. Dushkin. - M.: Rosselkhozizdat, 1980. - 48 C.
4. **ZAPADNYUK V. I.** To a question of an age periodization laboratory animals [Text] / V. I. Zapadnyuk // Gerontology and geriatrics. Annual. - To.: Health, - 1971. - 1972. - Page 433 – 438 p.
5. **ZAPADNYUK I. P.** Laboratory animal [Texts] / nominative Zapadnyuk, V. I. Zapadnyuk, E. A. Zachariah // - Kiev: "Vishcha school". - 1983. - 381 p.
6. **ZAKHAROV, YU. M.** Eritroblastichesky island / Yu.M. Zakharov, A. G. Rassokhin. - M.: "Medicine". - 2002. 280 p.

7. **KARNAUKHOVA N. G.** Determination of age gray and black rats [Text] / N. G. Karnaukhova//Ecology. – 1971. – No. 2. – P. 97–100.
8. **KUTSENKO S. A.** Fundamentals of toxicology: scientific and methodical edition / S. A. Kutsenko. SPb.: Volume, 2004. – 720 pages.
9. **MAZHITOVA, M. V.** Free radical processes and antioxidant protection of various departments of the central nervous system at stages of post-natal ontogenesis of white rats are normal Ypres action of industrial sulfur-containing pollyutant: avropeф. yew ... Dr.s биол. sciences/M. In Mazhitov. – Astrakhan, 2012. – 44 p.
11. **PAVLOVA M. M.** Functioning of eritrotsitary system in case of the anemicheskikh conditions at the workers occupied with conversion of the Astrakhan gas condensate [Text] / M. M. Pavlova, T. A. Esaulov//the Astrakhan medical magazine. – 2007. – No. 2. – Page 140.
12. Principles and evaluation methods of toxicity of chemicals. P.1. Geneva. WHO, 1981. – 312 pages.
13. **WARM D. D.** Age features of erythrocytes of peripheral blood of white rats and their reaction to effect of biological and synthetic antioxidants [Text] / D. D. Teply//Natural sciences. - 2009. – N 3. –P. 143–151.
14. **ESAULOVA T. A.** Features of forming of ecologically caused pathology at workers of large-scale gas-processing production: prevention, rehabilitation: yew.... doctors of medical sciences. / T. A. Esaulova. – Astrakhan, 2009. – 283 p.
15. **YAROSHINSKAYA, A. P.** The functional and morphological condition of plasma of blood and erythrocytes of the person at youthful, adult and mature age is normal also in the conditions of impact of sulfur-containing pollyutant: abstract yew.... doctors биол. sciences / A.P. Yaroshinskaya. – Astrakhan, 2011. – 34 p.
16. **YARYGA V. V.** Studying of erythrocytes and hemoglobin in dispensary groups with high risk of emergence of professional pathology on AGPZ [Text] / V. V. Yaryga//Works AGMA, t.iv (XXVIII). Materials of scientific research in the main directions of HIGHER EDUCATION INSTITUTION. – Astrakhan, 1996. – page 34–36.

# TREATMENT OF PATIENTS WITH ACUTE PARAPROCTITIS AGAINST THE BACKGROUND OF THE INOPERABLE MALIGNANT TUMORS OF THE RECTUM

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**ABSTRACT** — In all developed countries there is a clear upward trend in the incidence of colorectal cancer. The presence of highly virulent infection in the contents of the colon causes the inflammatory component of the process, the penetration of infection in adrectal fiber and as a result — the emergence adrectal abscesses. The aim is to analyze the results of treatment of patients with suppurative processes in adrectal tissue on a background of colon cancer. It was found that the operation, aimed at opening and drainage of a pararectal abscess or phlegmon of perineum allows you to temporarily stop the purulent process. New onset of inflammation in adrectal tissue is often repeated. It is advisable to consider the implementation of sanitary resection operations in such group of patients aimed at eliminating the primary malignant tumor.

**KEYWORDS** — tumor of the rectum, the destruction of the tumor, abscess of perirectal cellular tissue, acute paraproctitis

## INTRODUCTION

In all economically developed countries there is a clear upward trend in the incidence of colorectal cancer [1]. Now cancer of the colon and rectum is ranked third in the world in the structure of malignant tumors [2]. In Russia, over the last 20 years colon cancer has moved from 6th to 4th place among women and to the third among men's behind only cancer of lung, stomach and breast [3]. Increase in the absolute number of patients with cancer of the rectum and

colon in Russia from 2002 to 2009 was 12.7% among men and 14.5% among women [1].

Malignant tumors of the rectum are characterized by slow growth and the gradual appearance of clinical symptoms. Expressed symptoms of the disease occur when the tumor reaches large size. In most cases of colorectal cancers, tumor growth is noted mainly in depth, on the body wall, and its thickness, which is the cause of infection in adrectal fiber. The presence of highly virulent infection in the contents of the colon leads to instant connection of inflammatory component, the penetration of infection in pararectal fiber and as a result — the emergence of pararectal ulcers. At the same time questions of diagnostics and treatment of patients with suppurative pararectal diseases are not lose their relevance [4, 5].

### *Purpose of the research:*

analyze the results of treatment of patients with suppurative processes pararectal tissue against the background of colon cancer.

## MATERIALS AND METHODS OF RESEARCH

In total from 2012 to 2014 we have observed 18 cases of suppurative diseases pararectal tissue against the background of the tumor process of rectum.

It should be noted that in 9 (50%) cases, patients admitted to hospital several times over the period of

observation, namely, 3 patients — twice, and 1 patient — three times. From the total number of men was 16 (90%), women — 2 (10%). The age of patients ranged from 54 to 79 years. According to the classification of WHO (World Health Organization (2000)), half of the patients ( $n = 9$ ) was included in the category of older (60—74 years), 6 patients — the elderly (over 75 years) and in 3 cases — elder middle age (45–59 years). The distribution of patients according to the stages of cancer of the rectum was the next: 10 patients (55.6%) had the third stage of the disease, 8 patients (44.4%) — the fourth.

In 8 (44.4%) cases, patients are admitted to hospital with a diagnosis of the colorectal cancer (while in 7 cases (38.9%) patients with a history of suffered the imposition of a discharge loop sigmoidostoma, and in 10 (56.6%) observations It was diagnosed in this hospitalization.

Time since beginning of disease according to the anamnestic data was the next: on 4 day after appearing complaints 2 (11.1%) patients admitted to the hospital, from 5 to 11 days 7 (38.9%) patients was hospitalized, 12 to 15 days of beginning of disease — 5 (27.8%) patients, finally, after 16 days from the beginning of the first symptoms of the disease 4 (22.2%) patients was hospitalized.

Surgical intervention for pararectal suppurative processes against the background of the decaying tumors of the rectum is performed always on an emergency basis for urgent indications. Sometimes, delay of 1–3 hours was associated with severe general condition of the patient and intensive preoperative preparation. The antibacterial therapy started perioperatively. According to the testimony we carried out intensive infusion, transfusion therapy, detoxification and symptomatic treatment.

Operations of opening purulent pararectal cavity is performed under general anesthesia: we perform a wide opening pararectal abscess (phlegmon of perineum), which allowed us to carry out an adequate audit with assessment of the scope of affected tissues. We finish the surgical intervention by abundant washing wounds with an antiseptic solution, drainage of ischiorectal and pelviorectal spaces.

In the postoperative period we performed daily often dressings under intravenous sedation or neuroleptic analgesia with participation of anesthesiologist. During these dressings wound surface was sanitize antiseptic solutions, carried out by washing the cavity drains. At revealing during dressings more deeply drained streaks, we performed repeated operative interventions under general anesthesia.

## RESULTS

The maximum number of days, which patients was hospitalized with suppurative processes in the tissue on a background of inoperable rectal cancer, was 16, the minimum is 8.

The number of operations concerning pararectal suppurative disease on the background of rectal tumors for one patient was next: 12 (66.7%) cases, when patients needed only one operative intervention, which we made on emergency conditions on admission of the patient to the hospital.

In 6 (33.3%) cases we made 2 surgical interventions. In the next postoperative period treatment of these patients was limited by symptomatic conservative therapy and performing everyday dressing.

In 2 cases, in addition to operations was aimed to opening and sanitation pararectal abscess (phlegmon of the perineum), after 3–4 days the initial operation we made imposition of the loop sigmoidostoma and took into account the increasing acute colonic obstruction.

In the one case we use non-standard way of the treatment of the patient. Patient S., 63 years old, in May 2011 suffered to opening phlegmon of the perineum, in the same time diagnosis of rectal adenocarcinoma was verified. In August of that year loopsigmoidostoma was imposed. Radical surgical treatment is considered unwise, because patient had the multiple metastases of the right lobe of the liver. In February and July 2012, the patient was hospitalized with recurrent phlegmon of perineum, about which he has been repeatedly operated. Considering recurrence of inflammation pararectal fiber, in August 2012 we made obstructive low anterior resection rectal. The postoperative period was well. After discharge, patient was examined twice (December 2013 and May 2014) and recurrence of phlegmon of the perineum was not found. He died in November 2014 by reason of cancer cachexia.

Deaths during hospitalization among patients with suppurative pararectal diseases with the presence of rectal cancer have not been fixed.

## CONCLUSION

While treatment of suppurative tissue processes in the background of malignant tumors rectal, it is necessary to take into account that performed operation (opening and drainage pararectal abscess or phlegmon of the perineum) allows you to stop purulent process temporarily, but it does not eliminate the disease, because the cause of the disease is a tumor rectal. The new attacks of inflammation in pararectal tissue often repeat. That's why it's possibly to consider the question about performing for these patients sanitary resection



operations, which aimed for liquidation initial malignant tumor what can prevent recurrence of inflammation in pararectal tissue, which require to repeated surgical interventions.

## REFERENCES

1. **MESHKOV A.V., KRIVOSHEKOV E.P.** (Surgical treatment of patients with colorectal cancer complicated by intestinal obstruction, in a specialized cancer center). *The fundamental researches*, 2015, №1 (vol.1), pp. 103–106. (in Russian).
2. **JEMAL A., BRAY F., CENTER M. M., FERLAY J.** Global cancer statistics // *CA Cancer J Clin.* 2011. № 61. pp. 69–90.
3. **VOROB'EV G.I.** (Basis of coloproctology). Moscow: "Medical informative agency", 2006, 330 p. (in Russian).
4. **SERGATSKIY K.I., NIKOLSKY V.I., KLIMASHEVICH A.V., GERASIMOV A.V., KOSTIUKOVA I.M.** (Determination of dynamic of inflammatory processes of soft tissue in acute anaerobic non-clostridial paraproctitis based on data of joulemetry). *Vestnik of experimental and clinical surgery*, 2015, №4 (vol. 8), pp. 357–362. (in Russian).
5. **PERERA A.P., HOWELL A.M., SODERGREN M.H.** A pilot randomised controlled trial evaluating postoperative packing of the perianal abscess // *Langenbecks Arch. Surg.* 2015. (vol. 400). №2. pp. 267–271.

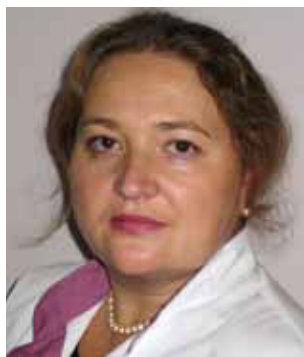
# SEARCH FOR NEW APPROACHES TO TREATING PATIENTS WITH SPINAL MUSCULAR ATROPHY, 2 TYPE AS PART OF CLINICAL-EXPERIMENTAL STUDY

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**ABSTRACT** — in the framework of the performed clinical-experimental study it was shown that SMA-2 patients have elevated level of blood serum neurotrophins and have strong correlation between an inhibition of neurite growth in sensory ganglion neurons and neurotrophins concentration. In our opinion an influence of pharmaceuticals on tyrosine kinase receptors for the purpose of intensification of neurotrophic effect in the nervous tissue of SMA 2 patients is inexpedient.

**KEYWORDS** — spinal muscle atrophy of type 2 (SMA), blood serum, brain derived neurotrophic factor (BDNF), nerve growth factor (NGF), ciliary neurotrophic factor (CNTF), organotypic culture, nerve, neurite-inhibitory effect, therapy



**V.A. Penniyaynen**



**M.V. Rezvantsev**

## INTRODUCTION

Spinal muscular atrophy of type 2 (SMA) is autosomal recessive disorder, characterized by progressive degeneration of alfa-motor neurons of spinal cord [1]. With an incidence of 1 in 6000–10000 live births and a carrier frequency of 1 in 40–50. The disease manifests itself as a weakness of proximal muscles, pareses, respiratory insufficiency and early mortality. Spinal muscular atrophy (SMA) is an incurable disease. Thus, the development of new approaches to symptomatic treatment, which may be related to augmentation of neurotrophic regulation, is of interest at this time.

## MATERIALS AND METHODS

Clinical-neurologic and neurophysiological examination of 12 patients with 2 type SMA was carried out. Level Beta-NGF, BDNF, CNTF in 12 patients (SMA 2 type) was determined in serum using ELISA Kit (RayBiotech, Inc). The experiments were performed in the organotypic culture of a 10–11 day old chicken embryos dorsal root ganglion. Study blood serum in an organotypic tissue culture.

The research was performed on 600 explants of dorsal root ganglia of 10–12-day old chicken embryos. The culture media contained Eagle's Basal Medium with Earle's salt (BME) supplemented with 2 mg/ml D-glucose, 10 ng/ml insulin, 2 mM glutamine, 75 IU penicillin and 15% bovine fetal serum. The explants were grown on collagen at 36.5° C. Growth of the neurites was investigated using a phase-contrast microscope. The square index (SI) was calculated as the ratio of

the whole explant square area (peripheral growth zone included) to the central zone square area. The Student's criteria were used for statistical analysis. Data are expressed as means + SE. Differences were considered significant when  $P < 0.05$ . SI was expressed as a percentage, the SI of control explants was set as 100%. To visualize objects, microscope «Axio Observer ZI» («Carl Zeiss», Germany) and program ImageJ were used.

The work was based on the following methods of statistical analysis: determination of numerical characteristics of variables; estimation of conformity of empirical law of distribution of quantitative variables to theoretical law of Gaussian distribution according to Shapiro-Wilk test; an estimation of influence of qualitative factor on a dispersion of quantity indicator using ANOVA dispersion method, an estimation of a force and direction of linear relationship between the quantity indicators using parametrical Pearson correlation coefficient, nonlinear relationship — using Spearman's correlation coefficient. Description of quantitative signs was carried out using arithmetic mean value and standard deviation. Zero statistical hypothesis was rejected at significance value  $p < 0.05$ . The statistical analysis was carried out using STATISTICA 8.0 package (StatSoft®, Inc., USA).

## RESULTS

12 patients with 2 type spinal muscular atrophy were examined, among them: 4 girls and 6 boys at the age from 8 up to 12 years old. All patients with 2 type SMA have been under medical observation for 3 years, during this period of time the disease was progressing. Motor defect was manifested since birth. Genetic defect was identified at the long arm of 5th chromosome (within the interval between D5S629 and D5S557). Clinical-neurologic picture includes flaccid pareses of hands and feet with prevalence of the process in the proximal parts, active movements were only in distal parts of the hands, neck muscles, mimic and respiratory muscles. There were generalized fibrillations and fasciculations of the muscles, intense diffuse hypomyotonia. 85% of children had intense atrophies of intercostal muscles with respiratory insufficiency and minor bulbar disorders. Changes of osteoarticular system were manifested as intense contractures of large joints of extremities and kyphoscoliosis. Functions of pelvic bodies were normal. There were no sensitivity and cognitive disorders.

The results of enzyme-linked immunosorbent assay showed that NGF (nerve growth factor) level ( $3899 \pm 1058$  pg/ml) in blood serum of patients with type 2 SMA was significantly ( $p < 0.001$ ) higher than in the control group ( $782 \pm 582$  pg/ml). The values of NGF levels in blood serum of the control group were

in the range from 110 pg/ml to 2237 pg/ml. Meanwhile, in patients with type 2 SMA they were in the range from 1387 pg/ml to 5411 pg/ml. We detected that patients with type 2 SMA had higher levels of NGF in blood serum. BDGF (brain-derived growth factor) level ( $36653 \pm 3606$  pg/ml) in blood serum of patients with type 2 SMA is significantly ( $p < 0.05$ ) higher than in the control group ( $27313 \pm 7260$  pg/ml). The analysis of parameter scatter detected that BDGF level in blood serum of the control group was ranging from 16040 pg/ml to 41960 pg/ml, while in patients with type 2 SMA — from 22523 pg/ml to 63700 pg/ml. The analysis of CNTF (ciliary neurotrophic factor) in blood serum did not reveal any statistically significant differences between control and study groups ( $23.0 \pm 14.3$  pg/ml versus  $21.3 \pm 13.2$  pg/ml, respectively). CNTF values in the control group ranged from 1.1 to 62.9 pg/ml, while in type 2 SMA patients — from 3.1 to 49.7 pg/ml. The following patterns of neurotrophin changes were detected: BDGF and NGF levels in blood serum of patients with type 2 SMA were significantly higher than in the control group; CNTF level did not significantly differ between control and study groups, but the values of this protein were within age limits, and no deficit of it was detected in the study group.

## EXPERIMENTAL STUDY

The next study comprised a series of experiments, which purpose was to analyze the impact of the blood plasma of type 2 SMA patients on the growth of axons of sensory ganglia in 10–12-day chicken embryos using the method of organotypic tissue culture. The following series of experiments was aimed at investigation of an influence of blood plasma of patients with 2 type SMA on growth of neurons of dorsal root ganglia of 10–12-day chicken embryos. After three days of culturing in the control and experimental explants of dorsal root ganglia there are two zones: central, consisting of not erratic differentiated neuroblasts and peripheral, so-called growth zone. The growth zone of explants of dorsal root ganglia contains mostly growth of neurites (processes of nervous cells), to a lesser degree — migrating and proliferating fibroblast-like and glial cells. Blood serum of 5 patients with type 2 SMA was researched in a wide range of dilution (1:100–1:2). In dilutions 1:2, 1:10, 1:50 the serum of patients blocked completely the growth of dorsal root ganglion neurites. When adding in cultural medium blood serum in dilution 1:70, a positive neurite inhibitory effect was observed. Area index of the studied explants was below the control value on the average by 25% and has made  $75.5 \pm 7.4\%$  (Fig. 1). Further dilution of blood serum practically did not affect the growth

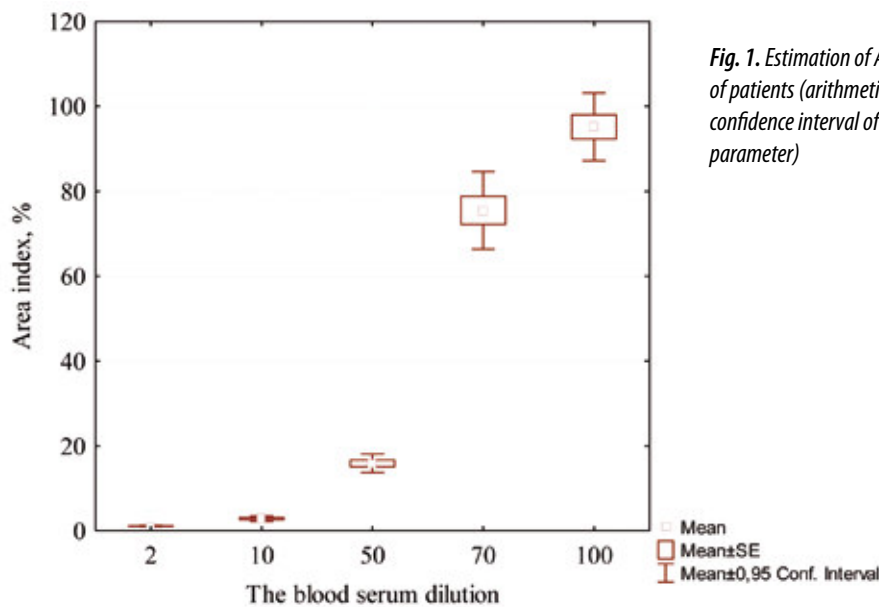


Fig. 1. Estimation of Area index in studied blood serum dilutions of patients (arithmetic mean values are shown, error bars – 95% confidence interval of mathematical expectation of Area index parameter)

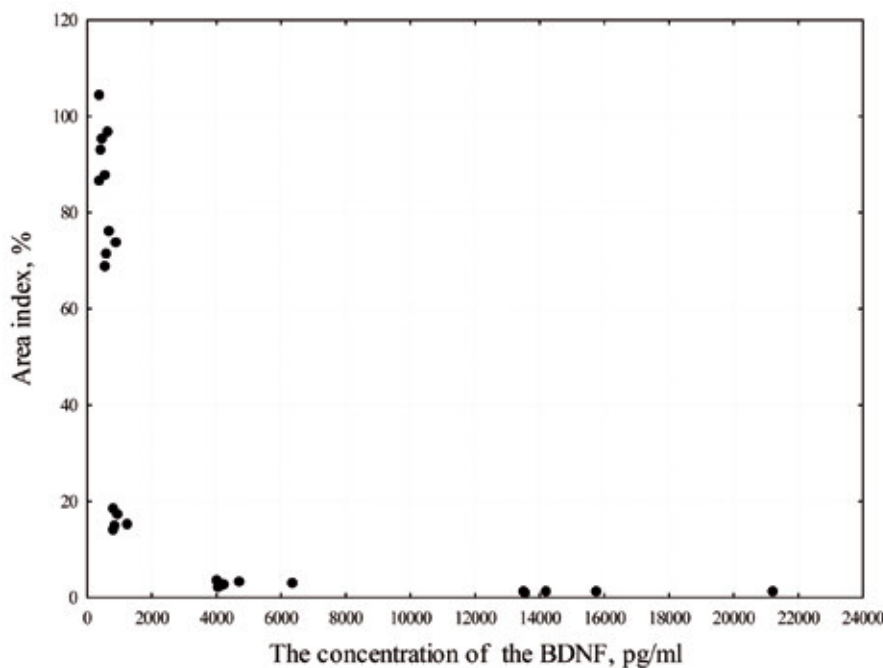


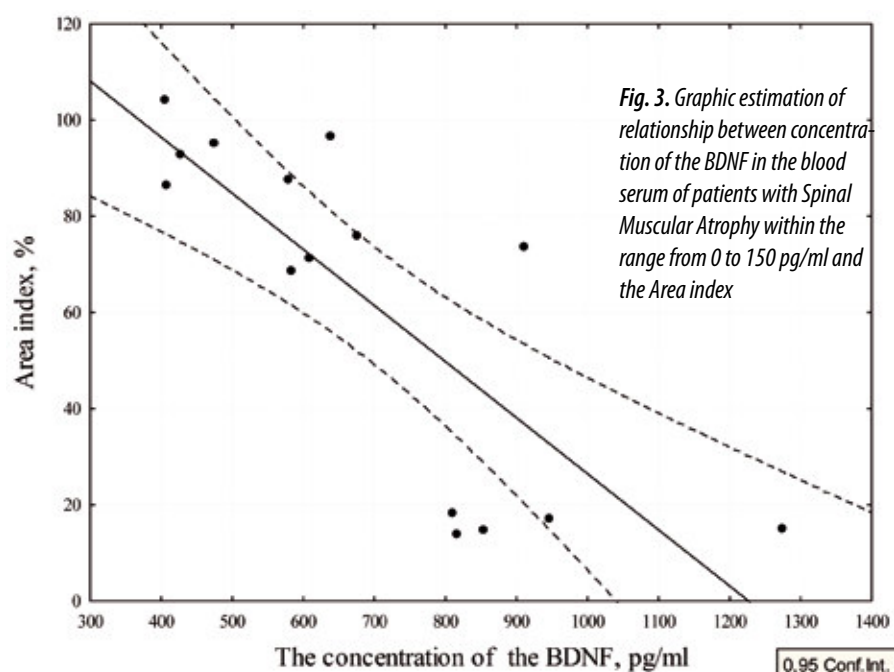
Fig. 2. Graphic assessment of relation between concentration of the BDNF in blood serum of patients with Spinal Muscular Atrophy and the Area index

of explants. The carried out studies have shown that blood serum of patients with 2 type SMA dose-dependently inhibits growth of neurites of sensory neurons of spinal ganglions. Results of estimation of the Area index for studied dilutions were analyzed using dispersion analysis. It is shown that blood serum dilution factor statistically significantly (F-test  $F=489,2$ ;  $p < 0,001$ ) influences the area index value registered in the study.

Correlation of clinical-laboratory and experimental data. Our previous study showed the presence of correlation relationship between the NGF level in

the blood serum of patients with SMA and AI (area index) [2]. Statistically significant ( $p < 0.001$ ) strong inverse (Spearman  $R = -0.90$ ) correlation relationship was detected. Thus, it was revealed that the degree of inhibition of axon growth in spinal ganglia of chicken embryos depended on the NGF level in the blood serum of patients with type 2 SMA. In this study we conducted the correlation analysis between BDGF and CNTF parameters in the blood serum of patients with type 2 SMA and AI. To evaluate the type of statistical relationship between the BDGF level in the blood serum of patients with SMA and IA, a



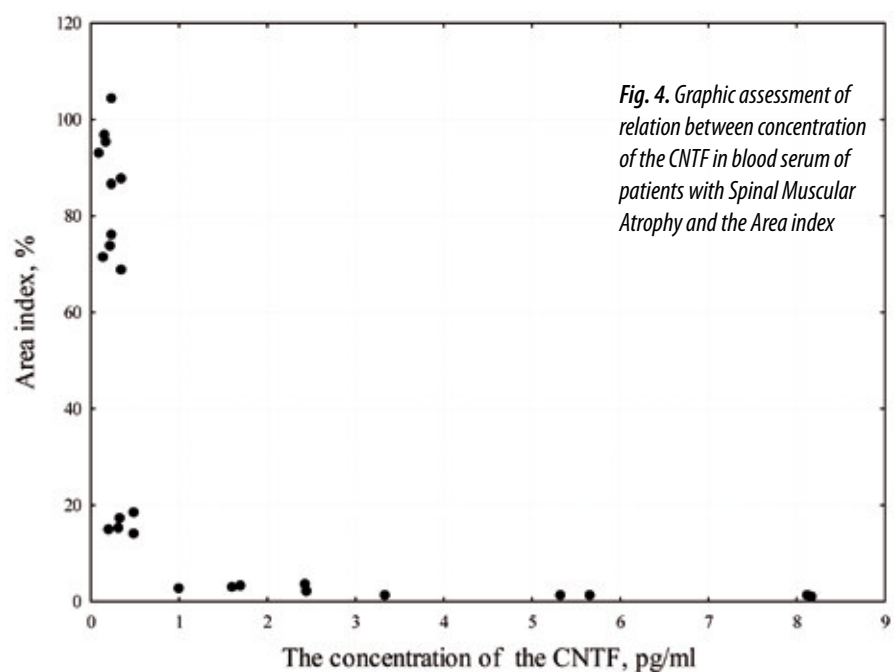


SMA and AI in the level interval from 0 to 1500 pg/ml, which was confirmed when plotting the additional scatter diagram for this interval of the BDNF levels (Fig. 3). The quantitative evaluation of linear relationship showed the presence of the statistically significant ( $p < 0.001$ ) strong inverse (Pearson correlation coefficient  $r = -0.80$ ) correlation relationship between the BDNF level in the blood serum of patients with SMA and AI in the level interval from 0 to 1500 pg/ml. Likewise, the relationship between the CNTF level in the blood serum of patients with SMA and AI was analyzed. The character of the correlation field on the scatter diagram plotted (Fig. 4) revealed the presence of the non-linear negative correlation relationship between the parameters.

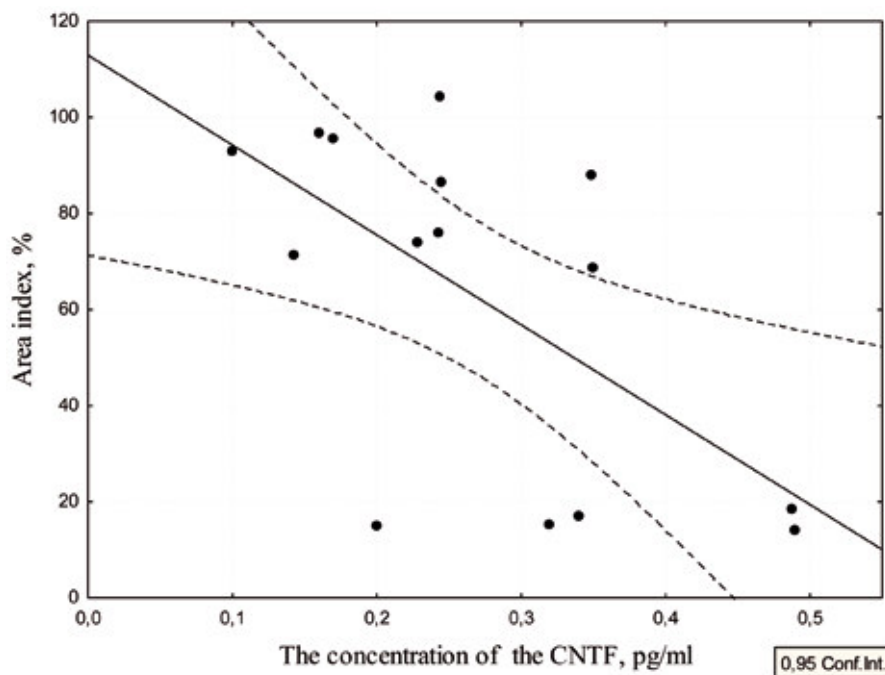
The quantitative evaluation conducted using the non-parametric Spearman correlation coefficient showed the presence of the statistically significant ( $p < 0.001$ ) strong inverse (Spearman  $R = -0.88$ ) correlation relationship between the parameters. While the CNTF levels in the blood serum of patients with SMA exceeded 1 pg/ml, the area index approached minimal values. While the CNTF levels were below 0.5 pg/ml, the AI parameter increased. Plotted scatter diagram for the interval of CNTF levels from 0 to 0.5 pg/ml proved the hypothesis about the presence of the partial linear connection for the parameters mentioned (Fig. 5). The quantitative evaluation of linear relationship showed the presence of the statistically significant ( $p = 0.014$ ) strong inverse (Pearson correlation coefficient  $r = -0.62$ ) correlation relationship between the CNTF level in the blood serum of patients with SMA and AI in the level interval from 0 to 0.5 pg/ml. Thus, it was revealed that the degree of inhibition of axon growth in spinal ganglia of chicken embryos correlated with the BDGF and CNTF levels in the blood serum of patients with type 2 SMA.

## DISCUSSION

Our study showed that patients with type 2 SMA had increased levels of the NGF and BDGF neurotrophins,



scatter diagram was plotted for the parameters described (Fig. 2). The analysis of the diagram revealed the presence of the non-linear negative correlation relationship between the parameters. The quantitative evaluation conducted using the non-parametric Spearman correlation coefficient showed the presence of the statistically significant ( $p < 0.001$ ) strong inverse (Spearman  $R = -0.94$ ) correlation relationship between the parameters. The character of the correlation field on the scatter diagram allowed to suppose the presence of partial linear connection between the BDNF level in the blood serum of patients with



**Fig. 5.** Graphic estimation of relationship between concentration of the CNTF in the blood serum of patients with Spinal Muscular Atrophy within the range from 0 to 150 pg/ml and the Area index

while the CNTF levels in them were normal. Presumably, the increase of neurotrophin synthesis is related to the development of compensatory & adaptive processes aimed to increase the reparative function of the nervous tissue. But, according to our studies, the increased level of neurotrophins does not lead to restoration or partial compensation of lost motor functions in patients with type 2 SMA. The experiment in the organotypic tissue culture showed that the serum of patients with type 2 SMA inhibited the axon growth in sensory ganglia [3]. The strong correlation relationship was detected between the fact of inhibition of axon growth in neurons of sensory ganglia and the NGF, BDGF, CNTF levels in the blood serum of patients with type 2 SMA. These data were confirmed by the results of electroneuromyography in patients with type 2 SMA, which showed the absence or decrease of reinnervation process [4].

## CONCLUSION

At present there are active attempts to treat neurodegenerative diseases using neurotrophins or by activating receptors, through which neurotrophins exercise their biological function [5, 6]. Probably, this therapeutic direction is important for diseases which are accompanied by the deficit of growth factors, but no deficit of neurotrophins (BDGF, CNTF, NGF) was detected in the blood serum of patients with type 2 SMA. The results of this study show that excessive stimulation of tyrosine kinase receptors using pharmacological drugs to augment the neurotrophic effect in

the nervous tissue of patients with type 2 SMA is not considered an efficient therapeutic approach.

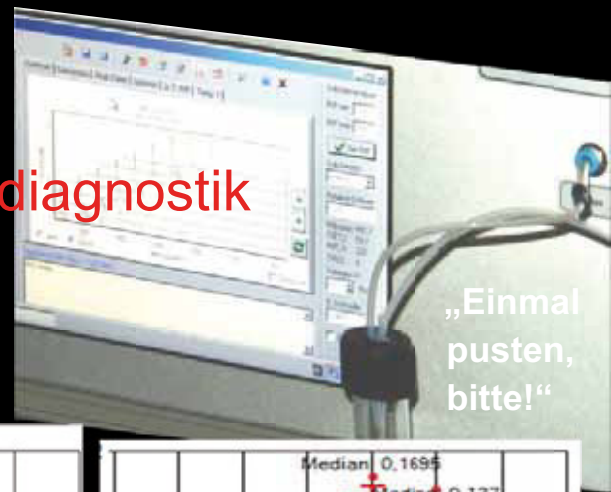
## REFERENCES

1. Neurology – the national management. Under edition RAS academician Gusev E. I. Moscow: GJeOTAR-Media, 2009. P. 936. (in Russian)
2. **SOKOLOVA M. G.** Correlation of level NGF and of results neurotrophic impact of blood serum of patients with spinal muscle atrophy of 2 type with the purpose of studying sprouting in organotypic tissue culture / M.G. Sokolova, V.A. Penniyaynen // Proceedings of the 1st Congress of the European Academy of Neurology. Berlin. – 2015. – P. 148–150.
3. **SOKOLOVA M. G.** Analyse des neurotrophien einflusses von blutserum der patienten mit spinaler muskelatrophie typ 2 auf wachstum der neuriten sensorischer ganglien / M.G. Sokolova, V.A. Penniyaynen // Proceedings of the 2nd European Conference on Biology and Medical Sciences. «East West» Association for Advanced Studies and Higher Education GmbH. Vienna. – 2014. – P. 112–117.
4. **SOKOLOVA M. G. SOKOLOVA M.G., PENNIJAJNEN V.A., REZVANCEV M.V., LOBZIN S.V., ALEKSANDROV N.JU.** Study of reinnervation process in patients with 2 type of spinal muscular atrophy: clinical experimental study. Vestnik SZGMU. Saint-Petersburg, 2014. Vol.6, No 4. P. 45–52. (in Russian)
5. **SHOVAL G.** The possible role of neurotrophins in the pathogenesis and therapy of schizophrenia / G. Shoval [et al.] // Eur Neuropsychopharmacol. – 2005. – №8. – P. 19–22.
6. **TIWARI S.K.** Peptide Therapeutics in Neurodegenerative Disorders / S.K. Tiwari [et al.] // Curr. Med. Chem. – 2014. – №1. – P. 2–17.

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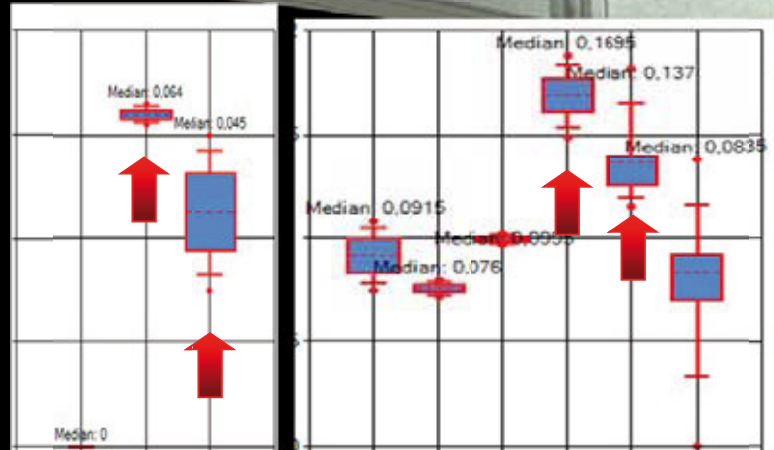
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# EDITORIAL

*Dear Colleagues!*

The annual medical forum Euromedica-2016 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.

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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