Proceedings of the 1st and the 2nd Japanese and Russian International Conference on Socially Significant Human Diseases: Medical, Environmental, and Technical Problems, and these Solutions

2014 - 2015

FAR EASTERN FEDERAL UNIVERSITY
HOKUTO SOCIAL MEDICAL CORPORATION

Book Title
PROCEEDINGS OF THE 1ST AND 2ND JAPANESE AND RUSSIAN INTERNATIONAL CONFERENCE ON SOCIALLY SIGNIFICANT HUMAN DISEASES: MEDICAL, ENVIRONMENT, AND TECHNICAL PROBLEMS, AND THESE SOLUTIONS, Edited by Kazushi Kishi

Published by
Hokuto Social medical Corporation (HSMC)
7-5, Kisen, Inada-Cho, Obihiro, Hokkaido, 080-0833 Japan,
Phone: +81-155－48－8000 Web Site: http://www.hokuto7.or.jp/
Far Eastern Federal University (FEFU)
10 Ayaks, Russian Island, Vladivostok, 690922 Russia
Phone: +7 (800) 555−0−888 Fax: +7 (423) 243−23−15
Web Site: http://www.dvfu.ru/en/web/fefu/

Chief Editor: Kazushi Kishi, HSMC
Co-editor in Russia: V. N. Bagryantsev, FEFU
Native English Editor: Aaron Stallard, Stallard Scientific Editing,
56 Brougham Street Nelson 7010 NEW ZEALAND
Design & layout: Masao Oshima, HSMC

First publihed: May 2015 on the web
Final published: December 2015 on the web

A free online edition of this book is available at
"http://www.hokuto7.or.jp/patient/info/publish"

ISBN 978-4-9908110-0-6

Academic collaboration with Far Eastern federal University

The Hokuto Social Medical Corporation was the first Japanese medical organization to perform medical activities in Russia with its involvement in the opening of the Hokuto Imaging Diagnostic Center in Vladivostok on 28 May 2013. The center is the result of cooperation between a consortium of four members with the common intention of bringing Japanese medical care to the Russian Far East: the Stroitel Sanatorium in suburban Vladivostok; Akira Co., Ltd.; PJL Co., Ltd., which is engaged in arranging medical treatment of Russian patients in Japan; and the Hokuto Social Medical Corporation.

The center has two primary goals: (1) to promote secondary preventive medicine by early and accurate diagnosis of disease by imaging modalities before it becomes symptomatic, thus preventing disease progression; and (2) to reappraise the diagnosis of the previously diagnosed diseases and the treatment plans. From June 2013 to May 2015 12,000 patients were checked at the center, demonstrating the high demand for these medical services in the Russian Far East region. To meet these demands, academic collaboration based on human exchanges is indispensable. Taking the preparations to open a rehabilitation center in Vladivostok later this year into consideration, and to assure that the present scientific conference truly fulfills the important role it has, it is vital that we continue with these academic exchanges to grow in a meaningful way. At the 29th General Assembly of The Japan Medical Congress, which was held in Kansai this year, the key concept was preemptive medicine. Let us bear this key concept in mind for the success of this meeting too.

May 2015

Hajime Kamada
President, Hokuto Social Medical Corporation

Editor's preface

This is the first volume of the proceedings of the Japanese–Russian International Conference on Socially Significant human Diseases (JRIC-SSD) series promoted by the Hokuto Social Medical Corporation (HSMC), Hokuto Hospital, Obihiro City, Japan, and by the Far East Federal University (FEFU), Vladivostok, Russia. The first conference was held on 22 May 2014, and the second on 27–28 May 2015, both at the conference hall of the FEFU. This series was jointly established by Hajime Kamada, MD, President of HSMC Hokuto Hospital, and Professor Valery N. Bagryantsev, MD, PhD, Chairman of Bioengineering Science, FEFU. After the first meeting, the conference series was named the Japanese–Russian International Conference on Medical, Environmental and Technical Problems in Socially Significant Human Diseases and their Solutions (JRIC-SSD), as proposed by Professor Bagryantsev. This conference will be subsequently held every year.

The contents of this book are presented at JRIC-SSD 2014 or 2015, and added thereafter till the end of year 2015 (Chaper 9, 30, and 38). These reports cover a wide range of topics in social and medical sciences, and divided into five sections which are (1) New Theory and Devices, (2) Regional Socioeconomic Analysis & Interpretations, (3) Epidemiology and Public Health, (4) Functional Foods, and (5) Therapy and Rehabilitation, of which all strongly intriguing. So I believe it is promised that readers will gain from these novel ideas presented herein, being inspired by the passion of the authors, and invigorated by the borderless spirit of socio-medical science.

I should apologize for any inconvenience as the Chief Editor. However, I sincerely thank all contributors, especially President Kamada and Professor Bagryantsev, without whom this project would not have been possible. I also give special thanks to Dr. Svetlana Denisova, General Director, Hokuto Healthcare Corporation, Vladivostok, who created and managed initial steps of this collaboration. Finally I thank to all of our staffs in HSMC HH, especially to Mr. Masao Oshima and Mr. Alexander Selivanov, Russian and International Project Division, Mrs. Kazuka Onishi, Secretary Division, and all who worked for this publication.

Kazushi Kishi MD, PhD
Chief Editor
Obihiro City, Hokkaido, Japan

11 May 2015

CONTENTS

SECTION 3, Epidemiology & Public Health

SECTION 4, Functional Foods

SECTION 5, Therapy and Rehabilitation

SECTION 1

New Theories and Devises

Chapter 1

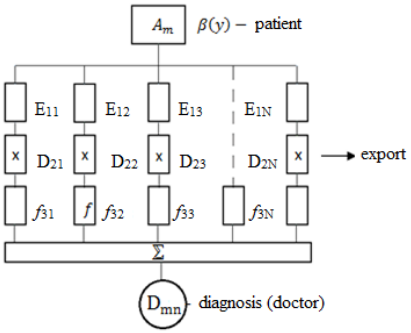
LINEAR MATHEMATICAL MODEL OF DIAGNOSTIC PROCESS

[1,2]Valery N. Bagryantsev, [1,2]Vladimir I. Korochentsev, [3]Alevtina V. Chigareva, [1]Sergy A. Atarshchicov, [1]Boris N. Yung
Far Eastern Federal University (FEFU)
10 Ajax, Russian Island, Vladivostok, 690922, Russia
[1]School of Biomedicine, FEFU, [2]Engineering School, FEFU,
[3]School of Regional and International Research, FEFU
e-mail: bagryantsev.vn@dvfu.ru, korochentsev.vi@dvfu.ru

Abstract. Improving diseases diagnostics using mathematical modeling has potential in health-care research [1, 2, 3].We attempted to develop a principal linear mathematical model to reduce the influence of subjective and variable factors on screening processes and disease diagnostics. A mathematical analysis of the possibility to improve the current diagnostic process was conducted, for modern schemes of laboratory and instrumental diagnostics. Recommendations are given for developing prospective mathematical models and systems for carrying out diagnostic medical biological research.

Keywords: mathematical model of laboratory and instrumental diagnostics, diagnostic process algorithms.

To understand the diagnostic process, we suggest a linear scheme that represents patient investigation realized in parallel in several directions.



Equation (1) then follows:

$$D_{mn} = \sum_{k=1}^{N} D_{2k} \int \beta(y) f_k(y-k)\mathrm{d}y = \int \beta(y)[\sum_{k=1}^{N} D_{2k} f_k(y-k)]\mathrm{d}y. \quad (1)$$

In this mathematical interpretation, the diagnosis D_{mn} is a response of a linear diagnostic system with "preliminary" diagnosis D_{2k} as the general signal received from a patient $A_m(\beta(y))$:

$$\Psi_m(y) = \sum_{k=1}^{N} D_{2k} f_k(y-k). \quad (2)$$

Here the model $f_k(y-k)$ is the transfer function of a signal with index "*k"*.

The task of system optimization of the linear signal processing from patient $A_m(\beta(y))$ is in the choice of the preliminary diagnoses D_{2k}, which supply the optimal (true) connection with the investigated function $\beta(y)$, describing the patient state A_m.

This task can mathematically be reduced to a feedback task (synthesis) of expression (1).

For example, consider the special case when all transfer functions of all channels are equal: i.e., $f_k(y)$=$f(y)$. If measured data (physical, chemical, microbiological, or other) comes to the multichannel system in the form of a signal from different analytes as function $\beta(y)$, then a complex signal is registered in the output of channel "*k"*.

$$a_k = \int \beta(y)_k(y-k)\mathrm{d}y. \quad (3)$$

One can choose a Kotelnikov`s series member for a linear instrumental research (radio, electronic, or other) function system:

$$f_k(y-k) = \frac{\sin \pi(y-k)}{\pi(y-k)}. \quad (4)$$

That is, the main contribution to coefficient a_k is made by the values $\beta(y)$ concentrated in proximity to the point $y = k$. However, function (4) has a value significantly away (by >20%) from the central maximum *y=k.*

Therefore, it is not possible to state the local diagnosis using only expression (3).

Information about value E_{1k} is distributed among the great number of preliminary diagnoses. To extract reliable information, one should conduct joint signal processing from all channels, (3).

$$D_n = \sum_{k=1}^{N} a_{mk} D_{2k}. \quad (5)$$

The optimal function describing a diagnosis is therefore formally determined as the sum of local diagnoses in expression (5).

References:

1. Gelfand I.M., Rosenfeld B.I., Shifrin M.A. Ocherki o sovmestnoy rabote matematikov i vrachey [Essays on Collaboration of Mathematicians and Physicians]. Moscow, Editorial URSS. – 2005. – 320 p.
2. Malykh V.L., Guliev Ya.I. Vrach i informatsionniye tekhnologii [Modeling of medical-diagnostic process in a class of controlled stochastic processes with memory], 2013. N. 2. – P. 6-15.
3. Nazarenko G.I., Osipov G.S. Osnovy I teorii meditsinskikh tehnologicheskikh protsessov [Fundamentals of the theory of medical technological processes]. Moscow, Fizmatlit, 2005.

Chapter 2

AUTONOMOUS DEVICE FOR CONJUNCTIVAL MICROSCOPY

[1]Dmitriy A. Polyansky, [2]Alexander N. Gumovsky, [2]Valeriy N. Bagryantsev
Far Eastern Federal University (FEFU)
10 Ajax, Russian Island, Vladivostok, 690922, Russia
[1]The School of Natural Sciences FEFU, [2]The School of Biomedicine FEFU
e-mail: rambo192@mail.ru

The major aim of this work was to create a device to film the microvascular bed of the bulbar conjunctiva, for use in both medical and preventive treatment facilities and in cases of emergency, extraordinary situations, and battle. It must also be highly sparing of the patient.

The device contains an optical system, including a video camera with a transfer system, an illuminator containing two white-light-emitting diodes that is rigidly mounted on the video camera in such a way that the direction of the luminous flux makes an angle of not less than 20° to the optical axes of the system, and a system for the control, registration, and analysis of the images realized on a computer base, as well as a communication unit to support the dynamic feedback between the optical system and the controlling system.

The system receives images from the video camera in real time and screens them on the monitoring device. The software analyzes the acuity, intensity, and contrast of each image and adjusts the camera transfer characteristics to use its dynamic range to the maximum effect. Each image is subjected to Fourier transform analysis and wavelet analysis to evaluate its frequency and contrast characteristics. Those meeting the required characteristics (input into the parameter unit) are saved to the memory or onto the computer hard drive. This is followed by the activation of the announcing wireless channel units that cause audible signals. The saved images and the preprocessing results can be displayed in a separate monitor window. This process is repeated until the number of images specified in the parameter block has been recorded. The announcing unit signal then stops, which signals to the operator to stop filming the conjunctiva. The set of recorded images is then analyzed in

detail in the morphological analysis unit, and the results are saved and displayed. The process of recording and analyzing the medical images takes no more than 2 minutes.

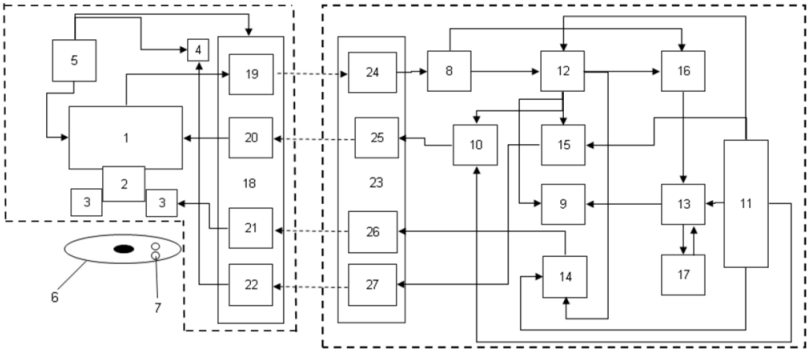


Figure 1 – Principal Diagram of the Device

1, Video camera; 2, image transfer system; 3, illuminator; 4, announcing unit; 5, power unit; 6, eye conjunctiva; 7, light spot; 8, display buffer; 9, video display unit; 10, unit for controlling the camera transferring characteristics; 11, parameter input unit; 12, preanalysis unit; 13, morphological analysis unit; 14, illumination-intensity controlling unit; 15, recorded frame counter; 16, image recording unit; 17, unit for recording the results of the morphological analysis; 18, unit for the optical system wireless communications; 19, first element for image wireless translation; 20, first element for image characteristic wireless translation; 21, first element for the wireless control of the illumination characteristics; 22, first element for the wireless announcing channel; 23, unit for the analysis of wireless communications; 24, second element for image wireless translation; 25, second element for image characteristic wireless translation; 26, second element for the wireless control of the illumination characteristics; 27, second element for the wireless announcing channel.

Functional units 8–17 and 23–27 of the device are used as a hardware–software complex on a notebook base, while units 1–7 and 18–22 are used on the mobile device itself.

Chapter 3

MATHEMATICAL MODELS OF DIAGNOSTICS USING ACTIVE WAVE DEVICES

[1,2]Vladimir I.Korochentsev, [1,2]Valery N.Bagryantsev, [3]Alevtina.V.Chigareva, [4]Vladimir Y. Startsev, [2]Sergy A. Atarshchicov, [2]Boris N. Yung
Far Eastern Federal University (FEFU)
10 Ajax, Russian Island, Vladivostok, 690922, Russia
[1]Engineering School FEFU; [2]School of Biomedicine FEFU;
[3]School of Regional and International Research FEFU
e-mail: korochentsev.vi@dvfu.ru;
[4]Saint Petersburg State Pediatric Medical University (SPbSPMU)
2 Litovskaya st., St. Petersburg, 194100, Russia;

Abstract. Algorithms and mathematical models are proposed to improve medical screening and early disease diagnosis by active wave medical devices. They are shown to be able to improve the existing systems and technologies used in medical imaging. Recommendations are also provided for creating new cybernetic developments and prospective devices for veterinary, medical, and biological research.

Key words: mathematical models of diagnostics, active wave devices for imaging.

Wave devices are appliances that use the properties of elastic and electromagnetic waves to determine the body's inner structures (body imaging). Active wave devices employ echo sounding to analyze wave reflections from inhomogeneities in the body; examples include ultrasonic research (USR) and electromagnetic sonars [1, 2].

Medical imaging devices include radio technical systems that use antenna and signal synthesis theory, wide-band lines matching, or other radio-physics techniques [3,4].

Inhomogeneities in the body that reflect detectable signals include bone structures and pathological formations such stones in the kidney or gallbladder and tumors.

Physically it is the task of reconstruction, when we find a continuous intensity function of intensity distribution of the signal,

reflected from different areas of inhomogeneity, measured in certain parts of the space.

Let us suppose that the experimentally measured function $\Phi(u)$is connected to a searched (or unknown) function $V(\zeta)$by an integral operator:

$$\Phi(u) = \int_a^b \sigma(u,\zeta)V(\zeta)\zeta, \quad (1)$$

where $\sigma(u,\zeta)$denotes a nucleus of integral equation, *u* denotes a generalized angular coordinate set in the interval $[c,d](c \le u \le d)$, and *a* and *b* denote the goal (stone) sizes $(a \le \zeta \le b)$.

The second type of restoring task can employ the $\Phi(\zeta)$antenna direction diagram calculation according to the experimentally measured power concentration of the reflected signal$W(u)$:

$$W(u) = \int_a^u \sigma(\zeta)\Phi(\zeta)\mathrm{d}\zeta, \quad (2)$$

where $\sigma(\zeta)$, $a \le \zeta \le b$are set parameters.

Operators (1) and (2) are linear. The solution of these integral equations refers to incorrect tasks of mathematical physics. Therefore, the devices, created according to these tasks of reconstruction, are not resistant to any type of interference of both external and internal origin.

Comparison of both mathematical models shows that measurement should be conducted by different methods. In the first case, the function $\Phi(u)$, measured at discrete points, can be interpolated to be continuous, and integral equation (1) can be solved in one of the known ways.

In task 2 the unknown function $\Phi(\zeta)$is determined in the area $[a,u]$. Therefore,

$$\Phi(\zeta) = \sigma^{-1}(u)\frac{\mathrm{d}}{\mathrm{d}u}W(u). \quad (3)$$

Fundamentally the last algorithm is not possible, because the function *W(u)* is known only at discrete points. Therefore, devices, created by these algorithms, are fundamentally different.

Let us consider the main mathematical problems facing the development and realization of medical devices working according to algorithm (1) using USR as an example.

The experimentally measured function of the response from an inner inhomogeneity (e.g., a stone) can be either complex or real. A

complex function occurs when the amplitude and phase of the signal, reflected from an inhomogeneity, are measured simultaneously. A material function occurs, when only the amplitude is analyzed. Most modern devices (e.g., USR) analyze only the reflected signal amplitude $|\Phi(u)|$.

In this respect the incorrectness of the solution of integral equation (1) is expressed not only in the instability of the derived solutions $V_n(\zeta)$ (n = 1, 2, 3…). That is, a great number of inhomogeneity (stone) types and configurations can be put to one and the same reflection function $\Phi(u)$.

In practice, the correct diagnosis (i.e., the choice of inhomogeneity type) depends on the subjective choice of the doctor (or operator), which depends on the individual's qualifications, experience, and ability to use the device software. Image analysis time and other factors can also affect the decision. To decrease the influence of subjective judgments requires mathematical processing of the derived experimental images $|\Phi(u)|$. One such method follows.

We create a matrix of the most likely types of inhomogeneity standards $|V_n(\zeta)|$, calculate the integral (1), and find functions $\Phi_m(u)$ that correspond to types $V_m(\zeta)$.

We make up a matrix of the images ($|\Phi_m(u)|$) that correspond to standard inhomogeneities $V_m(\zeta)$. Note that integration using formula (1) for a smooth kernel $\sigma(u,\zeta)$ is unambiguous and correct. That is why the created matrices can be the basis (foundation) for the whole class of USR devices working in accordance with the described algorithm.

As the integral equation solution is incorrect and gives many solutions $V_m(\zeta)$ that correspond to various inhomogeneity types, one must choose the only optimal solution $V_{\text{opt}}(\zeta)$ (i.e., the solution which corresponds to the probable correct description of the true form of the inhomogeneity).

Let us consider one of the probable algorithms of mean square error minimization σ_m^2between (recommended) standard images$|\Phi_m(u)|$ and those experimentally measured $\Phi(u)$:

$$\sigma_m^2 = \int_{-u_0}^{u_1} |\Phi_m(u) - \Phi(u)|^2 \, \mathrm{d}u. \qquad (4)$$

When chosen in accordance to mean square criterion (4), the function $\Phi(u)$can be found insufficient for investigation of the detailed

structure of an inhomogeneity. Detailed estimation requires other parameters such as the minimax proximity criterion.

$$\varepsilon_m(u) = \max|\Phi_m(u) - \Phi(u)| \qquad (5)$$

Specific mathematical algorithms of error minimization (4) and (5) could be developed for similar tasks of the mathematical function. These might be used, for example, in antenna synthesis theory, reconstructing structures of underground mineral deposits and other radio prospecting tasks.

Suggested algorithms for medical diagnostics can be used to develop new programs for processing the imagesfrom imaging devices.

References:

1. Korochentsev V.I. The wave theory of directed tasks and focusing antennas. Vladivostok, Publisher "Dal'nauka", 1998. - 198 p.
2. Korochentsev V.I., Rosenberg A.N. Analysis and synthesis of communications traffic control underwater objects on the anomalies of physical fields. Vladivostok, Publisher "Dal'nauka", 2007. - 188 p.
3. Rangayan R. M. Biomedical signal analysis. Practicalapproach. Transl. from Engl. Edited by A.P. Nemirko.-M..: FIZMATLIT. 2010. -440 p.
4. Ulin S.E., Mikhaylov V.N., Nikitayev V.G., Alexeyev A.N., Kirillov-Ugryumov V.G., Sergeyev F.M. Physical methods of medical imaging. Moscow, MIFI, 2009.- 308 p.

Chapter 4

PIEZOELECTRIC TRANSDUCER FOR ULTRASONIC CLEANING OF SURGICAL EQUIPMENT

[1]Anatoly V. Bondar, [1]Alexandr N. Gumovsky, [1] Natalia E. Boeva,
[1,2]Valery N. Bagryantsev, [3]Chigareva A.V.
Far Eastern Federal University (FEFU)
10 Ajax, Russian Island, Vladivostok, 690922, Russia
[1]School of Biomedicine FEFU, [2]Engineering School FEFU,
[3]School of Regional and International Research FEFU

Abstract: Calculations and apparatus are described here for the ultrasonic cleaning and sterilization of surgical instruments and equipment. Parameters of the piezoelectric transducer's working frequency are reported for most effective sterilization. The piezoelectric transducer is characterized through calculations.

Keywords: surgical equipment sterilization, physical methods of sterilization, piezoelectric transducer for sterilization

Ultrasound waves generated by a piezoelectric transducer are a useful means of sterilization. The transducer considered here oscillates at f_0 = 38 500 Hz. Define more precisely here the term f_0 a frequency that provides proper ultrasonic propagation in cleaning solutions [1]. As a piezo element material, we chose hard lead titanate zirconate containing sodium and bismuth, because an ideal speed of sound propagation in piezo-ceramics is 2 900 m/s. It ensures the lowest resonant frequency of co_p. In addition, the performance at low frequencies minimizes deterioration in the working medium. For optimum performance, the crystal width was chosen as half the ultrasonic wavelength. The plate was disk-shaped. An equivalent plate scheme close to the main resistance is shown in Fig. 1 for . $\boldsymbol{f_p \mp 0.7 f_p}$

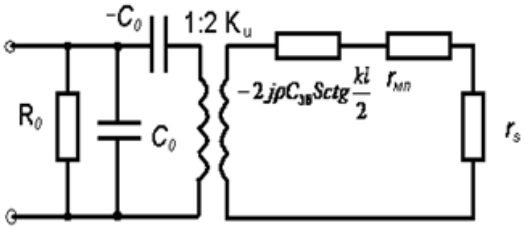


Figure 1 – The equivalent plate scheme close to the main resistance

Radiation power of $1,5 \times 10^4\ W/m^2$ was chosen from literature data as it satisfactorily provides cavitation in the cleaning medium [2].

The transducer characteristics were calculated using Mathcad 14.0 software.

The installation efficiency, η (1.1), including the electrical mechanical efficiency, η_{em} (1.2), and the acoustical mechanical efficiency, η_{am} (1.3), of the electrical mechanical transducer were calculated as follows.

$$\eta = \eta_{em} \cdot \eta_{am}\,, \tag{1.1}$$

$$\eta_{em} = \frac{R_0}{R_m + R_0}, \tag{1.2}$$

$$\eta_{am} = \frac{r_s}{r_s + r_{ml}}. \tag{1.3}$$

Here, R_0 is the mechanical loss resistance, R_m is the dynamic resistance, r_{ml} is the mechanical loss resistance, and r_s is the radiation resistance.

The calculated installation efficiency was 82%, which is acceptable for piezo-ceramic transducers.

The plot in Fig. 2 of the transducer's power $P(f)$ with respect to frequency, as calculated by equation (2.1), gives the device's optimal work at a given frequency.

$$P(f) = \frac{r_s}{2}\left| 2k_u U \times \left(\frac{-1}{i\omega C_0} + \frac{-2i\rho C_3^D S \frac{1}{\tan\left(\frac{kd}{2}\right)}}{4k_u^2} + \frac{r_s}{4k_u^2} + \frac{r_{ml}}{4k_u^2} \right)^{-1} \right|^2 \tag{2.1}$$

Here, S is the radiation surface area, C_3^D is the piezo-ceramic speed measured at the open electrodes, C_0 is the electrical capacity, k is the wavenumber, k_u is the voltage conversion coefficient, d is the transducer width, and U is the working voltage.

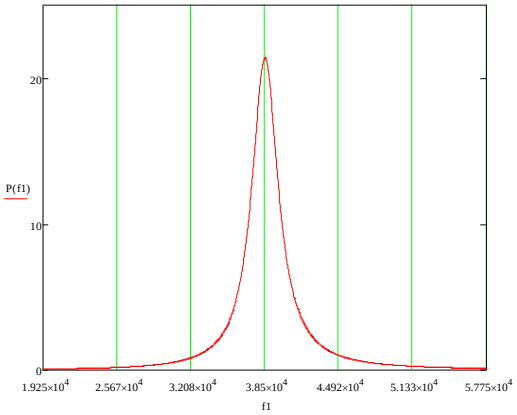


Figure 2 – Radiated power in the frequency range 19,250–57,750 Hz.

The mechanical part of the electromechanical transducer's resistance is calculated by equation (2.2) and is plotted in Fig. 3.

$$\zeta_{mec} = \frac{-4K_U}{i\omega C_0} - 2i\rho C_3^D S ctg\frac{kd}{2} + r_{ml} + r_s \qquad (2.2)$$

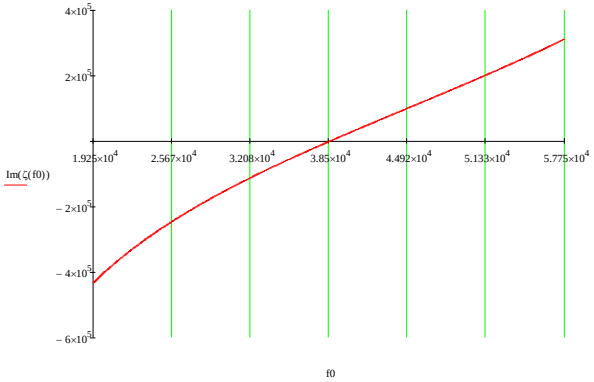


Figure 3 – The mechanical part of the electrical mechanical transducer's resistance plotted with respect to f_0.

The experimental setup is shown in Fig. 4.

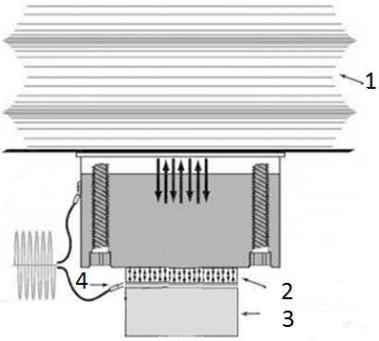


Figure 4 – Schematic of the experimental installation.

1: Induced ultrasonic medium; 2: piezo element; 3: massive support; and 4: electrode.

The obtained frequency characteristics, which describe the dependence of the calculated parameters on frequency, indicate that the transducer's working frequency was chosen appropriately, and show that the transducer would perform well as a result.

References:

1. Demin I.Y., Pronchatov-Rubtsov N.V. Electronical textbook on the course of lectures (special course) "Acoustic investigation methods in biology and medicine (medical acoustics)" // I.Y. Demin, N.V. Pronchatov-Rubtsov Electronical course of lectures, Nizhniy Novgorod. – 2010.
2. URL:http://www.profmt.ru/statyi/Osnovy_vzaimodejstviya_ultrazvuka_s_biologicheskimi_obektami.pdf - electronical resource.
3. Galiyarova N.M., Strelyaeva A.B. The structure of modified piezo ceramics on the basis of lead circonate-titanate at mezzo-,micro-, and nano-levels.// Internet-vestnikVolgGASY. Ser. Politematicheskaya. Vyip.2 – 2012.

Chapter 5

DEVELOPMENT OF AN OPTICAL SYSTEM AND A RADIO COMMUNICATION ANALYZER DEVICE FOR CONJUNCTIVAL MICROSCOPY

Anatoly V. Bondar, Alexandr N. Gumovsky, Eugenia. A. Pavlyuk, Valery N. Bagryantsev
Far Eastern Federal University, School of Biomedicine,
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: hcl36@mail.ru, alexandr_2k@rambler.ru, pavlyk.ea@students.dvfu.ru

Current apparatus for monitoring the general condition of a patient is examined. Parameters associated with circulation in the conjunctiva are estimated by using equipment that includes a morphological analyzer electrically connected to an optical system and video camera with a resolution of 1280 × 1024 pixels, recording at 60 fpsin 24 bit color [1]. The main drawback of this device is the wired USB 2.0 interface, which limits the maximum distance of the interaction to 3 m. The use of wireless communication could improve the device, and allow a specialist to work remotely from the patient. It could also allow the development of self-diagnosis protocols and for complex cases to be considered remotely.

This paper investigates wireless data transmission between the analyzer (A) and the optical system (OS) in device conjunctival microscopy (DCM).

The aims of the study are as follows.

1) Determine of the capacity of the radio channel.

2) Examine the current apparatus and check that the standards of the system meet the specifications of the wireless A and OS.

3) Investigate the effect of the system on the human body.

***Materials and methods*.** We used the theoretical foundations of radio communication based on the theory of microwave fields, and licensing documents for different frequency bands.

The content of the work. First, we obtained a preliminary estimate of the volume of information transmitted. Channel capacity restricts the parameters of filming, such as the frame rate, image resolution, and color

depth. In this work, the largest possible transmission (2400 Mbit/s) was for optimal resolution of 1280 ×°1024 pixels at 60 fps with 24 bit color quality. Including scope for superimposed technical data in the communication protocol increased the estimated data transmission rate to 2500 Mbit/s. This capacity assessment was used to select the communication channel. The Wi-Fi protocol fulfills these requirements.

The IEEE 802.11ad communication protocol at a frequency of 60 GHz was selected to ensuring that the wireless information is transmitted at the maximum capacity to get the highest quality images possible [2]. However, a 60 GHz signal attenuates in atmospheric oxygen, but the absorbance of approximately 1.5 dB per 100 m will not have a substantial effect over small distances. It would be desirable to use the 97 GHz microwave band, because this frequency is within the transparency window of the atmosphere and would increase the range of the wireless unit. Therefore, the use of the 97 GHz band is a priority for development.

Accordingly, when working in the 802.11ad protocol at short distances for the transmission of basic visual information natural signal attenuation occurs. This disadvantage is offset by the elimination of signal interference between different sources, which provides a solution to the problem of frequency distribution. Operation in tight spaces requires a repeater, which will accept the data from the DCM and transmit it to the medical center. This eliminates the problem of short-range radio communication in the selected range.

This frequency range is unlicensed in most developed countries. This table lists the standards for frequency bands, power transmitters, and the isotropic power of antennae. In 2009, the 802.11ad protocol was declared license-free and available for developing new products and services. The range was later expanded to 57–64 GHz, with work rules formulated in the FCC Rules Part 15.255. For the Russian Federation, the permitted frequency range is 61–61.5 GHz. [3, 4]

This network protocol achieves communication security (non-detect ability), integrity (resistance to impact noise), and resistance to unauthorized connections (inability to falsify the mobile station or access point).

Furthermore, millimeter wavelengths significantly reduce the size of the antenna systems.

The 7 GHz width of the available bandwidth makes the 60 GHz range extremely attractive for high-UWB transmission. For example, the

US FCC defines UWB as all frequencies greater than 500 MHz. This allows UWB_to transmit high-speed data streams, including multiple video streams from broadcast cameras, high-resolution video transmission (Table 1), which indicates the need to load the channel in high-definition video in different formats.

Table 1 – Approximate bandwidth requirements for uncompressed high-definition video signals of various formats Gbit/s.

Format	8- bit RGB	10- bit RGB	12- bit RGB
480p	0,5	0,625	0,75
720p	1,4	1,75	2,1
1080i	1,5	1,9	2,25
1080p	3,0	3,75	4,5

The spectral mask ensures that the signal is maintained within a certain bandwidth (Figure 1).

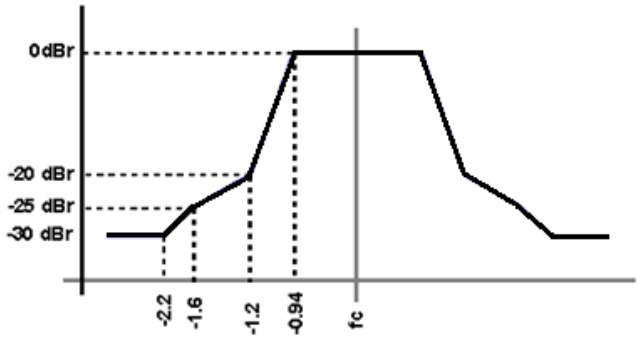


Figure 1 – Spectrum mask for transmission channels in the standard 802.11ad protocol.

Noise immunity is achieved by a number of factors: the wide 7 GHz bandwidth; the protection of WEP, WPA/WPA2, and MAC address filtering by the IEEE protocols 802.11a/b/n; and data integrity provided by poCKIP-encryption.

Considering the effects of the signals on the body is also important. Electromagnetic waves in the millimeter wavelength region have low penetrating power in biological tissue (0.2–0.8 mm), and are almost completely absorbed by the surface layers of the skin (e.g., water molecules, hydrated proteins, molecules of collagen, connective tissue)

without causing heating. Nevertheless, FCC regulations limit the surface power density to 1 mW/cm^2 average exposure over 30 min and 5 mW/cm^{2}average exposure over6 min. This ensures that the radiofrequency does not have pathological effects on biological tissues.

Conclusion. We found that the 60 GHz radio frequency band is suitable for wireless transmission of data between the OS, A, and DCM in this study. The bandwidth of the information exchange channel can achieve sufficient noise immunity, but RFI_susceptibility remains. The main problem with the use of the 802.11ad protocol over low distances is signal attenuation in the atmosphere. However, repeaters operating on different frequencies or other means of communication can provide links to remote medical institutions in a telemedicine system, while not exposing the patient or operator to microwaves.

References:

1. Patent - 58020 RF IPC A61 B 3/14 N 2006100363. device conjunctival microscopy / V.V. Usov, P.A. Pavlov, T.N. Obydennikova, O.G. Konstantinov; Pacific Institute of Oceanology them. V.I. Ilicheva Far Eastern Branch of the Russian Academy of Sciences (POI) (RU), State Educational Institution of Higher Professional Education "Vladivostok State Medical University, Federal Agency for Health and Social Development" (GOU VPO VSMU Federal Agency of Health and Social Development) (FEFU); Appl. 10.10.2006; Publ. 10.01.2006, Bull. N14.
2. 802.11ad-2012 - IEEE Standard for Information technology - Telecommunications and information exchange between systems - Local and metropolitan area networks - Specific requirements-Part 11: Wireless LAN Medium Access Control (MAC) and Physical Layer (PHY) Specifications Amendment 3: Enhancements for Very High Throughput in the 60 GHz Band, 8802-11-2012_Amd.3-2014.
3. ISO / IEC JTC 1 / SC 6, ISO / IEC 13156: 2011. Information Technology. Telecommunications and information exchange between systems. High system PHY, MAC and PAL 60 Hz., 01.10.2011. - 282c.
4. Appendix №1 to the table of distribution of frequently between the Russian Federation radio.

Chapter 6

EXPRESS DIAGNOSTIC SYSTEM FOR RESPIRATORY DISORDERS

Alexey M. Cherednichenko, Vladimir A. Kantur
Far Eastern Federal University, Engineering School
10 Ajax, Russian Island, Vladivostok, Russia, 690922
e-mail: aleksey3909@yandex.ru

Socially significant diseases account for the majority of all human diseases. An important example of such diseases is sudden respiratory failure, which is often lethal. Mortality caused by sudden respiratory failure can be caused by many different diseases of the respiratory organs. There are standard diagnostic methods to assess breathing, which range from auscultation to spirometry; however, they all require the presence of a doctor. This can be problematic, as respiratory failure is sudden and unexpected. [1]

Keywords: respiratory failure, breath control, respiratory devices, continuous monitoring of breathing, socially significant diseases.

Breathing indicators are constantly monitored in patients in intensive care or undergoing resuscitation using various specialized equipment, including IVL devices (for newborns, children, and adults, using different operating modes), breathing monitors, fans for IVL, active CPAP therapy for newborns, general anesthetic respiratory stations, general anesthetic respiratory devices, anesthesiology monitors, bedside monitors, central stations, pulse oximeter, capnography, and oximeter.

Patients are only in wardswith monitoring equipment for a short period of time, before being transferred to a general ward for further treatment. Death from sudden respiratory failure[2] is often connected with a sharp decrease in blood circulation to the brain caused by a sudden increase of arterial pressure. The greatest risk of respiratory failureis generally at night (from 01:00 to06:00).

In a general ward there are no systems to detectsudden respiratory failureor to treat it, particularly in patients with arterial hypertension or other vascular diseases.Therefore, the development of methods and

devices for the early detection and treatment of sudden respiratory failure is important.

Data measured during continuous monitoring in resuscitation or intensive care units can be used to detect respiratory failure, and it has various advantages and shortcomings, asstated above. [3,4,5] However, there are no continuous monitoring systems for use outside these specialized areas that are compact and sufficiently convenient for patients to use without discomfort. This type of system for diagnosing sudden respiratory failure remains to be developed.

The proposed system includes the following main components: a microphone, a signal amplifier, a unit for comparing signal levels, an alarm module (comprising both audio and visual alarms), an externally connected signal-processing module, and a microphone adjustment system.

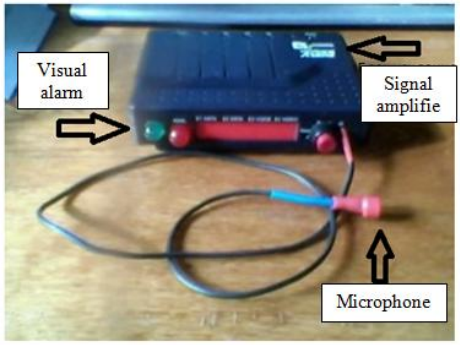


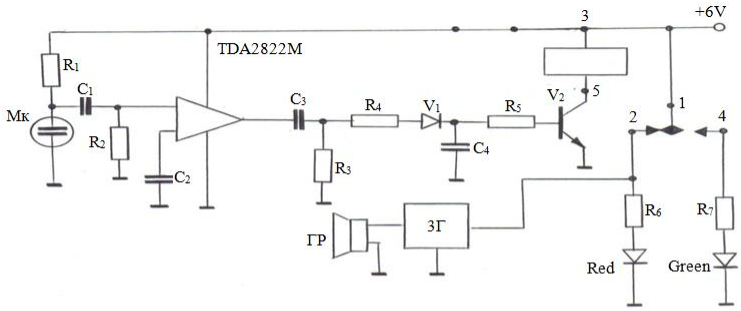
Figure 1 - The proposed system and its components

Description of the system. Figure 1 shows a photograph of the system. The microphone is a special carbon microphone 22 (MKE-395-2) that contains carbon powder between two metal plates, and it is encased in a sealed capsule. The walls of the capsule or one of the metal plates connects to a membrane. The changes in air pressure on the carbon powder caused by breathing alter the area of contact between the separate grains of carbon, which leads to variations in the resistance between the metal plates. Assessment of themicrophone established that signal amplification was required. Becausethe microphone has poor amplitude–frequency characteristics (AFC) and a narrow passband (it is insensitive to low and high frequencies), it suffers from high levels of noise and distortions.To receive a cleansignal for breathing, suitable signal amplification wasnecessary. This included the addition of resistors and a condenser with suitable parameters. It was experimentally established that the microphone should not be placed on the throat to avoid the highlysensitive microphone recording noises in the throat. It was concluded that the microphone should be fastened to the chin by straps or

a mask so that the microphone was aligned with the nose to record only the breathing.

The signal amplifier unit, the signal comparison unit, the power unit, the alarm module, and the signal-processing module weremounted together on a belt.

Figure 2 shows the amplifier and filters in the amplifier for removing noise. The signal from the microphone enters the dividing condenser withan alternating voltage of C_1. R_1 is the resistor at the input ofthe microphone. The signal is provided by C_1 and is fed to the TDA2822M amplifier. R_2 and C_2provide feedback on the direct/alternating current of the chip (chip mode). $R_2$is a divider forthe alternating current ofthechip (the signal is either increased or decreased by it).



Resistance:

R_1=10 kohm
R_2=4.7 kohm
R_3=130 kohm
R_4=10 kohm
R_5=4.7 kohm
R_6=75 kohm
R_7=75 kohm

Condenser:

C_1=0.3 μF
C_2=47 μF
C_3=47 μF
C_4=470 μF

Figure 2 – Scheme for the signal amplifier

The signal from the chip exits through C_3 (the dividing condenser for the alternating current),and is fed to the R_3–R_4 divider.

From the divider the signal goes to the half-wave rectifier consisting of diode V_1 and condenserC_4. The direct current through R_5 goes to transistor V_2 (a direct current divider). The loading of the collector of this transistor goes to the relay. The contacts at the relay switch between either normal or emergency operation.In normal mode a

green light-emitting diode (LED) with resistorR_7 is lit;the other contact of the relay occurs in emergency operation.

The contacts are closed when the person breathes normally,and the relay is in "on duty" mode,and its contacts 1 and 4 are constantly closed, food + 6V.Current from the power supply moves through contacts 1 and 4 of the relay, via the limiting R_7 resistor,and on to the green LED.

In an emergency,a signal from themicrophone goes to the amplifier, the management signal of the relay is absent, the relay switches, and contacts 1 and 2 become isolated. Current from the power supply then flows through contacts 1 and 2, via resistor R_6 and the red LED. As the red LED lights up, the green LED blinks, and asignal is given to the sound generator, which gives an alarm signal through theloudspeaker.

The LED and loudspeaker (Figure 2) will be placed in the alarm system module. The system, which consists of separate STM32 modules, outputs a signal to the computer for subsequent digitization, digital processing, and wireless broadcast to medical personnel. The system is intended to function as a signal-processing module.

Conclusions: the system is suitable formonitoringsudden respiratory failureas it develops in patients with cardiovascular diseases (e.g., arterial hypertension andcoronary heart disease) andbronchopulmonary diseases (e.g., COPD, bronchial asthma, and ENT).

Reference:

1. L. A. Bockeria report on the implementation of the interdepartmental program of the Russian Academy of medical Sciences: "Improvement of methods of prevention, diagnosis and treatment of life-threatening cardiac arrhythmias (sudden cardiac death)" / A. S. Revishvili, Z. E. Golukhova, Bazaev V. A. // Annals of Arrhythmology in 2008.Murphy, R.L. Automated lung sound analysis in patients with pneumonia / R.L.Murphy, A.Vyshedskiy, V.A.Power-Charnitsky, D.S.Bana, P.M.Marinelli, A.Wong-Tse, R.Paciej / Respir. Care – 2004. – 49. – P.1490 – 1497.
2. Kraman, S.S. Comparison of lung sound transducers using a bioacoustic transducer testing system / S.S.Kraman, G.R.Wodicka, G.A.Pressler, H.Pasterkamp // J.Appl.Physiol. – 2006. – 101. – P.469 – 476.
3. Kraman, S.S. Design, construction, and evaluation of a bioacoustic transducer testing (BATT) system for respiratory

sounds / S.S.Kraman, G.A.Pressler, H.Pasterkamp, G.R.Wodicka // IEEE Trans. Biomed. Eng. – 2006. – 53. – P.1711 – 1715.

4. Nakano, H. Validation of a new system of tracheal sound analysis for the diagnosis of sleep apnea-hypopnea syndrome / H.Nakano, M.Hayashi, E.Ohshima, N.Nishikata, T.Shinohara // Sleep. –2006.- 27.-P.951-957.

Chapter 7

DIAGNOSIS OF EARLY STAGE PATHOLOGICAL PROCESSES BY ANALYZING BRAIN RHYTHMS

A.A. Ribchenko, G.A. Shabanov, A.L. Maksimov, Y.A. Lebedev
R&D Center "Arktica", Russian Academy of Sciences Far Eastern Branch, Vladivostok–Magadan, Russia.

Multiple investigations into the monitoring and correction of patient-specific health conditions are conducted based on the registration and analysis of brain rhythms. In personalized medicine, the most important tasks are evaluating disease and providing a prognosis, controlling changes in health and recovery, and correcting any functional disturbances before pathological changes occur.

We have developed diagnostic technology based on neurophysiology and neurocybernetics. It is based on the idea that the human brain constantly controls, and is capable of correcting, the internal organs and the body as a whole, including its operation and conditions.

The decentralization index for screening patients with cancer was developed based on previous work. For cancer differential diagnostics, a specificity of Se = 0.85 and a sensitivity of Sp = 0.95 was achieved. Preclinical trials were carried out, where patients were screened with our method to diagnose early epithelial tumors and visually diagnosed diseases (e.g., glaucoma and ischemic optic neuropathy Preceded by many years fundamental research showed that induced oscillations (IO) in the brain's reticular structures bear information about the conditions of other visceral systems. We showed that specific IO occurred in response to different stimuli. The brain's reticular structures can be represented as a matrix of multiple functional conditions ("multiple arousal"), which reflect different normal conditions, functional disturbances, and pathological conditions in the body.

A cybernetic model of the brain's activating system was created by using a hardware–software system "PC MEGI-01". Total electro-biological brain activity is registered at the input, and a multi-frequency matrix of multiple functional conditions ("multiple arousal") is created as the output. The "PC MEGI-01" system and the methods of separation and

spectral analysis of the long current spectral components of the brain's rhythmic activity were patented. The diagnostic system simulates the brain's analytical function. It analyzes the information flow from the internal organ's receptors, and the functional corrector simulates the autonomic control of functions through centrifugal correction. The principal idea of the technology is aimed at assisting the body in its self-regulation processes through its incorporation into the control loop to prevent dysfunction and structural changes in the organs and systems of the body. The technology is a vicious cycle: diagnosis expressed dysfunctions - correction expressed dysfunctions - control resulting effect and its monitoring at the individual or population levels of health status.

The complex hardware consists of three function-associated hardware–software systems, which operate using a uniform spatial-frequency segmental system of coordinates that reflect the structure of the peripheral divisions of the autonomic nervous system and the main principles of viscero-somatic integration: a computer dermatograph (DgKTD-01), an inductive magneto-encephalograph (MEGI-01), and a functional resonance adjuster (ANKF-01).

Health of top scientists are being monitored in partnership with the Medical Association of the Russian Academy of Sciences Far Eastern Branch. Resulting in monitoring data allow health in the early stages not only to determine the degree of tension of adaptation mechanisms, but also to identify the group of persons with severe dysfunction in need of active prevention, treatment, and of corrective measures.

This technology allows fast, easy examinations that are noninvasive, reliable, available, and accurate. It also allows the possibility of automated processing and monitoring. These advantages make this technology applicable in health centers, preventive medicine, and rehabilitation. Family doctors could use this technology to monitor health conditions in individual patients and population groups.

Preclinical investigations and verification are held in partnership with the Medical Association of the Russian Academy of Sciences Far Eastern Branch, Pacific State Medical University, Far Eastern Federal University (Vladivostok), the Academician V.I. Kulakov Research Center of Obstetrics, Gynecology and Perinatology of the Health Ministry of Russia (Moscow).

Chapter 8

ASSESSMENT AND TREATMENTS OF HUMAN PSYCHOPHYSIOLOGICAL STATES

V.A. Kantur, V.V. Petrosyants
Far Eastern Federal University, Engineering School
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: vkantur@gmail.com

Abstract. It is previously proposed that human psychophysiological states can be assessed based on the measurement of information-wave resonance by a device that detects the information markers produced by an information-wave generator. The functional design of the information-wave test is described and assessed in this study. We also demonstrate differences between the established vegetative-resonance test and the proposed information-wave test. Additionally, we report the results obtained in volunteers who underwent information-wave testing, and the detection of markers generated using a pulse-code modulator. The relationships between blocks in the human energetic centers and mental disorders or functional deviations in the human body were defined experimentally using the proposed information-wave test. The results also confirm the feasibility of using an information-wave generator to treat a human psychophysical state. In conclusion, the present study demonstrates the feasibility of assessing and treating a human functional state using the information-wave test based on the relationship between the information-wave markers and a human information field.

Key words: Information-wave test, Psychophysical assessment and treatment

In the 1980s, V.P. Kaznacheev, a member of the Russian Academy of Sciences, proposed the phenomenon of cell-to-cell cooperation among neighboring living cells in the human body [1]. According to this theory, there is a cycle by which energy is distributed among the organs and ensures the organs have sufficient energy at certain times of the day and night. This implies the presence of energo-informational exchange among cells in some organs, between functional systems, and between the body and the external environment [2]. Considering that the human body is an

open system, it may be assumed that the body has canals, which provide a link to the external environment. If these canals are acupunctural meridians with acupunctural points responsible for linking the cells and organs within the body, then the energetic centers and chakra might provide a link between the body and the external environment. Both Russian and international researchers have sought to locate these centers in the human body [3, 4, 5]. Their research suggests that blocking these centers affects energo-informational homeostasis, impairing information and energy exchange by disrupting the bioelectrical potential of functional cells in the human body, and ultimately resulting in changes to the psychological state. Because human behaviors and their roles in life are defined by environment awareness, it should be assumed that the energo-information plays a key role in the development of blocks in the body's energetic centers. The development of blocks in the energy centers and energo-informational homeostatic disorders caused by metabolic processes, disorders, and diseases (according to the classical conception of disease) result in dysfunction of the organs connected to these centers and in the organ's cells. Therefore, it can be assumed that blocks in the energy centers are the result of psychophysiological problems.

Yu.V. Gotovskiy [6] revealed that electromagnetic radiation at fixed frequencies removed the blocks in the human energetic centers, restoring energo-informational homeostasis in the cells, metabolic processes, and the structure of damaged cells, and ultimately recovery of the psychophysical condition. Because electromagnetic radiation at fixed frequencies is capable of removing the blocks in the human energetic centers, it may be possible to obtain the energo-information associated with removal of these blocks.

The objective of this work was to investigate the effects of electromagnetic signals generated by pulse-code modulation on the human energo-informational centers, and to develop a method for assessing and treating human psychophysiological states. Figure 1 shows the functional scheme of the proposed information-wave test (IWT).

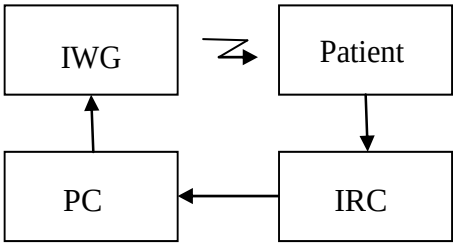


Figure 1 - Schematic diagram of the information-wave test.

IWG - information-wave generator; IRC - information reader and converter; PC - personal computer

The IWT system comprises an information-wave generator (IWG), a personal computer (PC), and an information reader and converter (IRC) consisting of a measuring transducer, detector, and analog-to-digital converter.

The device is operated as follows: the operator uses a PC to generate a pulse-code modulated signal (the informational marker), which enters the IWG. The electrical signal is transformed in the IWG into an electromagnetic signal, which is transmitted to the patient via a suitable antenna. Depending on the resonance of the information wave, a proportional signal is formed between the human information field and the information-wave marker detected by the IRC, and is observed on the PC screen.

To test the function of the proposed IWT, we performed this study using the Emed is BRT system to perform electropunctural vegetative resonance tests (VRT), which are approved by the Russian Federation Ministry of Health. The VRT registers the changes in markers at the reproduction points of electrical conductivity at the test preparations inclusion into the measurement line. This method allows the operator to detect blocks in the energy centers and, if necessary, to remove them by applying electromagnetic radiation at a fixed frequency using a loop inductor. The output of the VRT is measured in relative units (RU).

Ten healthy male volunteers aged 25–35 years participated in the study. The conditions of the seven main energy centers were determined in each patient using the BRT system. The mean X value, the mean M error value, and accuracy were calculated. Then, the catabolic and anabolic processes in the organs and the emotional behaviors of the participants before and after removing the blocks in the energy centers were determined.

In this experiment, we created a block in one of the energy centers and tested it using the BRT system. Next, we removed this block using the proposed IWT (Fig.1). The experiment was repeated for each energy center.

The experimental results are shown for a representative example of blocking the second energy center. After assessing the state of the energy center using the Emed is system, a block was created in the second energy center and this was treated using the VRT. Then, we assessed the catabolic and anabolic processes that occurred in organs that are functionally related and unrelated to the target organs, as well as the

characteristics and emotional behaviors of the participants. Finally, the block in the second energy center was removed using the VRT.

The VRT values obtained in this experiment were 74.5±0.9 R.U. for the first energy center,75.1±1.2 R.U. for the second energy center, 76.3±0.9 R.U. for the third energy center, 78.5±0.9 R.U. for the fourth energy center, 79.1±0.6 R.U. for the fifth energy center, 80.1±0.4 R.U. for the sixth energy center, and 78.9±0.4 R.U. for the seventh energy center. The VRT values were unaffected by blocking the second energy center. The value for the second energy center was 38.2±1.2 R.U., which confirmed that the block developed as expected in this center.

To confirm that the IWT detected the block generated using the VRT method, we assessed the changes induced by the IWG. The values obtained after applying the information-wave marker to the block in the second energy center were 72.3±0.8 R.U. for the first energy center, 70.1±1.1 R.U. for the second energy center, 73.3±0.6 R.U. for the third energy center, 77.5±0.5 R.U. for the fourth energy center, 72.1±0.4 R.U. for the fifth energy center, 77.1±0.4 R.U. for the sixth energy center, and 72.9±0.3 R.U. for the seventh energy center.

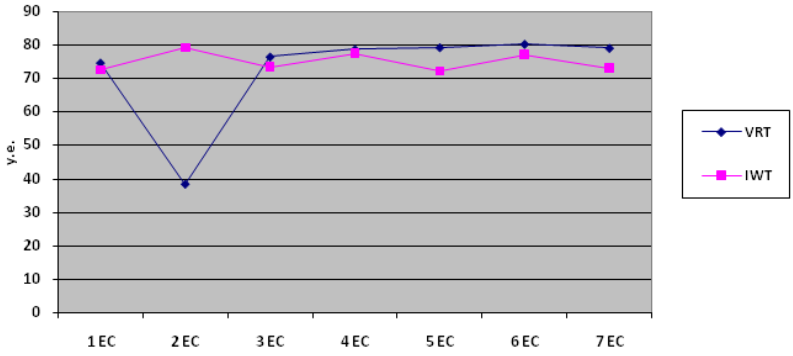


Figure 2 - Vegetative resonance test and information-wave test values obtained after blocking the second energy center.
VRT - vegetative resonance test; IWT - information-wave test

Anabolic processes are involved in synthetic process in organs while catabolic processes are involved in decay processes. According to the VRT, six degrees of catabolism–anabolism are defined in organs. The synthetic and decay processes occur continuously in normal conditions and do not exceed the first or second degrees. Any deviations from the

first or second degrees are indicative of pathological changes. According to Gerbera [4], each energy center is connected to specific organs. In particular, the second energy center is connected to the kidneys and the blind gut. The third center is connected to the stomach, pancreas, gall bladder, bile duct, liver, esophagus, and small intestine. The fourth center is connected to the bronchi, lungs, and heart.

After blocking the second energy center, we found that the catabolic processes dominated over the anabolic processes in the organs connected to this energy center. In particular, the anabolic processes were of the first degree in kidneys (39.2±0.8 R.U.) while the catabolic processes were of the fourth degree (35.3±0.5 R.U.), which indicates that catabolic processes were underway in the kidney. Similarly, catabolic processes were dominant and active in the blind gut, because the anabolic processes were of the second degree (37.2±0.7 R.U.) and the catabolic processes were of the fourth degree (33.3±0.4 R.U.). The catabolic–anabolic markers in organs unrelated to the second energy center were of the first or second degrees. After blocking the second energy center, all of the participants reported an unexplainable feeling of guilt.

After exposing the participants to electromagnetic radiation generated by a pulse-code modulator to remove the block in the given center, the VRT value of the second energy center was 79.3±0.7 R.U., confirming that the block was successfully removed. As expected, this information did not remove the blocks from the other energy centers. The same experiments were repeated for each energy center. All of the values were statistically significant, with *P*-values of <0.001.

Electromagnetic radiation generated using a pulse-code modulatorand applied to the body using the IWG successfully removed blocks in the energy centers. This method can be applied to correct human psychophysiological (functional) states. Exposing the body to energo-information is certainly the main mechanism that initiates the related intracellular processes. Considering that we now have methods to control this information, it may be possible to control the processes occurring in cells, organs, and functional systems using the IWG with a pulse-code modulator.

Conclusion. This study has demonstrated the feasibility of assessing the psychophysiological state and treating functional disorders by using the IWT, which is based on the relationship between the human information field and the information-wave markers irradiated using the IWG with a pulse-code modulator.

References:

1. V.P. Kaznacheev, L.P. Mikhaylova. Bioinformation function of the natural electromagnetic fields. – Novosibirsk: Nauka, Sib. Branch, 1985.- 182p.
2. G. Luvsan. Traditional and current aspects of the oriental reflexotherapy. –M: Nauka, 1992.
3. V. Biryukov. Vibration therapy.- Saint-Petersburg: Krilov publishers, 2010.- 185p.
4. R. Gerber. Vibration medicine. Transl. from Eng. – M: Sofia, 2008.- 592p.
5. R. Miller, "Bridging the Gap: An Interview with Valerie Hunt, Ed. D." Science of Mind, October 1983.
6. Yu.V. Gotovskiy, L. Kosareva. Exogenic bioresonance therapy by the fixed frequencies. Guidance Manual. – M.: Emedis, 2011.

Chapter 9

SURGICAL MASKS OF PEDIATRIC ONCOLOGY

O.N. Enaki, A.S. Shevchuk
Pacific State Medical University, Department of Pediatric Surgery
2 Ostryakova Ave, Vladivostok, 690002, Russia
e-mail: oksana.enaki@gmail.com, tel.: +7(914)072-47-42

***Background*:** Malignancies in childhood are very actual problem, increasing from year to year. Abdominal solid malignant tumors have their specific features in the younger are, particularly in histology. Lymphomas are more common in children and the growth of these lesions can be so fast that can imitate the acute abdomen and even the obstruction, so the patients have to be examined by the pediatric surgeon.

Our purpose was to analyze the ratio of malignancies revealed in children consulted primarily for the acute abdominal pathology.

Materials and Methods. All patients admitted to the Urgent Surgical Unit #1 of the Regional Children's Hospital, Vladivostok since 01.01.2001 till 30.06.2015 with the abdominal pain and/or obstruction, who underwent physical examination, standard laboratory and Ultrasound/X-Rays/CT-examination and were operated on with the pre-op Ds: Susp. Abdominal Tumor.

Results. During the total period of 14.5 years 21836 children in the age from 1 month to 14 years 11 months old were hospitalized to the above mentioned unit. 13108 had abdominal pain and Susp. Appendicitis (60.02%-1st group), 8728 had pain and obstruction (39.98%-2ndgroup). After the standard examination abdominal tumors were revealed in 11cases (0.05%): 4 – in the 1st group (2004, 2009, 2010, and 2014), 7 – in the 2nd(2012, 2013, 2014-3 cases, 2015-2 cases). Four of them were proved by pathologists to be not benign: 3 were lymphomas, 1 – histologically benign mixoma with malignant growth. Outcomes: two – remission, one – relapse (mixoma) and one child died during the chemotherapy.

Conclusions. Despite the rarity of malignancies in surgical patients it's socially significant disease. Such cases should be suspected by every pediatrician, pediatric or general surgeon and the fast differential diagnosis is a corner stone of the successful outcome revealing the problem in the early stage. Cooperation with the oncologists and pathologists is essential.

SECTION 2

Regional Socio-Economic Analysis and Interpretation

Chapter 10

INFLUENCE OF ECOLOGICAL AND HYGIENE FACTORS ON THE PREVALENCE OF ONCOLOGICAL DISEASES IN THE PRIMORYE TERRITORY

[1]Pavel F. Kiku, [1]Ludmila V. Veremchuk,
[1]Valentina G. Moreva, [2]Sergey V. Yudin
[1]Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia; e-mail: lme@list.ru
[2]Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia

Abstract. The prevalence of oncological pathologies under the multifactorial environmental influences during the period of 2000–2013 was evaluated based on the systems analysis methodology. The environmental dependence of the prevalence of cancer in the Primorsky region characterized by a complex mechanism of interaction of various factors and functional relationships. A direct correlation was identified between the zones of ecological stress and the levels of morbidity in the population associated with lung and stomach cancer, skin neoplasms, intestinal cancer, and oncological urological pathology (bladder and kidney cancer). The extent of factor modules impact on the oncological pathology features of different localization forms had a multidirectional character. The results obtained were used to develop a comprehensive regional program, "Oncology".

Key words: systems analysis, prevalence, oncological diseases, ecological and hygiene module factors.

Introduction. Malignant neoplasms are one of the major health-care key issues in all developed and developing countries, and ten million new cases and more than six million deaths are registered globally every year. According to rough estimates by the world health organization, 25 million people suffered from malignant neoplasms worldwide in 2000, one million have been diagnosed for the first time and seven million died. The number of new cases of cancer should increase to 27 million by 2030 and the number of patients living with cancer will be 75 million [13].

The discontinuity in the prevalence of oncological diseases in different regions and the changes in morbidity that occur with population migration conclusively confirm the relationship between cancer development and the ecological aspects of human existence [1].

As reported by the International Agency for Research on Cancer, 85% of human tumors can be attributed to the influence of environmental factors [13]. More in-depth investigations of these ecological factors are required to understand the epidemiology of cancer because the factors contributing to oncogenic risk in a population are closely related to the ecological conditions of different climatic and geographical zones [4, 9, 10, 15, 17]. Studies devoted to the issue of malignant neoplasms show that the main etiopathogenetic and epidemiological elements that define the prevalence of malignant neoplasms are environmental conditions [2, 5, 6]. Some authors have demonstrated that 70%–90% of human tumors are related to lifestyle characteristics and the impact of carcinogenic factors in the environment [11, 12, 16]. Malignant neoplasms are considered indicators of the health of the population, and depend heavily on the quality of the environment, so any increase in cancer incidence linked with environmental problemsin a region [3, 4, 7]. The dependence of the prevalence and frequency of malignant neoplasms on the anthropogenic load and environmental quality has been confirmed in domestic and foreign studies [1, 2, 9, 13, 14, 15, 16].

The incidence rate of malignant neoplasms has increased in Russia in recent years. This is attributed to unfavorable population processes, the ecological condition of the environment, and social and economic problems [1]. Unfavorable conditions for the development of oncological diseases have been created in the Primorye Territory, an outlying region of Russia, in the last 15–20 years, in terms of its natural and climatic features and specific ecological and social problems. In the period from 2000 to 2013, the level of oncological diseases for both sexes increased from 2720.76 cases per 100,000 head of population to 3834.21 cases, and increase was 30.1% over that period. It must be noted that the oncological pathology levels increased in all the cities and regions of the Primorye Territory, and the incidence in the cities was higher than in the rural areas because environmental pollution was higher in the cities. An investigation of environmental quality in the Primorye Territory showed unfavorable natural, climatic, ecological, and social parameters for the environment, increasing the risk of malignant neoplasm [4].

Study objective: The purpose of this study was a systems analysis of the dependence of the prevalence of oncological disease on the ecological and hygiene conditions in the Primorye Region.

Results and Discussions: In assessing whether the prevalence of oncological diseases depends on the ecological situation, we identified relationships between the levels of all forms of oncological disease and the status of the ecological zones. A direct correlation was identified between zones of ecological stress and the level of population morbidity in terms of lung and stomach cancer, skin neoplasms, intestinal cancer, and oncological urological pathologies (bladder and kidney cancer). However, no correlation was identified between the environment and the prevalence of diseases such as breast, ovarian, and cervical cancer. The prevalence of these diseases must be attributable to other factors.

The prevalence of oncological pathology increases in zones of critical ecological stress, where coal mining and chemical industries, ship repair enterprises, construction and machine building industries are located, and in regions of intensive agricultural chemicalization and melioration. These are present in cities and towns such as Artem, Spassk, Vladivostok, Ussuriysk, and Dalnegorsk, and regions such as Spasskiy, Dalnegorskiy, Kavalerovskiy, Shkotovskiy, Khohorolskiy, Chernigovskiy, and Khankayskiy. In these cities, towns, and regions are more than half of all enterprises with harmful working conditions. The levels of harmful substances in the air, soil, and water of these areas often exceed 10-fold the maximum allowable concentrations.

Our next goal is to examine a set of factors (modules) that are affected by oncological pathologies [8]. For this purpose, grouped factors were weighted against the oncological pathology indices of newly diagnosed morbidity, sickness, and mortality. The following facts were identified with this analysis. Sickness and mortality were most often attributed to environmental factors, which influenced the general indices of oncological pathology in the Primorye Territory. On the prevalence of cancer pathology is most strongly influenced by the hygiene module (in the cities, this module has influenced 52.8% morbidity, 54.0% of the disease, and 55.3% mortality) and socio-economic module influenced the structure of common indicators.

The most common nosological entity, lung cancer, was predominantly affected by the hygiene module in all three categories (morbidity, sickness, and mortality), and this dependence was the same in

the cities, regional areas, and all over the Primorye Territory. The influence of the social and economic module on cancer prevalence was smaller, and the influence of the ecological module was much smaller.

Colon cancer morbidity was predominantly attributed to the factors of the hygiene and social and economic modules, and the influence of these two modules was approximately equal in the cities. The prevalence of skin neoplasms and bladder cancer was similarly dependent on environment influences in the cities and all over the Primorye Territory.

We also defined the influence of environmental factors on hemoblastosis. The factors of the social and economic module were most influential on the population morbidity, illness, and mortality in the cities (on 46.3% of morbidity, 34.2% of illness, and 35.1% of mortality). The factors of the hygiene module were less influential. However, the influence of the ecological module was high, and was almost equal in the cities, rural regions, and all over the Primorye Territory.

It must be noted that the module factors relating to anthropogenic impact and the module factors characterizing the social infrastructure were more influential on the oncological pathology of malignant neoplasms and their prevalence in the cities, whereas in the region areas, the ecological module factors were more influential. From the results of this analysis, it can be inferred that different environmental factors influence the levels of oncological morbidity differently throughout the Primorye Territory. The factors of hygiene module predominantly influence the level of oncological morbidity in cities such as Arsenyev, Vladivostok, Spassk-Dalniy, and Dalnegorsk, and in the Nadezhdinskiy, Kavalerovskiy, Khankaiskiy, and Chernigovskiy regions. The factors of the social and economic module defined the levels of oncological pathology in cities such as Dalnegorsk, Artem, Partizansk, and Ussuriysk, and in regions such as Olginskiy, Partizanskiy, Mikhailovskiy, and Khorolskiy. Ecological factors influenced the prevalence of oncological pathology in Nakhodka, Dalnegorsk, Dalnerechensk, Lesozavodsk, and BolshoyKamen, and in the Terneyskiy, and Krasnoarmeiskiy regions. Therefore, using the systems approach to analyze these multifactorial influences, the cause and effect relationships were defined in the system "environmental conditions–oncopathology". To determine the effect of factor modules on the level of cancer morbidity and mortality in the Primorye territory, and their quantification allows us to determine appropriate medical and preventive measures. Understanding of key trends in the prevalence of malignant neoplasms in the Primorye territory

in response to environmental factors allows us to predict cancer incidence in defined periods in the future, and was the basis for the Primorsky territory program “Oncology”.

References:

1. Pisareva L.F, Ananina O.A., Odintsova I.N. et. al. Malignant neoplasms morbidity of the population in the Siberian and Far Eastern Administrative Centers (1998-2012)/ Siberian Oncological journal.2014, 4; P. 5-8.
2. Zaridze D.G. Carcinogenesis. M.: Scientific World; 2000.
3. Kiku P.F., Geltser B.I. Ecological problems of Health. Vladivostok: Dalnauka; 2004.
4. Kiku P.F., Veremchuk L.V., Zhernovoy M.V. The role of ecological and social and hygienic factors in oncological morbidity prevalence. Vladivostok: Izdat-Dom: Far Eastern Federal University; 2012.
5. Meshkov N.A. Epidemiological analysis of the dynamics and structure of the population mortality from malignant neoplasms in Tomsk//Hygiene and Sanitation. 2014; 1: P. 25-30.
6. Rusakov N.V., Mukhin N.A., Briko N.I. et. al. The features of sarcoidosis prevalence in Moscow/ Hygiene and Sanitation. 2012; 4: P. 16-19.
7. Rakhmanin Yu.A. Updating of human ecological issues and environment hygiene and the ways for their solving/ Hygiene and Sanitation. 2012; 5: P. 4-8.
8. Information theory in medicine. Minsk; 1974.
9. Tyulyandin S.A., Moiseenko V.M. Practical oncology: the selected lectures. St Petersburg: Center TOMM; 2004.
10. Chisov V.I., Starinskiy V.V., PetrovaG.V. Malignant neoplasms in Russia in 2005 (morbidity and mortality). M.: Gertsen FSI MSROI Roszdrav; 2007.
11. Akhtar R. Medical Geography and Epidemiology. Geographia Medica. 2009. Vol. 20: P. 77-83.
12. Doll R. The epidemiology of cancer. Eds. J. G. Forter. Philadelphia. Toronto, 2010; Vol P. 5: 103-121.
13. Global geocancerology. Ed. by G.M. Howe. Edinburg: Churchill Livingstone, 2011.

14. Higginson J. Cancer etiology and prevention. An approach to cancer etiology and control. New York: Acad. Press. 2009; P. 385-398.
15. Hirayama T. Life-style and cancer: from epidemiological evidence to public behavior change to mortality reduction of target cancer. Monogr. Natl. Cancer Inst. 2012;Vol 1: P. 65-74.
16. Muir C.S. Etiology of cancer. Eds. J. G. Fortner J. E. Rhads. Philadelphia. 2006; Vol.11: P.108 – 121.
17. 17.Smulevich V. Ecological approach to cancer epidemiology. Ecol. Disease. 2012;N 8: P. 75-79.

Chapter 11

PREVALENCE AND ORIGIN OF HIV-1 RESISTANCE IN PRIMORSKY KRAI, RUSSIA

V.S. Eliseeva, S.P. Kruglyak, L.F. Sklyar, A.V. Kalinin, T.A. Ginevskaya
Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: Vic-eliseeva@mail.ru, ms.eva2009@mail.ru

Variants of drug-resistant human immunodeficiency virus (HIV) have become increasingly widespread; genotyping of HIV isolate is an important method for identifying the mutations associated with drug resistance. This article addresses the prevalence of different HIV subtypes and circulatory recombinant forms and describes the molecular structure of drug-resistant HIV-1.

Key words: HIV, drug resistance, sequencing, subtype.

The prevalence of drug-resistant HIV strains, whichis associated with high replication rates of HIV and the high incidence of replication errors, is one of the reasons thatantivirus therapies are ineffective in some patients. Molecular genetic methods are therefore necessary to select therapies that are tailored to individual patients.

Research objective:To analyze the prevalence of mutations in drug-resistant protease genes and HIV-1 reverse transcriptase strains, and to examine the prevalence of HIV-1 subtypes.

*Materials and methods:*Genetic data were obtained by sequence analysis of HIV RNA in 61 patients. Mutation resistance was determined by virological and/or immunological response in patients.

Results:A survey of genetic variants of HIV-1 among HIV-infected patients living continuously in the territory of PrimorskyKrai revealed a prevalence ofHIV-1 subtype B of 49% (39 individuals), anda prevalence of subtypes A and C of 21% and 23%, respectively. In addition, we detected a low prevalence of circulating recombinant forms:1 occurrence each of CRF01_AE/A and B/a, and 2 occurrences of CRF02_AG.

Polyformmutations in proteasegenesand reverse transcriptase strains were present in all patients. The prevalence of mutations was: minor mutations in 20 (33%)patients, mutations of the protease inhibitor gene in 3 (5%) patients, mutations of the reverse protease inhibitor gene in 34 (56%) patients, and no mutations in primary or secondary resistance genes in 26 (42.6%) patients.

Conclusions: The dominant HIV subtype among the examined patients was subtype B, along with several circulating recombinant forms; these results confirm previously reported data. It is known that CRF01 occurs in Southeast Asia and is the prevailing form in Thailand. Recombinant gene formscould appear in PrimorskyKrai and nearby inland areas.Patients could have become infected with an active recombinant form or subsequently these forms could have arisen in the population. Subtype CRF02_AGis widespread in African countries, Kazakhstan, and in the territories of Russia–Altai and Novosibirsk.

The first mutations resistant to HIV protease inhibitor may have arisen in isolated instances, and may have been unrelated to the administration of drug therapies. Mutations conferringresistant to reverse transcriptase inhibitors occur in response to commonlyused therapies, such as highly active antiretroviral therapy (HAART); it is therefore necessary to conduct further research on the prevalence of HIV drug resistance to HAART.

References:

1. M.R. Bobkova. HIV drug resistance. - M.: Human, 2014. -288.
2. E.V. Kazennova, D.A. Neshumaev,V.Y. Laga,I.A. Lapovokand others. Molecular epidemiological characteristics of the HIV epidemic in the regions of Siberia and the Russian Far East. Collection of works of VIII All-Russian scientific-practical conference with international participation. Vol. 1 - 2014 - P.45-46.
3. Easterbrook P. J. et al. Impact of HIV-1 viral subtype on disease progression and response to antiretroviral therapy // J.Int. AIDS Soc. — 2010. — Vol.13. — Published online 2010 February 3. Doi : 10.1186/1758-2652-13-4.
4. Tebit D.M., Arts E.J. Tracking a century of global expansion and evolution of HIV to drive understanding and to combat disease // Lancet Infect. Dis. – 2011. – Vol.11. – P.45-56.

Chapter 12

PHILOSOPHICAL FOUNDATIONS OF SOCIALLY SIGNIFICANT DISEASES AND IMPLICATIONS FOR INTERVENTION

[1]N.Y. Prikhodko, [2]A.V. Chigareva
Far Eastern Federal University (FEFU),
10 Ajax, Russian Island, Vladivostok, 690922, Russia,
[1]School of Humanities FEFU, [2]School of Regional and International Research FEFU; e-mail: prihodko.ny@dvfu.ru, e-mail: chigareva.av@dvfu.ru

Abstract. This paper addresses key problems raised by the prevalence of socially significant diseases (SSDs) in modern society. We examine fundamental social–philosophical issues raised by SSDs, in an effort to systematize and understand the social dimensions of problems associated with SSDs in today's global civilization.

Keywords: social problems, socially significant diseases, social risks

In the mid-20th century, a new concept of *social diseases* appeared in social–philosophical discourse, according to which diseases arise in the context of socio-economic conditions, and that resulting impacts on society must be addressed in terms of social and human security [1]. In modern society, the problem of *socially significant diseases* (SSDs) comprises both social and medical dimensions. A fundamental assertion of modern social–philosophical discourse is that social well-being is a critical existential issue in today's world, and well-known contemporary social philosophers (e.g., Beck, Giddens, and Luhmann) are addressing the essential nature of modern global civilization in this from this viewpoint [1]. Giddens considers today's societal problems to be intensifying as a consequence of scientific and technological progress [2].

Social problems and vectors of social change are integral components of life in every society, and they define the social space in which we live. In modern sociology, the analysis and understanding of social problems represents a growing field of investigation. Recently, Yamrotsis and Notsella presented a powerful model to address the world's social problems [3], and their conceptual model serves as a basis for understanding the social problems associated with SSDs. According

to Yamrotsis and Notsella, the concept of social problems can be applied both to the social processes and the conditions that most people perceive as undesirable and threatening to basic society values, such as social order, justice, and the stability of social institutions. Publically accepted agreements—formalized as laws and regulations, or informally represented by public opinion—can be perceived as social problems as well, if they are contrary to the interests of specific social or socially defined demographic groups. Societal problems can arise due to a sense of collective guilt, caused by public neglect and a lack of awareness regarding specific social phenomena and conditions, thus resulting in negative impacts on some sectors of society.

The concept of social problems and their consequences can be applied to a wide variety of phenomena. The impacts of social problems can be devastating if adequate preventive measures are not undertaken to preclude or eliminate the consequences of those events, or if the problems are not suitably evaluated by society or by individual communities as unsatisfactory. In addition, the main characteristic feature of social problems is the possibility, or at least the potential possibility, of their inherent solvability. Generally, the state is responsible for solving social problems, and within this framework one can single out specific dimensions of various phenomena for which some aspect or aspects are social; i.e., those with an identifiable social origin or which exhibit a real or potential threat to societal values or interests. The identification of the nature of the social problem is thus necessary for its resolution.

The SSDs, which are sometimes thought of as socially dangerous in some way, are one of the most prominent social problems facing modern society. The spread of SSDs threatens the core values and fabric of society by threatening human life itself. Moreover, SSDs negatively impact demographic and economic stability. The SSDs that are most prominent, and that receive the most recognition, are those that pose a threat to other individuals [2, 3], as such diseases require the formulation of numerous legal and social norms. In general, the state and society are responsible for both the spread and the containment of SSDs, and in this respect, a sense of collective responsibility is a primary motivator for the state to reduce the risks of SSDs.

An understanding of the social problems associated with SSDs provides the basis for current social–philosophical discourse, which often revolves around societal transformations from a modern to postmodern civilization—in other words, the transformation from an industrial to a

post-industrial society. Such a transformation is associated with the transition from social norms based on certainty and rationality, which are inherent in modernity, to those based on relativity and uncertainty, which are inherent in a postmodern society. Within the realm of social–philosophical discourse, postmodernism arose at the end of the 20th century, associated mainly with the works of Foucault and Lyotar [4]. A postmodern view of relativism has become a critical attitude not only within the sciences, but also in the context of social values and normative structures.

We here define some characteristic features of contemporary society that are critical for the ensuing analysis of SSDs, in the context of social processes using postmodern terminology. We first address the characteristics of social structures. Social classes in postmodern society are related to capitalistic economic structures. This limits their importance as essential elements of social order. To replace the social class structure with a more complex and heterogeneous organizational foundation requires an inter-weaving of economic, gender-related, age-related, and cultural factors. As compared with traditional social structures, the social structure of a postmodern society is more fragmented and more differentiated.

Moreover, factors related to health and health behavior become critical structure-forming components of a postmodern society, and the presence or absence of certain kinds of diseases becomes a basis for social differentiation. Relevant diseases include both socially acceptable and socially unacceptable diseases. For example, diseases of the musculoskeletal system are acceptable in society, and people with such disabilities form a separate social stratum for which an entire infrastructure has been created and developed. Diseases associated in the public mind with socially unaccep table behaviors affect the social structures of modern society. For example, HIV has become a structure-forming factor, and HIV-infected individuals have been relegated to independent social communities in modern society.

Beck identified an important characteristic feature of modern society, which he referred to in his famous work *Risk Society* [5]; this feature is the presence of imminent danger, as the differentiation of secure and insecure zones in the modern world are increasingly blurred. Modern society is characterized by certain kinds of social risks, which, according to Beck, are typified by the Chernobyl melt down. The Chernobyl disaster and its sequelae represented the end of an era in which

we could distance ourselves from one another, as the essential feature of radioactive contamination is worldwide connectivity. Borders can provide protection from poverty, but not from the dangers of atomic contamination. Therefore, the cultural and political forces behind the Chernobyl disaster symbolize the underpinnings of modern society [6].

Threats to life and well-being posed by the dangers of social conflicts create heavy existential social burdens, which have serious short- and long-term consequences. To eliminate the constraints imposed by one's social identify, and to allow opportunities to make decisions that secure the individual a place in the social structure by virtue of his or her merits alone, a new model of ascriptive variety must emerge in society. In contrast to the system of caste and class, an ascriptive model develops without regard to financial status, fear, or traditional norms; such a model represents the highest stage of social development in a postmodern society. Technological developments have redefined the risks and hazards associated with SSDs, such that they are unevenly distributed globally, and as the borders of nation states are permeable and transparent to SSDs, the prevalence of fears and risks associated with SSDs have created new social–psychological community structures Social movements are now founded in the context of a global community, and measures of the success of current policies can only be assessed at national and international levels.

The recognition of the new and evolving context of modern society has led contemporary social analysts to consider post-industrial society to be a risk society, with the risks associated with SSDs constituting one of the basic risks of life in modern society. It should be emphasized that, within the inclusive list of behaviors resulting in SSDs, many are determined by institutional factors, including the lack of preventive strategies for disease, generally inadequate preventive medicine, the lack of satisfactory educational systems, and problems related to the legal dimensions of SSDs.

A consideration of SSDsin the context of risk prevention requires a review and reinforcement of policies supporting social workers, as social workers play a central role in the management and mitigation of risk in a risk society. Thus, in addition to medicine, the fields of social work and psychology should play key roles in developing adequate preventive strategies in the battle against SSDs [8].

The national and global scope of social problems related to SSDs must be addressed, particularly in the case of socially dangerous diseases,

which often result in stigmatization and discrimination. Stigmatization associated with SSDs has a hugely negative impact, not only on individuals, but also on the community in general. At the individual level, stigmatization affects self-esteem, causing despair, low self-worth, and depression. Often, social stigmas associated with an illness cause a negative emotional feedback loop to arise in an individual. For instance, if a man identifies himself as an outlaw, the social consequences are exclusion from normative social structures, and a deterrent response by law enforcement, manifesting society's moral assumption that good people live according to the law. Social stigmatization can devalue a person and challenge his or her social identity. This destabilizes that person's emotional well-being, promoting actions that are deemed socially unacceptable [9].

At a societal level, stigmatization undermines efforts at disease prevention, and more subtle and diffuse forms of behavior may replace those that are more obvious or severe. Despite new and more supportive forms of social control, new social interaction models describe downward trajectories in individuals with diseases, especially socially dangerous diseases. For example, Foucault describes trajectories leading to insanity, involving alienation, control, and exclusion; such trajectories are prevalent in postmodern society[10].

Modern social–philosophical discourse on the problems and risks associated with SSDsin a postmodern society offers avenues for addressing these problems. For example, Giddens describes a neoliberal project that develops planned policies as a response to a risk society. Regulation, rather than risk management, is the hallmark of such a neoliberal social policy. Giddens`s neoliberal project reduces the risks associated with the modern world by taking social work and psychological care as a central tenet. Developers of this neoliberal project claim that any intervention to reduce risk, including interventions associated with SSDs, should include social work as a main component of the solution. Social workers help individuals maximize self-improvement as a means of solving problems; thus, goals include building new relationships between clients and resource systems, developing interactions between individuals and resource systems that improve the efficiency of such interactions, and developing policies that improve social assistance and change. State policies under these circumstances must be linked to providing basic social protection, and the

accompanying social services should be associated with citizens' activities and the development of personal responsibility.

Thus, we conclude that the best way to prevent SSDs is to establish state-specific legal and social institutions that strengthen the capacity of citizens to take individual responsibility for their physical and social well-being; however, such personal achievements should not reduce the responsibility of states to create programs that appropriately manage risk.

References:

1. Beck U., Giddens A., Lash S. Reflexive Modernization: Politics, Tradition and aesthetics in the modern social order. Cambridge, UK: Polity Press, 1994; Giddens A. The Third Way: the Renewal of Social Democracy. Cambridge: Polity Press, 1998; Beck U. Risk Society. Toward to New Modernity. London: Sage Publications, 1992; Luman N. Community of society. Evolution. M: Logos, 2005.
2. Giddens A. The Third Way: the Renewal of Social Democracy. Cambridge: Polity Press, 1998.
3. Jamrozik A., Nocella L. The sociology of social problems: theoretical perspectives and methods of intervention. Cambridge UK: Cambridge University Press, 1998.
4. Foucault M. The history of madness in the classical age. St. Petersburg: University book, 1997; Foucault M. Discipline and Punish: The birth of the prison. London, Tavistok, 1977.Lyotard JF. The postmodern state. M., Aletheya, 1998.
5. Beck U. Risk Society. Toward to New Modernity. London: Sage Publications, 1992.
6. Beck U. About this book (1986) //. Beck U Risk Society. Toward to New Modernity. Moscow: Progress -Tradition, 2000, p. 5.
7. Risk Society. Toward to New Modernity. Moscow: Progress - Tradition, 2000, p. 6.
8. Webb S. Social Work in Risk Society. New York: Palgrave Macmillan, 2006.
9. Goffman E. Stigma: Notes of the Management of Spoiled Identity. New York: Prentice- Hall, Inc.; Englewood Cliffs, 1963.

10. Foucault M. The history of madness in the classical age. St. Petersburg: University book, 1997; Foucault M. Discipline and Punish: The birth of the prison. London, Tavistok, 1977.
11. "On approval of practical guidance and methodical manual on health statistics" Order of the Federal State Statistics ServiceNo.409, accepted November 22, 2010.
12. "On approval of SSD list and the list of diseases that pose a danger to others" Russian Federation Government Resolution No.715, accepted, December 1, 2004.

Chapter 13

ORGANIZATION OF MEDICAL REHABILITATION OF PATIENTS WITH SOCIALLY SIGNIFICANT DISEASES IN RUSSIA

Anatoly F. Belyaev
State Budgetary Educational Institution of Higher Professional Education, Pacific State Medical University, Russian Ministry of Health, Primorsky Institute of Vertebroneurology and Manual Medicine, Vladivostok, Russia
e-mail: inmanmed@mail.ru, tel.: 8(423)245-93-84

Abstract. In this article, I review the Russian legal and regulatory guidelines for the medical rehabilitation of patients with socially significant diseases. I describe the regional regulations in this field, and the legal framework for training students and doctors involved in medical rehabilitation.

Key words: socially important diseases, medical rehabilitation, regulations

Socially important diseases are specified by the Russian Federation Government Regulation 715, dated December 2004, "Approved list of socially significant diseases, which may pose a risk to the general public", amended on July 13, 2012. The most severe of these diseases are associated with hypertensive blood pressure (International Classification of Diseases classes I 10.0–I 13.9), which may damage vital organs, especially the heart and brain. In terms of the possible strategies for overcoming the problems of socially significant diseases, the implementation of preventive measures may be the most effective and low-cost approach. The tangible benefits of changing the behavior and lifestyle of the general public include reduced rates of morbidity and mortality; however, the number of people disabled by socially significant diseases is increasing, with a resulting economic loss to society. Medical rehabilitation appears to be the most effective way of improving quality of life and functional activity, and decreasing the effects of disability in survivors of cerebral and cardiac accidents [1-3].

Medical rehabilitation is a priority in domestic healthcare services. The legal regulations for medical rehabilitation are specified by the

Russian Federation Federal Law no. 323-FL, dated November 21, 2011, "The Fundamentals of Public Health Protection in the Russian Federation". In particular, article 40 "Medical Rehabilitation and Sanatorium Resort Therapy" describes medical rehabilitation as follows: 1) a set of medical and psychological measures designed to rehabilitate the patient's functional reserves, improve the quality of life, improve the patient's survivability, and facilitate the integration of the patient back into the community; 2) medical rehabilitation should achieve complete or partial recovery of the damaged organ/system, compensate for any missing function, maintain the body's functions during treatment of the underlying pathologic processes, facilitate the prevention, early diagnosis and correction of pathophysiologic disorders, and prevent or attenuate potential disabilities; 3) medical rehabilitation involves the complex application of natural therapies, medicinal drugs, non-drug therapies, and other methods; 4) medical rehabilitation should be performed at healthcare organizations by specialists with higher and secondary medical education, professionally trained clinicians, and other specialists; and 5) the therapeutic procedures available at medical rehabilitation centers and sanatorium resorts must be approved by the authorized federal executive.

Because healthcare issues are under the joint jurisdiction of the Russian Federation and the Territory in accordance with the Constitution of the Russian Federation, Legislation no. 750-PTL, April 8, 2011, "The Healthcare in Primorye Territory", which has since been amended, and article no. 24 "Medical Rehabilitation and Sanatorium Resort Therapy".

The structure of medical rehabilitation is specified in bylaws established by the Russian Federation Ministry of Health, and is approved under Order no. 1705n, dated December 29, 2012 "The Procedures of the Medical Rehabilitation Arrangement". This Order describes three stages of medical rehabilitation: 1) resuscitation, 2) hospital care, and 3) outpatient care with multidisciplinary mobile teams. A clear structure has been established to implement this Order.

In the first stage of medical rehabilitation, regional vascular centers and primary vascular centers have been established in all federation subjects, including Primorye Territory. The medical rehabilitation delivered at these centers is regulated by the Russian Federation Ministry of Health Order no. 928, dated November 15, 2012, "The Approval of the Procedures for Health Care Delivering to the Patients with Acute Cerebrovascular Disorders" and by the Ministry of Health of the Russian Federation Order no. 1750n, dated December 29, 2012, "The Approval of

the Standard for the Specialized Medical Aid in Cerebrovascular Accident". The funding for medical rehabilitation is provided by the Federal Compulsory Medical Insurance Fund according to the main diagnosis.

In the second stage, medical rehabilitation is delivered as hospital care in medical units specialized to perform medical rehabilitation, and are licensed for this purpose. The cost of medical rehabilitation services in this stage are included in the tariff for medical rehabilitation and are reimbursed by the Federal Compulsory Medical Insurance Fund according to diagnosis-related groups developed by the International Classification of Functioning and the Russian Federation Government Regulation no. 1273, dated November 28, 2014, "The State Program for Guaranteeing Free Medical Care to the Citizens of the Russian Federation".

In the third stage, outpatient care, payments are made according to the patient's main condition or according to the diagnosis-related groups developed in accordance with the International Classification of Functioning for medical rehabilitation purposes.

The positions Doctor of Medical Rehabilitation and Rehabilitation Nurse were inaugurated by the Administrative Order no. 1183n, dated December 20, 2012, "The Approval of the Positions Nomenclature for Medical and Pharmaceutical Professionals". The approved types of medical rehabilitation organizations are described in Administrative Order no. 529n, dated August 6, 2013, "The Approval of the Nomenclature for Medical Organizations".

The nomenclature of medical services for medical rehabilitation was developed under the auspices of Article no. 14 323-FL "The Fundamentals of Public Health Protection in the Russian Federation" of the Order of the Russian Federation Ministry of Health and Social Development no. 1664n, dated December 27, 2011, "The Approval of the Nomenclature for Medical Services", and the Order of the Russian Federation Ministry of Health no. 794n, dated October 28, 2013, "Amendments to the Order of the Ministry of Health and Social Development of the Russian Federation no. 1664n, dated December 27, 2011, 'Approved Nomenclature of Medical Services". Medical rehabilitation services are included in the list of licensed procedures, which is administered by the Russian Federation Government Regulation no. 291, dated April 16, 2012, "On Medical Licensing (excluding…)". In accordance with Administrative Order no. 121, dated March 11, 2013

"Approved Requirements for the Organization and Performance of Primary Medical and Sanitary, Specialized (including technological advanced), Emergency (including specialized emergency), and Palliative Care, and Medical Aid Provided at Sanatorium Resorts Therapy…" of medical rehabilitation services include specialized primary care medical centers, sanatoriums, and outpatient setting; specialized medical care in hospital settings; palliative medical care in outpatient settings; palliative medical care in hospital setting; and medical care in sanatorium resorts.

The position of Chief Medical Liaison Officer in Medical Rehabilitation was approved by The Russian Federation Ministry of Health, Administrative Order no. 444, dated October 25, 2012, "Chief Liaison Officers of the Ministry of Health of the Russian Federation". The Russian Federation Ministry of Health also established a Specialized Committee on Medical Rehabilitation. The nomenclature and regulation of chief officers in the Federal Districts are governed by Administrative Order no. 655, dated September 23, 2013, "Regulation of Chief Liaison Officers of the Russian Federation Ministry of Health".

The position of Chief Liaison Officer of Medical Rehabilitation was approved by the Ministry of Health in the Far Eastern Federal District in the Administrative Order no. 959, dated December 13, 2014, "The List of the Chief Liaison Officers of the Ministry of Health in the Federal Districts of the Russian Federation." The position of Chief Liaison Officer of Medical Rehabilitation was also approved by the Department of Health of Primorye Territory. To ensure the successful development of medical rehabilitation services in the far east of Russia, significant methodical and administrative work was required to improve the pedagogical skills of staff, prepare educational materials, and improve the quality of training. This preparation was undertaken at Pacific State Medical University. A Chair of Medical Rehabilitation and Sports Medicine has also been established at this university. An extended course on rehabilitation covering the most pressing challenges regarding the medical rehabilitation of patients following acute cerebrovascular disease has been run for two semesters since 2013. This course is also scheduled for spring, 2015. In accordance with Order no. 273 FL, dated December 29, 2012 "Education in the Russian Federation", and Order no. 16 of the Russian Federation Ministry of Education and Science, dated January 14, 2011, and the Federal State Educational Standard for higher professional education in the specialties "Medical Care", "Pediatrics", and "Dentistry", the faculty has developed appropriate teaching materials for students.

Pacific State Medical University started to teach medical rehabilitation to students in 2015, in accordance with the Federal State Educational Standard. A task group, including neurologists, rehabilitation specialists, and sports medicine specialists, has been established at Pacific State Medical University, and is concerned with the scientific issues related to medical rehabilitation in Primorye Terrority. The specialists are trained via full-time and extramural postgraduate courses in manual therapy, exercise therapy, and sports medicine within the clinical residency. Organizational and methodological work is now underway to establish medical residencies in medical rehabilitation and osteopathy.

In 2014, associations of rehabilitation professionals were established in 47 federation subjects, including Primorye Territory, followed by establishment of the Union of Rehabilitation Professionals of Russia at the Constituent Congress in Moscow. This Union is an important institution aimed at fostering partnerships between the government and professionals in the field of medical rehabilitation. It has also developed various professional standards, including those for specialists in the field of medical rehabilitation and in social rehabilitation. Some clinical recommendations and treatment protocols have also been developed by the Union. Section five of the Federal Targeted Program of Healthcare Development in the Russian Federation up to 2020 is devoted to specialists in the field of medical rehabilitation. In accordance with the Federal Program, the Department of Health of Primorye Territory has implemented a medical rehabilitation development program, which will continue until 2020. The objectives of the Federal Targeted Program are as follows: increase life expectancy to 74 years; increase the longevity of physically active individuals to 65 years for women and 70 years for men; reduce the length of hospital stay in healthcare organizations providing high-tech medical care by as much as 25%; decrease the number of disabilities by up to 20%; decrease the severity of disabilities by up to 15%; decrease the hospitalization requirements by up to 20%; improve the quality of healthcare delivery; decrease secondary expenditure related to the provision of minimal care of seriously ill and disabled patients; and decrease the morbidity rate of working citizens by up to 15%.

The Russian Federation Ministry of Health Order no. 05/1701, dated January 13, 2015, implemented pilot medical rehabilitation projects in 12 federation subjects, in accordance with the protocol developed at a meeting at the Russian Federation Ministry of Health. The projects will be structured on the three-stage medical rehabilitation system.

Accordingly, the Department of Health of Primorye Territory and the Federal Compulsory Medical Insurance Fund have conducted some meetings and seminars to discuss these pilot projects. The Department of Health of Primorye Territory introduced the Order "Organization of medical care and medical rehabilitation of patients with central and peripheral nervous system, and musculoskeletal system diseases" which approves the following items in Primorye Territory: 1) provisional regulation of the medical care and rehabilitation of patients with central and peripheral nervous system or musculoskeletal system disorders in healthcare organizations; 2) a list of healthcare organizations approved to deliver medical care to these patients; 3) provision for a Selection Board to approve the delivery of medical rehabilitation at the healthcare organizations; 4) and routing for the medical rehabilitation of patients with central and peripheral nervous system and musculoskeletal system disorders.

In conclusion, in this article, I have summarized the rules and regulations involved in establishing the medical rehabilitation of patients with socially significant diseases in the Russian Federation.

References:

1. A.F. Belyaev. Sailors' health: problems and their solution. M.: Vladivostok: Russian Island; 2010; 312p.
2. G.E. Ivanova. Medical Rehabilitation in Russia. Prospects for development.// Newsletter of the rehabilitation medicine. 2013; 5:3-8.
3. G.E. Ivanova, L.V. Stakhovskaya, A.P. Repyev. Legislative principles for delivering medical rehabilitation aid.// Newsletter of the rehabilitation medicine. 2014; 1:2-5.

Chapter 14

OPINIONS OF DOCTORS CONCERNING THE FEDERAL STANDARDS OF MEDICAL CARE

Yu.I. Gainullina, A.V. Gundobina, O.V. Loginova
Far Eastern Federal University, School of Biomedical Science
10 Ajax, Russian Island, Vladivostok, 690922, Russia

One of the aims of implementing the health care modernization program in the Russian Federation is the practical application of federal standards for secondary care in medical institutions. These federal standards were implemented by the issuance of relevant orders and regulations. However, the implementation of federal standards from the top down did not take into account the opinions of doctors concerning the development of a standardized system.

Purpose: To survey the opinions of doctors in in-patient hospitals concerning their ability toimplement federal standards in secondary care.

Materials and methods: We performed an anonymous survey of 539 doctors in public health organizations in the Russian Federation, where the federal standards are implemented. Statistical analyses were performed using Statistic a software version 10.

Results: The survey revealed that the doctors held controversial attitudes to the implementation of federal standards. Just 48.1% of the respondents had a favorable view regarding the federal standards, 28.0% reported that the federal standards restricted their professional activities, 2.3%did not want to use the standards, and 21.6%were undecided. The quality of the federal standards was evaluated using a five-point scale. Only 37.2% of the respondents rated the quality of the standards as high (= 5 or 4 points), 33.0% as satisfactory (= 3 points), 14.1% as unsatisfactory (= 2 or 1 points), and 18.6% were undecided. The reasons for poor compliance with the federal standards that were reported by the respondents included limited financial resources for purchasing drugs and reagents (63.0%), poorquality of the federal standards (42.3%), and limited equipment (56.0%) and facilities (27.9%) for delivering medical care. Meanwhile,

60.4% of the respondents reported that they are not ready to adopt the standards now; 2.7% of the surveyed doctors did not answer the question.

Conclusion: The results indicate that many doctors have developed a negative attitude towards implementing the federal standards of medical care. Someof the reasons included the poorquality of the standards of care and a lack of educational programs for doctors.It will be necessary to better motivate doctors to implement the federal standards of medical care.

SECTION 3

Epidemiology and Public Health

Chapter 15

SCREENING METHODS FOR PRECANCEROUS CONDITIONS

Natalia G. Plekhova
Pacific State Medical University, Central Research Laboratory
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: pl_nat@hotmail.com, tel.: +7(423)242-97-78, +7(423)245-17-19

Abstract. The feasibility of combining modern innovative techniques and research methods (liquid-based cytology, automated cytological scanning, PCR detection of human papilloma virus) for the diagnostic screening of precancerous cervical pathologies is demonstrated.

Keywords: screening, cervical cancer, Pap test, human papillomavirus.

The screening methods used to monitor human health incorporate recent developments not only in medicine, but also in interdisciplinary areas of the fundamental sciences, especially the biomedical sciences. The main objective of these methods is to identify disease in the early, clinically asymptomatic stages of its course, to allow an accurate clinical examination and the prompt identification of the appropriate measures for the management of the disease. The use of screening to determine the pathological changes in the body that can presage malignant neoplasms is especially relevant. According to World Health Organization data, screening for malignant neoplasms in the lung, breast, stomach, colon, and uterine cervix is reasonable in Russia, and accords with the high level of morbidity in the population. The effectiveness of the screening methods used has already been demonstrated in the cases of mammography for breast cancer, the fecal occult blood test for colon pathologies, and cytological screening for pathologies of the uterine cervix.

Special attention must be paid to uterine cervical cancer because it is the third most common malignant neoplasm and the fourth most common cause of death from oncological disease in women throughout the world. The development of extensive modern technologies has made it possible to improve traditional diagnostic methods, including cytological screening of cervical smears as a screening method. These methods allow the condition of cervical cells to be monitored in the stage

of the pathological process preceding the formation of a malignant neoplasm. Unfortunately, ~30% of cervical cancers are not detected in time, which is attributable to improper sampling, uninformative samples generated when preanalytical processing procedures are violated, and the subjective assessment of the cells' condition by cytologists [4]. The application of new material-processing technologies at the preanalytical stage has considerably improved the effectiveness of screening methods. These methods include liquid-based cytology for cell suspensions obtained from liquid biomaterials; rapid cell fixation on different types of slides; purification and separation of liquid samples using cell gradient centrifugation or filtration centrifugation; and suspension treatments before the cells are placed onto slides, which include the differential lysis of specific cell types, deproteinization, solution purification to remove cell debris, and the correction of the cell concentration in the final volume. The manipulations performed with these techniques allow thin-film preparations to be made that can be used for diagnosis not only with traditional cytological screening of cervical material (Papanicolaou staining method) using optical microscopy, but also with an automated cytological scanning system. This system consists of three components: automatic sample scanning, database creation or accumulation in the computer memory images, and the ranking of cellular elements according to the signs of atypia (presence and degree) with a software package and the expertise of a professional cytologist. Thin-layer preparations treated with these techniques can be used for additional research to narrow the diagnosis, including the direct, immune, or cytochemical identification of the virus.

In this context, the recent important discovery of the role of human papillomavirus (HPV) in the genesis of cervical cancer, which was recognized by the Nobel committee, suggest that viral testing is warranted in patients in whom dysplastic processes have been identified in the epithelium of the uterine cervix. According to randomized controlled and cohort studies of HPV, testing for the virus is more sensitive than cytological screening in detecting precancerous changes in the uterine cervix and invasive cancer (cervical intraepithelial neoplasia II and III, adenocarcinoma *in situ*, invasive cancer) [2, 3]. However, the detection of HPV and the identification of the viral genotype using molecular methods (PCR) as part of the screening process are limited or does not always provide accurate information because they can detect transient infections, especially in young women [1]. In the USA and Europe, testing for high-

risk HPV (HR-HPV) is recommended for women with atypical squamous cells of undetermined significance (ASCUS) and is performed in addition to cervical cytological screening in patients aged over 30 years. However, the combination cervical cytological screening with HPV testing produces somewhat different results than when using only one method. Therefore, if in the imperceptible cervical diseases test on HPV is negative, the number of colposcopies can be reduced, which increases the cost-effectiveness of screening. The assignment of patients with ASCUS and positive HR-HPV results to a specific high-risk group of patients using this method will circumvent unnecessary appointments for colposcopy and interventions for women who do not need them. The results of the multicenter ATHENA (Addressing the Need for Advanced HPV Diagnostics) study in the United States, in which more than 47,000 women participated, showed that the genotype of the virus must be determined and the condition of the precancerous uterine cervix established when the combined screening method is used. The application of cervical cytological screening using modern material-processing technologies at the preanalytical stage and HPV testing, with the definition of the virus type, can significantly improve the diagnosis of precancerous pathological changes in the uterine cervix. The combination of these methods allows the organization of medical practices to be optimized and guarantees rational and economically effective cervical screening.

Referencese:

1. Cuzick J. , Ho L., Terry G. et al. Individual detection of 14 high risk human papilloma virus genotypes by the PapType test for the prediction of high grade cervical lesions // J. Clin. Virol., Vol. 60, Is. 1, 2014, pp. 44-49
2. Farnsworth A. Screening for the prevention of cervical cancer in the era of human papillomavirus vaccination: An australian perspective // ActaCytologica, 2011, 55 (4), pp. 307-312.
3. Ibanez R., Autonell J., Sardà M. et al. Protecting the underscreened women in developed countries: The value of HPV test // BMC Cancer, Vol. 14, Is. 1, 2014, pp. 574-582.
4. Minkina G.N., Savicheva A.M., Hall K. et al. The prevalence of different types of human papillomavirus in women with cervical intraepithelial neoplasia severe // Questions of Gynecology, Obstetrics and Perinatology, 2013.N 3, P.32-37.

Chapter 16

CLINICAL INFLUENZA CAUSED BY DIFFERENT VIRAL SEROTYPES

A.I. Simakova, K.A. Dmitrenko
Pacific State Medical University
2 Ostryakova Ave, Vladivostok, 690002, Russia
e-mail: ksdmitrenko@mail.ru, tel.: +7(968)165-32-96

Hospital records (n = 531) for the last six years (2009–2014) were analyzed. The diagnoses of influenza were confirmed with nasopharyngeal swabs using real-time polymerase chain reaction. The etiological analysis showed that influenza A (H1N1) pdm09 occurred in 261 patients, accounting for 46.5% of patients; influenza A (H1N1) was diagnosed in 148 patients (26.4%); influenza A (H3N2) in 102 patients (18.2%); and influenza B in 50 patients (8.9 %). Influenza A (H1N1) pdm09 caused disease that was clinically more severe than seasonal influenza.

Influenza is one of the most widespread diseases in the world. According to World Health Organization data, influenza and other respiratory viral infections make up 60%–70% of the total world morbidity.

Objective: Our objective was to examine the clinical features of influenza, according to the viral serotype.

Materials and methods: The hospital records of 531 influenza patients treated at the Infectious Disease Department of the Primorye Territory Regional Clinical Hospital #2 in the past 6 years (2009–2014) were analyzed retrospectively.

Results: All patients were divided into four groups: patients with influenza A (H1N1) pdm09 (group 1, n = 261); or those with seasonal influenza: influenza A (H1N1) (group 2, n = 148), influenza A (H3N2) (group 3, n = 102), or influenza B (group 4, n = 50). All influenza diagnoses were confirmed with the polymerase chain reaction. Patient age ranged from 21 to 64 years (mean, 26.9), and the major proportion (36.3%) of patients were 20–29 years old. The sample population

contained 51.2% women and 48.8% men. Moderate disease severity prevailed (87.4%), but 12.6% of patients experienced severe disease. The disease started abruptly, with pyrexia, headache, and muscle and joint pain in 89% of patients. The patients with influenza A (H1N1) pdm09 were febrile (39.5 ± 0.04 °C), and their fever lasted for 5.0 ± 0.9 days on average, whereas those with seasonal influenza were subfebrile (37.5 ± 0.06 °C), and their fever lasted for 2.5 ± 0.6 days. Catarrhal syndrome affected 74% of group 1 patients, 29% of group 2 patients, 34% of group 3 patients, and 7% of group 4 patients on the first day of the disease. Among the complications reported, sinusitis was most frequently observed (16.2%), pneumonia was recorded in 9% of patients, and myocarditis was a complication in 0.5% of patients. The average duration of hospitalization in group 1 was 7.5 ± 0.5 days, but only 5.5 ± 0.4 days in groups 2, 3, and 4 ($p < 0.05$). As antiviral therapies, 7.2% of patients received oseltamivir, 76.1% received umifenovir, and 16.7% received symptomatic treatment. The mortality rate was 1.6%, and only patients infected with influenza A (H1N1) pdm09 died.

Conclusion: Infection with th 2 e highly pathogenic influenza A (H1N1) pdm09 virus was characterized by more severe disease progression than the seasonal disease.

Chapter 17

MARKERS OF INTERFERON AND CELLULAR IMMUNITY IN MEN WITH RECURRENT GENITAL HERPES AND CHLAMYDIAL CO-INFECTION

Elena V. Markelova, Natalia S. Chepurnova, Marina S. Tulupova
Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: markev2010@mail.ru, tel.: +7(423)245-07-00

Abstract. In this study, we sought to identify markers of interferon and cellular immunity in patients with genital herpes and *Chlamydia trachomatis* co-infection. The cell profile of herpetic urethritis was characterized by an increased frequency of lymphocytes expressing a marker of early activation ($CD25^+$) among normal cells expressing HLA-DR, and by an increased frequency of apoptotic-capable cells. These profiles are associated with abnormal activation, switching from early to late activation, together with a functional defect of T cell immunity. Patients with herpetic urethritis co-infected with *C. trachomatis* showed a significant increase in the frequency of $CD3^+CD25^+$ cells and increases in the markers of later negative activation against the background of lower phagocytosis. These results are consistent with chronic cell activation, and priming of T lymphocytes for the induction and activation of apoptosis in these patients. Co-infected patients also exhibited relative interferon-γ insufficiency.

Key words: genital herpes, *C. trachomatis*, immune status, interferon.

Genital herpes is associated with significant morbidity. In 20th century, it was classified as one of the 70 most common diseases, and is associated with major social and healthcare problems. About 1 billion people, about 1/6th of the world's population, are infected with herpes simplex virus (HSV) type 2 [1]. In the Russian Federation, the incidence of HSV-2 was estimated to be 18.4 per 100,000 people in 2011 [2]. Many studies have focused on the clinical manifestations and treatment of genital herpes, as well as its adverse effects on the female reproductive system. However, there is limited information regarding the role of HSV as an etiological factor in genitourinary system diseases in men. The

deleterious effects of HSV on various organs are widely accepted, and its role in carcinogenesis and secondary infertility is well established. For example, studies examining the effects of HSV and human cytomegalovirus using semen revealed that HSV was more common in idiopathic infertility, and was associated with reductions in active mobile spermatozoa and the proportion of morphologically normal germ cells [3]. Thus, there is no doubt that HSV modifies the immune responses of humans to various pathogens [4]. Studies of sexually transmitted infections showed that genital herpes was commonly associated with chlamydial infection owing to the common epidemiologic characteristics of the causative pathogens [5, 6]. In addition, persistent asymptomatic infections, particularly *Chlamydia trachomatis*, may trigger immune responses and delay hypersensitivity reactions, key factors in male infertility. Immunologic homeostasis is especially important in the persistence of viral and bacterial urogenital infections. HSV type 2 is associated with disturbed interferon (IFN) and cytokine activities [7]. Some qualitative changes were found in the course of infection because the causative pathogens could substantially change their pathogenic properties through interactions with other pathogens. Therefore, clinically, patients with co-infection acquire certain characteristics, which vary considerably from those of patients infected with a single pathogen. Immune disorders are more apparent in co-infected patients and are less susceptible to traditional treatment regimens, reducing the therapy's effectiveness, activating pathogenic microflora, changing the causative pathogen's properties, and increasing the risk of super-infection.

Purpose. To evaluate the immunologic features and measure the concentrations of IFNα and IFNγ in men with recurrent genital herpes and chlamydial co-infection.

Materials and methods. We analyzed venous blood samples from 30 men aged 20–45 years with chronic urethritis. There were 13 (43.3%) patients with chronic recurrent herpetic urethritis and 17 (56.7%) with chronic urethritis with a mixed bacterial and viral etiology (genital herpes co-infected with *C. trachomatis*). We also analyzed venous blood samples from 30 healthy male volunteers as a control group. Lymphocyte phenotyping and markers of phagocytosis were assessed by flow cytometry using monoclonal antibodies from BD Biosciences (San Jose, CA, USA). The serum IFNγ concentration was measured using specific reagents from R&D Diagnostics Inc. (Minneapolis, MN, USA). The

serum IFNα concentration was measured using an enzyme-linked immunosorbent assay (sandwich method) from Vector Best (Novosibirsk, Russia) in accordance with the manufacturer's instructions. The results were recorded using an enzyme immunoassay analyzer (Multiscan, Helsinki, Finland). The cytokine concentrations (in pg/ml) were calculated by drawing a calibration curve using computer software. Data were analyzed descriptively using Student's *t* test with Biostat software (version 10, AnalystSoft Inc., Walnut, CA).

Results and discussion. Cells expressing CD markers and their combinations were identified in the major lymphocyte populations (i.e. T, B, natural killer [NK], and natural killer T [NKT] cells) using markers of positive ($CD25^+$ and $HLA\text{-}DR^+$) and negative ($CD95^+$) lymphocyte activation. We focused on two lymphocyte subpopulations, namely T helper cells ($CD3^+CD4^+$ cells) and cytotoxic T cells ($CD3^+CD8^+$ cells). The results of these analyses showed that the cellular profile in patients with chronic urethritis was significantly different from that in the control group (Table 1).

Table 1. Immunophenotyping of immunocompetent cells, immunoglobulin levels, and phagocytosis indices in patients with chronic urethritis and in healthy men

Indicators	Patients with urethritis			Healthy men n=30
	HSV-1.2 n=13		HSV-1.2 C. trachomatis n=17	
$CD3^+$ $CD19^+$	%	69.23±2.51	70.82±1.52	70.30±2.15
	cell/10^9/L.	1.01±0.07	1.33±0.12	1.42±0.14
$CD3^+CD4^+$	%	42.00±1.87	38.06±2.05**	47.50±2.20
	cell/10^9/L.	0.64±0,03	0.69±0.07	0.96±0.10
$CD3^+CD8^+$	%	25.08±0,89	28.70±1,98	31.10±1.90
	cell/10^9/L.	0.39±0.02	0.53±0.06	0.62±0.11
$CD3^-CD19^+$	%	13.62±1.18	11.88±0.81*	14.92±1.26
	cell/10^9/L.	0.20±0.02	0.22±0.02	0.30±0.05
$CD3^-16^+56^+$	%	13.40±1.98	14.15±1.32	13.85±0.80
	cell/10^9/L.	0.22±0.05	0.25±0.02	0.28±0.07
$CD3^+CD16^+$ 56^+	%	5.19±1.27	5.26±1.33	3.44±0.06
	cell/10^9/L.	0.08±0.02	0.09±0.02	0.07±0.02

$CD25^+$	%	13.69±1.28***	16.23±1.19***	9.12±0.82
	cell/10^9/L.	0.21±0.02	0.31±0.04	0.20±0.07
$CD3^+CD25^+$	%	7.53±0.92 p_{1-2} <0.05	10.30±0.86***	6.15±0.70
	cell/10^9/L.	0.11±0.01 p_{1-2}<0.05	0.20±0.03*	0.14±0.04
$CD95^+$	%	23.38±2.30*	23.77±2.67*	16.20±1.20
	cell/10^9/L.	0.36±0.03	0.42±0.05	0.32±0.06
$CD3^+$ $CD95^+$	%	15.36±1.81**	16.35±2.34***	7.14±0.12
	cell/10^9/L.	0.23±0.02*	0.30±0.05*	0.15±0.03
$HLA\text{-}DR^+$	%	15.37±1.30	14.62±0.74	13.90±0.86
	cell/10^9/L.	0.24±0.02	0.27±0.02	0.28±0.06
$CD3^+HLA\text{-}DR^+$	%	2.26±0.28	2.74±0.28	4.00±0.62
	cell/10^9/L.	0.03±0.002	0.05±0.008	0.09±0.02
$CD4^+/CD8^+$		1.69±0.09	1.55±0.16	1.55±0.15
phagocytic index	%	66.31±4.55	64.18±4.62*	76.3±1.4
phagocytic number		3.80±0.38	3.62±0.41*	4.80±0.20

Notes: *p < 0.05, **p < 0.01, and ***p < 0.001 versus the control group; p_{1-2}, p-value for the comparison between the two groups of patients with urethritis.

We observed several common patterns and characteristics in the distributions of the examined factors in men with herpetic urethritis and men with genital herpes co-infected with *C. trachomatis*. In particular, there were no significant differences in the frequencies of $CD3^+CD4^+$ cells and $CD3^+CD8^+$ cells between these two groups. However, the frequency of $CD3^+CD8^+$ cells was significantly lower in the co-infected group than in the control group. The ratio of $CD3^+CD4^+$ cells to $CD3^+CD8^+$ was not significantly different between both groups (men with herpetic urethritis and men with genital herpes co-infected with *C. trachomatis*). The correlation of $CD4^+/CD8^+$ did not extend beyond the reference range in any subject.

By analyzing the expression of markers of lymphocyte activation, we observed significant differences in the frequencies of cells expressing these markers among the study groups. In particular, the frequency of $CD25^+$ lymphocytes was increased in 6 (46.15%) patients with herpetic urethritis and in 12 (70.58%) patients with herpetic urethritis co-infected with *C. trachomatis*. In addition, we found a significant increase in the

frequency of $CD3^+CD25^+$ cells in patients with herpetic urethritis co-infected with *C. trachomatis* and an increase in the frequency of $CD3^+CD95^+$ cells (a marker for negative lymphocytes activation) in both groups of patients with urethritis. However, the frequency of cells expressing HLA-DR was not significantly different between patients with chronic urethritis and the control group. These results indicate that the lymphocytes have switched from early activation to late activation, which may reflect a functional defect of T cell immunity. There were no differences in the frequencies of NK cells or $CD3^+CD19^+CD56^+$ cells, a minor cell population, or of NKT cells. The phagocytic analysis showed that the quantitative indices of phagocytosis were significantly lower in patients with herpes co-infected with *C. trachomatis* than in the control group.

The serum IFNγ concentration was significantly elevated in patients with herpetic urethritis compared with the control group ($p<0.01$), but not in patients with herpes co-infected with *C. trachomatis* (Table 2). These results suggest that patients may have a relative shortage of IFNγ, consistent with a functional defect in T helper 1 lymphocytes.

Table 2. Serum cytokine profile in patients with chronic urethritis and healthy men

Indicators	Patients with urethritis		Healthy men n=30
	HSV-1.2 n=13	HSV-1.2 C. trachomatis n=17	
IFNγ	27.24±6.06** (p_{1-2} <0.01)	10.05±0.65	12.52±0.63
IFNα	10.8±0.9*	14.92±1.82**	4.6±0.4

Notes *p < 0.05 and **p < 0.01 versus the control group; p_{1-2}, p-value for the comparison between the two groups of patients with urethritis.

It was previously reported that a local deficit in IFNγ is associated with a reduction in T helper 1 lymphocytes and impaired macrophage function in patients with chlamydial urethritis or chlamydial urethritis co-infected with other pathogens [8]. IFNγ plays a key role in the eradication of *C. trachomatis*, and low IFNγ concentrations allow persistent infection. The serum IFNα concentrations were significantly greater in both groups of patients with chronic urethritis than in the control group, consistent with a compensatory reaction to viral infection and viral and bacterial co-infection.

Conclusions. The cell profile of patients with herpetic urethritis is characterized by an increased frequency of lymphocytes expressing the marker of early activation ($CD25^+$) despite a normal frequency of cells expressing HLA-DR, and an increased frequency of cells with apoptotic potential. These results are indicative of abnormal activation of immune cells, switching from early activation to late activation, together with functional defects in T cell immunity. Herpetic urethritis co-infected with *C. trachomatis* was associated with a significant increase in the frequency of $CD3^+CD25^+$ cells, increased expression of markers of later negative lymphocyte activation, reduced phagocytosis indices, and relative IFNγ deficiency. These findings are consistent with chronic cellular activation and priming of T lymphocytes for the induction and activation of apoptosis in patients with herpetic urethritis co-infected with *C. trachomatis.*

References:

1. A.A. Chentoufi, L. BenMohamed, P. Van De Perre and A.A. Ashkar, "Immunity to ocular and genital herpes simplex viruses infections," *Clinical and Developmental Immunology*. – Art. ID 732546. – p. 2. – doi: 10.1155/2012/732546.
2. P.R. Abakarova, "Genital herpes: therapy potential," *Gynecology*, vol. 15, no 2, pp. 47–50, 2013.
3. D.M. Sobchak, N.E. Volskiy, T.A. Svintsova et al., "The human immune system and peculiarities of herpes infection pathogenesis (Review)," *Modern technologies in medicine*, vol. 6, no 3, pp. 118–127, 2014.
4. J.A. Kagramanova, V.V. Malinovskaya, E.N. Vyzhlova and E.V. Serova, "The Gel "Viferon" treatment effectiveness of the recurrent genital herpes forms of viral infection for women local application," *Rus. journal for skin and venereal diseases, App. Herpes*, no 1, pp. 29–30, 2010.
5. L.A. Marchenko, I.P. Lushkova, "Genital herpes and carrier state of antigens of major class I histocompatibility complex," *Rus. journal for skin and venereal diseases*, no 2, pp. 4–11, 2009.
6. Yu.V. Egorova, A.S. Nesterov, N.A. Ilyina and A.V. Nesterova, "Immune system peculiarities in women with urogenital chlamydiosis," *Bulletin of I.Ya. Yakovlev CSPU*, no 4, pp. 69–73, 2012.

7. A.V. Melnichenko, M.V. Mezentseva, R.Ya. Podchernyaeva et al., "Interferon status and cytokine profile in patients with acute and chronic forms of the associated herpetic infection," *Medical Immunology*, vol. 13, no 4-5, pp. 411–412, 2011.
8. E.V. Markelova, I.A. Yutskovskaya, "Local cytokine status in men with chronic chlamydial and ureaplasma urethritis", *Far Eastern Medical Journal*, no 3, pp. 83–86, 2007.

Chapter 18

PREDICTION OF HCV THERAPY EFFECTIVENESS IN CO-INFECTED HCV/HIV PATIENTS

Li Yu A., Sklyar L.F., Kiku P.F., Markelova E.V., Simakova A.I.
Pacific State Medical University,
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: julianochka-li@rambler.ru, lidiya.sklyar@hotmail.com,
tel.: +7(423)242-97-78

Hepatitis C virus (HCV) is the most common cause of liver disease in HIV-infected patients. A combined analysis of baseline characteristics and data will allow a more accurate prediction of the results of HCV-treatment in these patients, significantly increase therapeutic efficiency and optimize treatments for co-infected patients, as well as improve existing methods of treatment. We investigated criteria for HCV-therapy effectiveness in HIV-infected patients and created a predictive scale for its outcome on the basis of monitoring of the clinical, laboratory and cytokine parameters. Because the scale is based on evaluation of the initial data, it can predict the probability of sustained virological response prior to the commencement of HCV treatment in HCV/HIV co-infected patients.

***Key words*:** HCV/HIV co-infection, HCV treatment, predicting scale

Introduction. Chronic infection by hepatitis C virus (HCV), contracted as a result of blood-to-blood transmission, is the most common cause of liver disease in HIV-infected patients. Among 35 million HIV-infected individuals, ~20% (7 million) are also infected with HCV. In the HIV population of the Russian Federation, the incidence of HCV is ~60%–70%, and most of these patients have a history of intravenous drug use [2, 3]. The last decade was marked by the introduction of highly active antiretroviral therapy (HAART) into clinical practice; HAART has reduced mortality and the incidence of opportunistic infections, and has significantly improved the expectancy and quality of life of HIV patients [5]. Under these conditions, chronic HCV has become one of the leading causes of death among HIV-infected patients [8].

The principal approaches to HCV treatment against the background of HIV infection are the same as those for mono-HCV-infection. However, the application of HAART for the treatment of HIV infection, as well as the treatment and prevention of opportunistic infections, determine the features of an integrated therapeutic approach for management and treatment of co-infected patients. The positive response probability of HCV treatment is largely determined by virological characteristics (e.g., genotype and viral load) as well as a variety of clinical and immunological criteria, all of which significantly influence therapeutic success.

Despite numerous studies, the mechanisms of immunological damage by HIV infection are still not entirely clear [4, 9]. The results of systemic cytokine profiling of HCV/HIV patients are often contradictory. In the future, a combined analysis of baseline characteristics and data will allow more accurate predictions of the efficacy of HCV treatment in HIV patients, and will also significantly increase therapeutic efficiency and optimize treatment protocols for co-infected patients.

The goal of this study was to investigate criteria for measuring the effectiveness of HCV therapies in co-infected HIV patients and to create a predictive scale for assessing therapeutic outcomes on the basis of clinical, laboratory, and cytokine profiling parameters.

Materials and methods. We examined 289 HCV/HIV co-infected patients treated for 48 weeks with PEG-IFN alfa-2a and ribavirin. We determined the cytokine status (IL-2, 4, 18, IFNα, γ, and antibodies to IFNα) in 120 of these patients, and analyzed case records retrospectively for all patients [7]. Patients were followed at an AIDS center in Vladivostok during the period 2006–2014.

The patients were divided into two groups according to results of the HCV therapy. The first group consisted of co-infected patients who had achieved a sustained virological response (SVR) at 24 weeks after the end of the therapy; the second group consisted of non-responders, i.e., patients who had not achieved SVR. Statistical analyses were conducted using SPSS IBM Statistics v. 22

Results. The study group consisted of 182 males (63%) and 107 females (37%). The average age of all individuals was 35.0 ± 4.7 years. Of the study group, 49% presented stage 4A HIV infection, 51.2% received HAART, and 59.5% achieved SVR.

We used neural network analysis to select predictors that were statistically associated with SVR achievement [6]. The predictors were classified according to the average value of the indices in the group that had achieved SVR. For the regression model, we selected a categorical regression with optimal scaling (CATREG). This model was chosen because, in addition to the standardized regression coefficients, the analysis yields "importance coefficients", with the absolute values of the coefficients being proportional to the importance of the regression coefficients; therefore, they are proportional to the degree of contribution of each predictor (i.e., the "weight") to the dependent variable (SVR achievement). The coefficients are selected as the importance of the weight values. For each predictors included into the regression model was calculated his score. Thus, the scale (Table 1).

Table 1. Evaluation scale for the sustained virological response (SVR)

Predictor	Value	Point
Age	>40 years	8.5
HCV viral load	≥500 000 IU/ml	0.15
IL-2 before treatment	> 4.3 pg/ml	2.5
IL-4 before treatment	> 0.75 pg/ml	30
IFNα before treatment	> 6.85 pg/ml	44
IFNγ before treatment	> 10.5 pg/ml	17
IL-18 before treatment	> 1230 pg/ml	0.3
Anti-IFNα-antibodies before treatment	> 0.44 pg/ml	2
HIV stage	4A–4B	0.3
HIV viral load	>150 cop/ml	0.07
CD4+ T-lymphocytes before treatment	>518	0.5
HAART	No	0.08
Stage of fibrosis	F3–F4	2.5
ALT	>2N U/l	1.3

**A total score of less than 50 is indicative of a high risk of HCV-treatment inefficiency.*

Next, to determine the threshold for the total score, a theoretical probability range was defined for which SVR had not been achieved. According to results of the regression analysis, the range of scores was constrained to the interval of 0–50. Thus, we determined a minimum indicative score (50) for which successful HCV-therapy was practically not observed, and this score was adopted as a preliminary threshold. The theoretical values of threshold points were tested by binary logistic regression, in which only one categorized predictor was used, i.e., the

total score of the patient (≤50 or >50); the dependent variable was SVR. This regression model based on the received program data is carried out within the forecast 83.3% (coefficient of determination, R^2 = 64.4%) [1].

Discussion. Predicting the effectiveness of various treatments is a promising area of medical science, regardless of field or specificity. Numerous new factors that directly or indirectly affect the outcomes of treatments are being examined to evaluate the effectiveness of chronic hepatitis C therapy, and the number of promising predictors is increasing daily. With regard to HCV infection, treatment is increasingly individualized, especially in cases of HCV/HIV co-infection; this individualization complicates the assessment of therapeutic effectiveness and thus the development of strategies for treating HCV/HIV patients.

In this study, we developed a scale that allows patients to be easily placed into one of two groups: those who are non-responsive to therapy, and those who have achieved SVR. The scale should be useful for clinicians, who must make decisions about patient management and care. Because it is based on an initial evaluation of patient status, the scale allows a prediction of the probability of SVR achievement prior to HCV treatment in HCV/HIV co-infected patients.

References:

1. Byuyul, A. SPSS: art of data processing. Analysis of statistical data and recovery hidden patterns: Tr. from Deutch. / A. Byuyul, P. Tsëfel. - M.: DiaSoft, 2005. – 608 p.
2. Hepatitis C and HIV infection: the tactics of co-infected patients. Clinical Protocol for the WHO European Region. [Electronic resource] / WHO. - Mode of access: http://www.euro.who.int/_data/assets/pdf_file/0010/781487HEP__C_rus.pdf. (Date of access: 10.05. 2010).
3. Hepatitis C in Russia: epidemiological characteristics and ways to improve the diagnosis and surveillance / N. Pimenov, V.P. Closets, S.V. Komarov [et al.] // Epidemiology and Infectious Diseases. - 2012. - № 3. - P. 4-9.
4. Zheleznikova, G. F. Cytokines as predictors of course and outcome of infections / G. F. Zheleznikova // Cytokines and Inflammation. - 2009. - T. 8, № 1. - P. 10-17.
5. Kravchenko, A.V. Features antiretroviral therapy with in co-infection of HIV and chronic hepatitis / A.V. Kravchenko,

N.Y. Gankin, V.G. Canestri // Farmateka. - 2008. - № 19. - P. 1-8.

6. Artificial neural networks for prediction in surgery [electronic resource] / S.D. Bogomolov, S. Kiselev, A. Medvedev, V. M. Nazarov. - M., 2003. - Access: http://www.medicum.nnov.ru/nmj/2003/1/26.php. (Date of access: 12.09. 2014).
7. Antiviral therapy of chronic hepatitis B and C in HIV-infected patients. Methodical letter of Health Ministry of the Russian Federation from 20.01.2006 № 163-PX / Health Minister. - M., 2007. - 32 p.
8. Meta-analysis: increased mortality associated with hepatitis C in HIV-infected persons is unrelated to HIV disease progression / T. Y. Chen, E. L. Ding, I. G. R. Seage, A. Y. Kim // Clin. Infect. Dis. – 2009. – Vol. 49, № 10. – P. 1605-1615.
9. Viral hepatitis and HIV co-infection / V. Soriano, E. Vispo, P. Labarga [et al.] // Antiviral. Res. – 2010. – Vol. 85, № 1. – P. 303-315.

Chapter 19

DEVELOPMENT OF MULTIDISCIPLINARY DIAGNOSTIC APPROACH FOR THE DETECTION OF BLADDER CANCER CAUSED BY URINARY SCHISTOSOMIASIS

[1] V.Y. Startsev, [2]A.Y. Kolmakov
[1]St.-Petersburg's state pediatric medical university, Department of Oncology with Course of Radiation Diagnosis and Radiotherapy
e-mail: vlad_startsev@mail.ru, tel. +7(921)942-79-40.
[2]Clinical Hospital, Lobitu-City, Province of Benguela, Angola
e-mail: Antonkol_030275@mail.ru, tel. +244(926)230-007.

Relevance. Urinary schistosomiasis (US) is common in humans infected with *Schistosoma haematobium*, and is associated with an increased risk of bladder cancer (BC). BC typically affects young, employable people and usually occurs within 10–20 years after primary US (El-Harvey M.A. et al., 2000; Lopatkin N.A. et al., 2010). US is endemic to many regions, especially parts of Africa and the Middle East. Owing to global migration, cases of US have also been reported in East-Asian and European residents [3].

In most endemic countries, schistosomiasis-associated BC (shBC) is detected mainly in invasive stage (80%), which requires radical surgical treatment and pelvic exenteration. Histologically, squamous BC is associated with a low degree of dissemination [5]. The World Health Organization recommends that patients who present with gross hematuria should be prescribed standard doses of antiparasitic drugs (e.g. praziquantel) [1, 6]. However, continued follow-up of patients with newly diagnosed US is a concern because, once gross hematuria is resolved following oral therapy, patients with US are often discharged from medical care and are not routinely followed up [7]. Unfortunately, many patients with shBC are hospitalized within a few months to 1 year because of repeated gross hematuria caused by cancer invasion into muscle tissue.

Purpose of the study: To improve the diagnosis and treatment of shBC.

Materials and methods: We analyzed 56 patients who originally presented with hematuria and weretreatedatour medical clinic in the

Provinceof Benguela (Angola) between 2009 and 2012. The duration of gross hematuria since the first manifestation ranged from 3 weeks to 12 months. All patients were black, with 49 (87.5%) rural and 7 (12.5%) urban residents. All patients used untreated water for domestic purposes.

The patients were divided into two subgroups (A and B) according to the diagnostic and treatment approaches. Group A comprised 35 patients, of which 19 (54.3%) were women (mean age 37 years) and 16 (45.7%) were men (mean age 35 years).This group of patients was analyzed retrospectively. This group of patients were initially prescribed praziquantel (40 mg/kg) and antibiotics. They were discharged once the gross hematuria had resolved. Patients with recurrent hematuria were prescribed praziquantel and underwent routine urological examinations: cytological examination of urine sediment (CEUS), ultrasonography of the pelvic organs and abdomen, and due to indications, cystoscopy followed by biopsy and excretory urography, and computed tomography of pelvic organs. Following the detection of BC, the patients were referred for specialized treatment.

Group B was a prospective group of 21 patients, of which 13 (61.9%) were women (mean age 31 years) and 8 (38.1%) were men (mean age 28 years).This group of patients received a modified diagnostic and treatment plan, as follows. First, the patients were directed to an urologist in the outpatient department of the regional hospital and then sent to a day-ward, where a wide range of diagnostic procedures were performed, including CEUS, ultrasonography, cystoscopy with biopsy of the bladder mucosa, and trans-urethral resection and biopsy (TURB), as indicated.

Results: BC was confirmed in the majority of patients (*n*=30) in group A, and surgery was performed in all of these patients. The pathology reports revealed the presence of squamous cell carcinoma with schistosome eggs in the inflamed mucous membranous areas in all of the remote tissue preparations that were assessed. In 1 (2.86%) patient with $pT_2N_0M_0$BC, we performed open segmental resection of the bladder. In 28 (80%) patients, we ascertained locally advanced and disseminated BC, which was classified as $pT_{3\text{-}4}N_{0\text{-}3}M_{0\text{-}1}$. Among these 28 patients, 23 (82.1%) underwent radical cystectomy with urinary diversion, while 5 (17.9%) underwent ureterocutaneostomy owing to advanced malignancy. One (2.9%) patient with gross hematuria was referred to us from the maternity hospital at week 37of pregnancy. After the diagnostic examinations, the patient underwent cesarean section and cystectomy with a neobladder

using a modification of the Mainz–Pouch II method. The patient and her baby were discharged from the hospital in a satisfactory condition. Malignancies affecting the female or male genitalia were found in 5 (14.3%) patients in group A.

In 4 (19.0%) patients in group B, cystoscopy revealed proliferative changes in the urothelium caused by the schistosomes. All of the patients underwent TURBon the same day as cytoscopy. The histological report confirmed the presence of schistosome eggs, but there was no evidence of urothelial malignant lesions. BC was confirmed in 12 (57.1%) with a grade of $_{p}T1\text{-}2N_0M_0$and required surgery. These patients underwent TURB (*n*=5, 41.7%) or open segmental resection of the bladder (*n*=7, 58.3%) including three pregnant women (week 35–39of pregnancy). In 1 (4.8%) patient, macrohematuria occurred because of reflux caused by kidney stones. Prostate cancer had spread to the bladderin 2 (9.5%) patients.

Schistosome eggs were detected by CEUSin 28.2% of patients. Based on the results of ultrasound diagnostic, shBC was suspected in 46.8% of patients. In 63.5% of patients, cystoscopy revealed urothelial neoplastic changes or gross (>1.5 cm in diameter) proliferative changes of the bladder mucosa, caused by schistosomal activity.

Conclusions: Using standard diagnostic methods, we observed a low sensitivity for and a long delay in the diagnosis of BC in group A. Only a combination of different diagnostic modalities (i.e. morphologic, radiologic, and endoscopic methods) together with diagnostic surgery in a ward setting was sufficient to reach an accurate diagnosis and treat these patients in a timely manner. The early detection of urothelial tumors allowed us to perform organ-sparing surgery for patients of group B, and we rely that it will provide better quality of life for them.

Prophylactic treatment with praziquantel did not help to prevent shBC. It is important that healthcare providers in regions endemic for US to organize their diagnostic strategies and implement a stepwise approach to ensuring patients with hematuria are quickly referred for comprehensive examinations in an outpatient center. Such centers should be equipped with the necessary diagnostic equipment and experienced staff.

The diagnostic and treatment strategy for patients with US should include cystoscopy and, if indicated, TURB. This approach allows us to identify shBC at an early stage. Early surgery because of gross urothelial changes in patients with US is justified for preventing the development of squamous cell BC. We need a landmark clinical marker to help identify

patients with early US symptoms because of the high risk of developing shBC within 10–20 years of the initial US infection.

References:

1. El-Harvey, M.A. The epidemiology of schistosomiasis in Egypt: Gharbia Governorate./M.A. El-Harvey [et al.] / Am. J. Trop. Med. Hyg.,2000. – Vol. **62. – P.** 42-48.
2. Urology: textbook for university. Moscow: "Geotar-Media", 2010. – 520 p. [on Russian].
3. Xue, K. Clinical presentations of schistosoma hematobium: three case reports and review / K. Xue [et al.] //Can. J. Urol., 2011. – Vol. 18, № 3. – P. 5757-5762.
4. Honeycutt, J. Controversies and challenges in research on urogenital schistosomiasis-associated bladder cancer / J. Honeycutt [et al.] // Trends Parasitol., 2014. – Vol. 30, № 7. – P. 324-332.
5. Ploeg, M. The present and future burden of urinary bladder cancer in the world / M. Ploeg [et al.] / World. J. Urol., 2009. – Vol. 27. – P. 289–293.
6. Salem, H.K. Changing patterns (age, incidence, and pathologic types) of schistosoma-associated bladder cancer in Egypt in the past decade / H.K. Salem [et al.] / Urol., 2012. – Vol. 79. – P. 379–383.
7. Shokeir, A.A. Squamous cell carcinoma of the bladder: pathology, diagnosis and treatment / A.A. Shokeir / BJU Int., 2004. – Vol. 93. – P. 216–220.

Chapter 20

GENDER FEATURES BASED ON A COMPARATIVE ANALYSIS OF CLINICAL RESERCH OF HIV-INFECTED MEN AND WOMEN

L. Sklyar, E. Miroshnichenko, G. Parashchenko, N. Belogolovkina, E. Ermolitskaya, E. Varavina

The Establishment of Health Care KKB No. 2, Center for Prevention and Control of AIDS and Infectious Diseases, 50 Borisenko Str., Vladivostok, 690057, Russia; e-mail: lidiya.sklyar@hotmail.com

Abstract: Studies of gender distribution in the cumulative number of patients with HIV infection in the Primorsky region show that men dominate, although the number of women is increasing. The nature of opportunistic infections is comparable for both sexes. However, significant differences were observed in the prevalence of *Candida* esophagitis and herpes infection. Numerous studies have been conducted on gender, HIV, therapeutic strategies, and their relationships. Over time, these studies will contribute to improved health advice for women. However, to this end, the influence of both sex and gender must be considered.

***Key words*:** HIV infection, gender, opportunistic infections

The total number of HIV-infected individuals in Russia exceeded 800 - 600 thousand in 2014 [2]. Approximately 80% of new HIV cases in Russia are in persons 18–29 years old [1]. Cases of HIV infection are registered with the Russian Federation. According to regional statistics, on 31 December 2014, 7732 HIV-infected persons resided in Primorsky territory, and the prevalence of HIV-infected inhabitants in the territory was 398.9 per 100,000 population. An analysis of the incidence and prevalence of the HIV-infected population of Primorsky during the 3-year period from 2011 to 2014 indicates that the number of HIV-infected individuals is increasing. All medical facilities in the region provide screening and examination for HIV, and treatment of patients with HIV. Sometimes gender plays an important role in access to, and availability of, medical care. Women face numerous challenges and barriers related to their health and well-being. For example, many women suffer from domestic violence, and their economic and social position is, on average,

lower than that of men, and they are often economically dependent on a partner. Many women are raising children alone, and their time, money, and effort go first and foremost to the health of their children, and their own health care needs are often neglected. These problems may prevent women from visiting a doctor or seeking medications, often this leads to mental and physical stress. Since it is known that many diseases occur in men and women with different frequencies, and that symptoms, complications, and manifestations of diseases vary with gender, it is likely that HIV infection in women presents itself differently than in men. The relationship of men and women to infection varies; for example, the likelihood of infection by opportunistic pathogens can be related with anatomical, biochemical, or neuroendocrine differences between men and women (for example, the pH of the vagina). Complex hormonal interactions and related differences may also play a role in the prevalence of HIV infection and the clinical manifestation of opportunistic infections [1, 3].

Purpose of the study. To conduct a comparative analysis of clinically examined HIV-infected men and women in terms of stages and severity of infection.

Materials and methods. We analyzed the dispensary treatment cards of 117 patients with a diagnosis of HIV infection. The total sample was divided into two groups based on gender and stage of the disease. The first group consisted of 59 men with stage III–IV (late) HIV infection. The second group consisted of 48 women at similar stages of infection.

Results of the study. An analysis of the cumulative number of patients with HIV infection in the territory of Primorsky showed that women comprise 36.3% and men 63.7% of the population (ratio of women to men of 1:1.75). However, an increasing number of women over the last 6 years are presenting with newly diagnosed cases of HIV infection, and the percentage of women in the cumulative population has increased from 30% in 2004 to 38.3% in 2014. According to the results of our study, the frequency of visits by women versus men with HIV for clinical examinations by infectious disease specialists was the same as the prevalence of HIV in women versus men (1:1.8). The frequency of visits to other specialists was also the same in women and for men (1:1). In general, the nature of opportunistic infections is comparable in both sexes. However, significant differences are observed in cases of *Candida* esophagitis, herpes infection, and cytomegalovirus infection. Related

diseases frequently observed in women include gynecological diseases of the ovaries, uterus, cervix, vagina, and labia, and menses disorders, inflammatory diseases of the pelvic organs, acute salpingitis, genital herpes infection, vaginal candidiasis, human papilloma virus infection, and lesions of the cervix (dysplasia, carcinoma). The relatively large number of manifestations in women is reflected in the increased number of clinical care visits among women as compared with men (80% versus 20%, respectively). Differences have also been observed in the incidence of other infections, such as skin disorders (rash, seborrhea, psoriasis, eczema, molluscum contagiosum, cellulite, tinea corporis and tinea), which are often more prevalent in women than in men. On the other hand, men visit specialists at a higher frequency than do women for certain disorders, such as those related to vision (37.5% versus 12.5%, respectively) and the nervous system (45.4% versus 20%, respectively). We also found an increased incidence of urinary tract infections, fungal infections, and infections of the skin and nails in women relative to men, but a higher frequency of diseases of the peripheral nerves and muscles in men. Women experience changes in otorhinolaryngological organs more often than do men (36.4% versus 25%, respectively).

Conclusions. Monitoring of the clinical treatment of individuals with HIV can provide useful information for making management decisions that improve the quality and efficiency of medical care for HIV patients. Information obtained about progress in the clinical treatment of HIV-infected individuals and versatile monitoring of clinical examinations allows for the prompt coordination of the activities of specialists in medical facilities when working with HIV-infected patients.

References:

1. HIV infection: clinical features, diagnosis, and treatment /in. A. Pokrovsky, I. N. Ermak in. A. Belyaeva, O. Yurin; Under the General Ed. in. A. Pokrovsky. - 2nd add
2. (Corr. and supplementary): GEOTAR-MED, 2013. -488pg.
3. European action plan for HIV/AIDS 2012-2015 / WHO.- Geneva, WHO, 2011.- 63 pg. URL: http://www.euro.who.int/ data/assets/pdf_file/0007/149281/RC61 rInfDoc8.the pdf. (accessed on 02.03.2013,).
4. Federal scientific and methodological Center for prevention and fight against AIDS. [Internet resource] - Mode of access: http:// www.hivrussia.ru

Chapter 21

SPECTRUM PULMONARY LESIONS AT HIV INFECTION

Zhelamkova M.P., Li Yu A., Sklyar L.F., Korolenko N.D., Yakovleva N.D.
Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia;
e-mail: lidiya.sklyar@hotmail.com, sarik007@mail.ru, tel.: +7(423)242-97-78

We conducted a study of clinical data on community-acquired pneumonia in immunocompromised patients with HIV infection. The data reveal the extent of the clinical course of the disease (pneumonia) and a wide spectrum of opportunistic infections caused by the disease.

***Keywords*:** HIV, pneumonia, etiology, clinical features

Background: HIV infection is one of the most severe medical problems worldwide [1]. Progression of immunosuppression in HIV-infected patients is associated with an increase in the incidence of related lung diseases [2]. Pneumonia caused by different infectious agents playsa leading role in such diseases.

Objective: To study the spectrum of lung diseases in patients with HIV-associated immunodeficiencybased on clinical, laboratory, and instrumental data.
Materials and methods: Case records of 50 HIV-infected patients with lung diseases, hospitalized at the Center for AIDS in 2014, were analyzed.

***Results of the study*:** Men prevailed (67%); the mean age of patients was 37 ± 7.8 years. Patients were diagnosed with stage 3B HIV infection (22% of cases; 11 patients), stage 4B infection (62% of cases; 31 patients), and stage 5 infection (16% of cases; 8 patients). The average CD4 + T-lymphocyte countvaried from 50 to 698/mcl. The preliminary diagnosis for all patients upon admission was community-acquired pneumonia, mixed etiology, moderate severity. During subsequent examination, treatment, and observation, and according to additional laboratory and instrumental tests and assessment of clinical symptoms, the causes of pneumonia in patients was identified as mixed bacterial and fungal

microflora with dominant *Streptococcus pneumonia* (56% of cases; 28 patients), tuberculosis (30% of cases; 15 patients), and pneumocystis pneumonia (10% of cases; 5 patients). Moreover, pulmonary tuberculosis and *Pneumocystis jirovecii* were more often detected in patients with CD4 + T-lymphocyte counts of <200 /mcl(41.6% and 12.5%, respectively)than in patients with CD4 + T-lymphocyte counts of >200 /mcl (19.2% and 7.7%, respectively). In addition, non-Hodgkin's lymphoma with metastasis to the lungs and pulmonary aspergillosis were diagnosed in patients with severe immunodeficiency.

Conclusions: The progression of HIVinfection is associated with an increased frequency of tuberculosis and rare opportunistic diseases in the spectrum of lung lesions.

References:

1. Kolosov V.P. Community-acquired pneumonia (clinical course, prognosis outcomes). - Blagoveshchensk, 2012. - 124 p.
2. Hoffman K. Treatment of HIV / 2011 K. Hoffman, Rokshtro J.K. - M .: R. Valent, 2012. - 736 p

Chapter 22

PREVALENCE AND ORIGIN OF HIV-1 RESISTANCE IN PRIMORSKY KRAI, RUSSIA

V.S. Eliseeva, S.P. Kruglyak, L.F. Sklyar, A.V. Kalinin, T.A. Ginevskaya
Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: Vic-eliseeva@mail.ru, ms.eva2009@mail.ru

Variants of drug-resistant human immunodeficiency virus (HIV) have become increasingly widespread; genotyping of HIV isolate is an important method for identifying the mutations associated with drug resistance. This article addresses the prevalence of different HIV subtypes and circulatory recombinant forms and describes the molecular structure of drug-resistant HIV-1.

Key words: HIV, drug resistance, sequencing, subtype.

The prevalence of drug-resistant HIV strains, whichis associated with high replication rates of HIV and the high incidence of replication errors, is one of the reasons thatantivirus therapies are ineffective in some patients. Molecular genetic methods are therefore necessary to select therapies that are tailored to individual patients.

Research objective:To analyze the prevalence of mutations in drug-resistant protease genes and HIV-1 reverse transcriptase strains, and to examine the prevalence of HIV-1 subtypes.

Materials and methods:Genetic data were obtained by sequence analysis of HIV RNA in 61 patients. Mutation resistance was determined by virological and/or immunological response in patients.

Results:A survey of genetic variants of HIV-1 among HIV-infected patients living continuously in the territory of PrimorskyKrai revealed a prevalence ofHIV-1 subtype B of 49% (39 individuals), anda prevalence of subtypes A and C of 21% and 23%, respectively. In addition, we detected a low prevalence of circulating recombinant forms:1 occurrence each of CRF01_AE/A and B/a, and 2 occurrences of CRF02_AG.

Polyformmutations in proteasegenesand reverse transcriptase strains were present in all patients. The prevalence of mutations was: minor mutations in 20 (33%)patients, mutations of the protease inhibitor gene in 3 (5%) patients, mutations of the reverse protease inhibitor gene in 34 (56%) patients, and no mutations in primary or secondary resistance genes in 26 (42.6%) patients.

Conclusions:The dominant HIV subtype among the examined patients was subtype B, along with several circulating recombinant forms; these results confirm previously reported data. It is known that CRF01 occurs in Southeast Asia and is the prevailing form in Thailand. Recombinant gene formscould appear in PrimorskyKrai and nearby inland areas.Patients could have become infected with an active recombinant form or subsequently these forms could have arisen in the population. Subtype CRF02_AGis widespread in African countries, Kazakhstan, and in the territories of Russia–Altai and Novosibirsk.

The first mutations resistant to HIV protease inhibitor may have arisen in isolated instances, and may have been unrelated to the administration of drug therapies. Mutations conferringresistant to reverse transcriptase inhibitors occur in response to commonlyused therapies, such as highly active antiretroviral therapy (HAART); it is therefore necessary to conduct further research on the prevalence of HIV drug resistance to HAART.

References:

1. M.R. Bobkova. HIV drug resistance. - M.: Human, 2014. -288.
2. E.V. Kazennova, D.A. Neshumaev,V.Y. Laga,I.A. Lapovokand others. Molecular epidemiological characteristics of the HIV epidemic in the regions of Siberia and the Russian Far East. Collection of works of VIII All-Russian scientific-practical conference with international participation. Vol. 1 - 2014 - P.45-46.
3. Easterbrook P. J. et al. Impact of HIV-1 viral subtype on disease progression and response to antiretroviral therapy // J.Int. AIDS Soc. — 2010. — Vol.13. — Published online 2010 February 3. Doi : 10.1186/1758-2652-13-4.
4. Tebit D.M., Arts E.J. Tracking a century of global expansion and evolution of HIV to drive understanding and to combat disease // Lancet Infect. Dis. – 2011. – Vol.11. – P.45-56.

Chapter 23

MITOCHONDRIAL MEMBRANE POTENTIAL AS AN INDICATOR OF THE ECOLOGICAL PROPERTIES OF ATMOSPHERIC MICROPARTICLES

[1,2]Anna V. Nazarenko, [1]Tatyana I. Vitkina, [1]Elena V. Kondratyeva, [2]Kirill S. Golokhvast

[1]Far Eastern Federal University
8 Sukhanova St., Vladivostok, 690950, Russia
e-mail: annie.nazarenko@gmail.com, tel: +7(423)243-34-72
[2]Vladivostok Branch of the Far Eastern Center of Physiology and Pathology of Respiration - Institute of Medical Climatology and Rehabilitative Treatment
73g Russkaya St., Vladivostok, 690105, Russia
e-mail: tash30@mail.ru, tel: +7(423)278-82-01

Abstract. We examined the effects of atmospheric microparticles on the leukocyte mitochondrial membrane potential *in vitro* using peripheral blood samples from healthy volunteers and patients with asthma. We also determined the dose-dependent effects of atmospheric microparticles on the mitochondrial membrane potential.

Keywords: mitochondrial membrane potential, atmospheric microparticles

Atmospheric pollution is a key factor related to human disease. In particular, the morbidity of respiratory infections, chronic obstructive pulmonary disease, and lung cancer is associated with air pollution, particularly suspended microparticles [2]. Suspended microparticles, especially particles < 10 μm, have the worst medical effects of all atmospheric particles. The mechanisms underlying their effects on the living body differ substantially from those of larger particles [1].

The mitochondrial membrane potential (MMP) is a critical factor in correct mitochondrial function and cell longevity. The MMP can be used to assess the cell's energy state in studies examining the pathological effects of environmental factors [3, 4].

The aim of this investigation was to determine the effects of atmospheric suspensions collected in coal mining regions on leukocyte

mitochondrial activity *in vitro* using cells obtained from healthy volunteers and patients with asthma.

The experiment was performed using venous blood samples from healthy volunteers and patients with asthma in remission. The MMP was determined in unexposed leukocytes and in leukocytes exposed to 10 or 100 mg/mL of native atmospheric suspension particles. The MMP was analyzed using a BD FACSC anto II flow cytometer with MitoProbe JC-1 stain.

Using unexposed leukocytes, the proportion of leukocytes with a low MMP, relative to the total number of leukocytes, was 1.2% in healthy volunteers versus 4.1% in patients with asthma. After exposing leukocytes to 10 ng/mL of native atmospheric suspension particles, the percentage of leukocytes with a low MMP was 1.8% in healthy volunteers versus 7.1% in patients with asthma. A larger change was observed when the leukocytes were exposed to 100 mg/mL of native atmospheric suspension particles, because the percentage of leukocytes with a low MMP was 72% in healthy volunteers and 60.9% in patients with asthma. These results indicate that at a dose of 10 mg/mL, the atmospheric suspensions had weaker effects on the MMP in healthy people than in patients with asthma. However, at a dose of 100 mg/mL, the atmospheric suspensions increased the proportion of cells with a low MMP by more than 60% in both groups, which indicates that these suspensions caused significant cellular dysfunction.

The results demonstrate a dose-dependent effect of atmospheric suspensions on MMP. The decrease in MMP was greatest in patients with asthma, perhaps because the compensatory processes were less effective in these patients. Therefore, pathologic disorders are likely to be exacerbated when patients with respiratory diseases (e.g., asthma) are exposed to deleterious environmental factors.

This work was supported by the Scientific Fund of the Far Eastern Federal University and a Russian Federation Presidential Grant for Young Scientists (MK-1547.2013.5).

References:

1. Brook R.D., Rajagopalan S., Pope C.A. et al. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation. 2010. 121(21): 2331–2378. doi: 10.1161/CIR.0b013e3181dbece1.

2. Lim S.S., Vos T., Flaxman A.D. et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet. 2012. 380(9859): 2224–2260. doi: 10.1016/S0140-6736(12)61766-8.
3. Lobanova E.G., Kondrat'eva E.V. Measurement of mitochondrial membrane potential in leukocyte suspension by fluorescent spectroscopy. Bull Exp Biol Med. 2014.157(2):288-290. doi: 10.1007/s10517-014-2547-4.
4. Matteucci E., Ghimenti M., Consani C. et al. Exploring leukocyte mitochondrial membrane potential in type 1 diabetes families. Cell Biochem Biophys. 2011. 59(2):121-126. doi: 10.1007/s12013-010-9124-x.

Chapter 24

INFLUENCE OF ANTIHISTAMINES ON PHAGOCYTIC CELLS IN PATIENTS WITH ALLERGIC DERMATITIS: INTERNAL PATHOLOGY AND REHABILITATION METHODS

[1]Igor N. Dubnyak, [1]Ekaterina V. Eliseeva, [1]Natalia S. Dubnyak, [2]Yana V. Dubnyak, [1]Konstantin N. Kirichek

[1] Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia; tel: +7(423)245-08-65
[2]Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: yana.prym@mail.ru, tel: +7(423)245-76-87

Abstract. Numerous studies have examined the internal pathology of patients with chronic skin diseases, including the responses of phagocytic cells to antihistamines. Several methods of rehabilitating patients, including diet therapy and massage, have been reported.

Key words: somatic organs, skin diseases, membranes, diet, massage.

Several theories have been reported for the pathogenesis of chronic skin diseases such as urticaria, eczema, psoriasis, lichen planus, and atopic dermatitis. In particular, the theory that describes the importance of internal physiological dysfunction in the development, persistence, and severe clinical course of these diseases is widely acknowledged [2, 3, 4]. Skin is a reactive surface covering of general environment. Any damage to the internal organs is instantly projected onto the skin, and irritation to the skin is transferred to the appropriate internal organ. Some researchers have proposed that changes in internal organs occur in some skin diseases, but others consider that skin diseases are the signs of lesions in a primary organ, altered metabolism, or changes in the immune system or the central nervous system [2, 3]. Considering this background, chronic dermatoses has been considerable researched because of its concurrence of disorders of organs and systems in order to identify possible treatments of these diseases, as well as methods for rehabilitating patients. The number of cases of chronic, unremarkable dermatosis has decreased in recent years. It is not uncommon that the internal pathologic disorder

becomes the dominant pathogenetic process that dictates the patient's clinical state, when there is an underlying background of skin disease. The main objective of this work was to determine the underlying systemic and organ pathologies in patients with chronic allergic dermatitis (urticaria, eczema, and atopic dermatitis) in patients treated at the dermatovenerologic dispensary of the Primorye Territory Hospital #2 and in ambulant patients. Our objective was to determine possible ways of treating and rehabilitating patients with these skin disorders.

Therefore, we performed a survey and clinical examination of patients, and analyzed the outcomes by reviewing the patients' medical histories and outpatient cards. Ultrasound and blood tests were performed to assess the functionality of the hepatobiliary system, pancreas, and kidneys. In total, 128 permanent residents of Primorye Territory (48% women and 52% men, mean age 38.6 ± 2.5 years) were analyzed in this study.

Table 1 – Distribution of patients according to their diagnosis

#	Diagnosis	Quantity	%
1.	Recurrent urticaria	65	50.8
2.	Atopic dermatitis	28	21.9
3.	Chronic eczema	35	27.3
4.	Total	128	100.0

According to the patients' medical histories and outpatient cards, dermatitis occurred in the majority (90.3%) of patients with pathological changes in the echo structure of the gallbladder, liver, pancreas, or kidney. Previous craniocerebral trauma was found in one-third of the patients. Dermatitis had a long disease course with frequent prolonged exacerbations in all of the patients who had combined pathologic disorders of the digestive system and kidneys. Therefore, a complex treatment regimen was administered to these patients [1, 2, 4]. In addition to the basic examinations, blood tests were performed in patients with chronic urticaria to determine the phagocytic activity of the immune system, as well as the effects of antihistamines on phagocytic cells by measuring the lysosomal membrane stability index (LMSI) of neutrophils and monocytes [5]. The dose of antihistamines was calculated according to the pharmaceutical dose of one tablet of the studied drugs.

Table 2 – Effects of antihistamines on the lysosomal membrane stability of neutrophils and monocytes in patients with skin allergies

LMSI of phagocy-tizing cells, in %	Studied drugs in μg /ml.								
	Chloropy-raminum 250 μg /ml	Error	Chifena-dinum 250 μg /ml	Error	Lorata-dinum 100 μg /ml	Error	Fexofena-dinum 1800 μg /ml	Error	With-out drugs
LMSI of neutrophils	82.6 ± 1.4	p<0.05	81.5 ±1.2	p<0,05	82.2 ±1.6	p< 0.05	78.3 ±1.2	p<0.05	79.3 ±1.2
LMSI of monocytes	71.2 ± 1.6	p<0.05	72.8 ± 1.9	p<0,05	73.6 ± 1.8	p< 0.05	64.9 ±1.2	p<0.05	66.0 ±1.0

LMSI: lysosomal membrane stability index.

The results showed that the antihistamines chloropyramine, quifenadine, and loratadine increased the LMSI of neutrophils and monocytes, and partly maintained the inflammatory process in patients using H1 receptor blockers, and supports the need for prescribing additional drugs to stabilize lysosomal membranes in patients with severe disease. Fexofenadinum stabilized the lysosomal membranes of phagocytic cells, and appeared to be the most favorable drug in allergic inflammation. The comorbidities were treated as appropriate and a hypoallergenic diet was initiated before starting rehabilitation. A chemically sparing, physiologically complete diet with appropriate amounts of protein, fat, and carbohydrates was developed. A light diet containing low levels of specific nutrients was only recommended if there were pathological changes in the digestive system (e.g. exacerbation of peptic ulcers, chronic enteritis, or pancreatitis). The diet comprised six meals per day in small portions and a hyposodium diet with salt restriction (not more than 4–6 g of salt per day). Simple carbohydrates were limited to 20–30 g per day. The patients were recommended to drink 1.2 l of water per day. In the remission period during ongoing diet therapy, the patients received massage therapy considering the fact that certain skin areas correspond to a specific organ. The rehabilitation program increased remission time, improved the quality of life, and was associated with full recovery in about 50% of patients with chronic recurrent urticaria, atopic dermatitis, or microbial eczema.

In conclusion, the present results suggest that the development and treatment of chronic dermatosis should be considered together with disorders in internal organs or the nervous system conditions. It is also important to consider the effects of antihistamines on the stability of the lysosomal membrane of phagocytic cells. The treatment and rehabilitation of patients with chronic allergic dermatosis should include combined diet and massage therapies.

References:

1. Gistamin and antihistamines / N.S. Khilchenko, E.V. Eliseeva, N.V. Plaksen, R.K. Goncharova. - Vladivostok: Far East Medicine, 2009. – p.58.
2. L.A. Goryachkina, Role of Helicobacter infection in chronic urticarial pathogenesis / L.A. Goryachkina, E.Yu. Borzova // Allergology. - 2004. - # 1. - p.p. 31-39.
3. N.S., Dubnyak, I.N.Dubnyak, E.A. Sharonova. Skin symptoms of internal diseases.- Vladivostok.- FSUE "TINRO center", 2005.- p.50.
4. O.L. Ivanov. Skin and venereal diseases.-M.-2013.- p.251.
5. A.S. Sharonov. Phagocytes, lysosomes, membranes / A.S. Sharonov, Yu.I. Shilov. - Vladivostok. -Dalnauka, 2007. – p.128.

Chapter 25

INFLUENZA IN HIGH-RISK PREGNANT WOMEN

I.V. Zenin, A.F. Popov
Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: geltok.127@mail.ru, tel.: +7(423)242-97-78

In this study, we examined the characteristics of influenza in pregnant women. We analyzed the medical records of 239 pregnant women who were diagnosed with influenza between 2009 and2014. Influenza A (H1N1) pdm09 was detected in 75 women while 164 women were diagnosed with seasonal types, including influenza A (H1N1), influenza A (H3N2), and influenza B. Pandemic strains of influenza were more severe than seasonal strains.

Background: It is important to determine the incidence and severity of influenza in high-risk groups, particularly pregnant women.

Purpose: To determine the incidence, virus serotype, and outcomes of causal treatment of influenza in pregnant women.

Materials and methods: We performed a retrospective review of the medical records of 239 pregnant women who were diagnosed with influenza and treated at Regional Hospital No. 2 between 2009 and 2014. The patients were divided into two groups according to the type of influenza. Overall, 75 patients were diagnosed with influenza A (H1N1) pdm09 (group 1) and 164 were diagnosed with seasonal types, including influenza A (H1N1), influenza A (H3N2), or influenza B (group 2). The diagnosis was confirmed by polymerase chain reaction in 69.5%.

Results: The mean age of patients in groups 1 and 2 was 22.4 and 23.9 years, respectively. Acute onset of the disease, the presence of intoxication and catarrhal syndromes were recorded for all patients. The severity of fever was similar in groups 1 and 2 (38.7 ± 0.5 °C vs. 38.4 ± 0.4°C, $P > 0.05$). The duration of fever was also similar in groups 1 and 2(4.5 ± 0.5 days vs. 4.1 ± 0.6 days, $P > 0.05$). Catarrhal syndrome was detected on the first day of illness in 80.2% of patients in group 1 and in

74% of patients in group 2. Pneumonia was a frequent complication of influenza and occurred in 24.5% of patients in group 1 compared with 8.7% of patients in group 2. Severe forms of influenza, including highly pathogenic avian influenza, were detected in seven times more patients in group 1 than in group 2. One patient with influenza A (H1N1) pdm09 died on day 6 of her illness at the age of 39 years in week 33–34 of gestation. The most common drugs prescribed to the pregnant women included umifenovir, oseltamivir, and interferon α2b. The disease resolved in nearly all of the patients.

Conclusion: Highly pathogenic avian influenza in pregnant women was characterized by more severe clinical conditions than seasonal influenza subtypes.

SECTION 4

Functional Foods

Chapter 26

EFFECTS OF SELENIUM-ENRICHED *LAMINARIA JAPONICA* ON EXPERIMENTAL HEPATITIS IN RATS

Nadezhda E. Struppul
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: struppul@mail.ru

Abstract. A powdered sample of the brown alga *Laminaria japonica*, with a selenium content meeting the recommended daily dose for human, was prepared. The positive effects of selenium-enriched laminaria on the liver and serum biochemical parameters of laboratory rats with experimentally induced toxic hepatitis were investigated.

Keywords: selenium, selenium-enriched *Laminaria japonica*, experimental toxic hepatitis.

Much attention has been paidto theinfluence of selenium on humanin recent decades. Selenium is a micronutrient and its deficiency in the human body causes reproductive dysfunction and damages the heart muscle, bone, and cartilaginous tissues. Selenium plays an essential role in the protection of cells from oxidants and in the maintenance of cellular immunity, and it is necessary for the normal function of the thyroid and prostate glands and the normal course of spermatogenesis [3, 6, 12, 15, 18, 19]. Selenium deficiency aggravates the diseases of the respiratory organs [5] and is found in patients with malignant diseases of the blood [2]. Experimental selenium deficiency is also reported to cause intestinal cancer in rats [9] and skin cancer in mice [14]. Positive correlations between blood selenium levels and the frequencies of some types of oncological diseases in humans have been reported. Seaweeds and their processed products are a potential source of organic selenium. We examined the capacity of a commercial species of macroseaweed to accumulate selenium, and the possibility of extracting this selenium-enriched biomass.

The samples of two-year old *Laminaria japonica* used in the experiments were collected in the Vostok Bay of the Japan/East Sea,

Primorye Territory, Russia. The dynamics of selenium accumulation by the *L. japonica* thallomes, maintained in water with a high concentration of selenium,were investigated under conditions corresponding to the optimum natural conditions for the seaweed's growth. The seaweed thallomeswere dried at 40 °C until they reached a constant weight and were then crushed to powder in a laboratory homogenizer.

Experimental hepatitis was induced in white rats by the daily oral administration of 50% tetrachloromethane (CCl_4) oil solution at a dose of 0.4 ml/100 g of bodyweight for 14 days. After treatment with the toxin for 14 days, the rats' food was supplemented for 21 days with crushed *Laminaria* enriched with selenium.

Two groups of experimental animals were used to assess the pharmacotherapeutic efficacy of the *Laminaria* powder. The rats' diet was supplemented with laminaria powder equivalent to a selenium dose of 10 μg/100 g of bodyweight (group I) or 0.4 μg/100 g of bodyweight (group II). The condition of the animals was evaluated on days 14 and 36 of the experiment by comparing their biochemical parameters with those of animals not treated with CCl_4 (intact group) and those of sensitized (CCL_4-treated) rats that were not treated with the laminaria preparation (control group).

The selenium concentration in the alga increased in proportion to its concentration in the environment (Table 1).

Table 1 – Selenium concentration in *L. japonica*thallomes in seawater with different selenium contents, μg/gd.w. (mean ± SD, N = 6)

Experimental days	0.01 mg/L	0.10 mg/L	0.50 mg/L	0.50 mg/L/day
0	1.34 ± 0.32	1.34 ± 0.32	1.34 ± 0.32	1.34 ± 0.32
3	1.47 ± 0.53	1.95 ± 0.47	3.64 ± 0.22	10.64 ± 1.8
6	1.59 ± 0.30	2.47 ± 0.26	5.18 ± 0.58	41,92 ± 7.1
10	2.35 ± 0.46	4.19 ± 0.36	9.83 ± 0.40	54.50 ± 9.3

The maximum selenium content in the *L. japonica* thallomeswas achieved on day 10 of the experiment, when it was 54.5 μg/g. This concentration was about 40 times greater than that in the control samples, and 1 g of this algal biomass had a selenium content equivalent to the recommended daily allowance for human consumption.

The protective properties of selenium against the actions of various toxicants depend upon the preparation in which it is administered. The effects of the dry selenium-enriched *L. japonica* powder on the pro- and

antioxidant systems of laboratory animals with experimental toxic hepatitis were investigated.

The selenium concentrations in the livers and sera of the control group rats tended to be lower than those in the intact groupon day 14 of the experiment (Table 2). This might be attributable to the activities of the selenium-containing compounds during the progression of the CCl_4-induced pathology. The selenium concentration in the blood is an objective measureof the body's selenium status, and reflects the total content of active selenium-containing enzymes, selenium-transporting proteins, and depositing selenium [1]. The localization of the excess selenium in animal tissues is unclear, but the accumulated selenium is thought to be associated with glycoprotein SelP, a basic selenium-containing protein in the mammalian plasma [17]. This protein transports intracellular selenium, is rapidly regenerated, and contains 9–12 selenocysteine residues, depending on the body type. SelP synthesis also increases with the administration of selenium-containing supplements to the diets of selenium-deficient animals [4].

Table 2 – Selenium concentrations in the livers (μg/g) and sera (μg/L) of rats administered selenium-enriched *L. japonica* powder to treat experimental toxic (CCl_4) hepatitis (mean±SD, N=5)

Experimental day	Intact rats	Rats with experimental toxic hepatitis		
		control	group I	group II
liver homogenates				
14	0.29 ± 0.07	0.20 ± 0.05	-	-
36	0.22 ± 0.06	0.12 ± 0.04	0.40 ± 0.09	0.84 ± 0.16
blood serum				
14	75 ± 9	86 ± 11	-	-
36	68 ± 10	74 ± 8	92 ± 10	274 ± 24

The consumption of selenium-enriched *L. japonica* in the daily food ration resulted in the dose-dependent accumulation of selenium in the livers and sera of the rats. On day 36 of the experiment, the selenium concentrations in the livers of the group I animals had increased up to three-fold relative to the levels in the control group animals. The selenium levels in the sera and livers of the group II rats had increased up to seven-fold and 3.7-fold, respectively.

Specific indicators of lipid peroxidation (LPO) include the concentration of diene conjugates of unsaturated polyunsaturated fatty acids(DK), which are products of the first stage of the oxidation process,

and the concentration of malondialdehyde (MDA), the final product of biomembrane oxidation. The dynamics of DK and MDA changed in the experimental rats treated with laminaria, as shown in Table 3.

Our results show that the selenium-enriched laminaria caused significant changes in the generation of DK and MDA. Strong liver damage was detected in the control group rats. The higher selenium dose in the diet of group II normalized the animals' selenium status.

MDA levels are not always an adequate measure of lipid peroxidation because the reaction is insufficiently specific [13]. However, even when the peroxidation products are not recorded, changes occur in other components of the antioxidant system, particularly reduced glutathione. When reduced glutathione increases, it indicates that free-radical oxidation processes are activated [1]. Therefore, we determined the reduced glutathione concentrations in the rat liver homogenates to establish the levels of free-radical oxidation (Table 3).

A two-fold increase in reduced glutathione in the liver of the rats fed selenium-enriched *L. japonica* indicated that the algal powder has antioxidant properties.

Table 3 – Biochemical parameters of the livers and sera of rats with experimental toxic (CCl_4) hepatitis treated with selenium-enriched *L. japonica* powder, on day 36 of the experiment (mean±SD, N=5)

Parameter	Intact rats	Rats with experimental toxic hepatitis		
		control	group I	group II
Diene conjugate concentration, *μmol/mg of protein*	liver homogenate			
	2.86 ± 0.56	3.81* ± 0.28	3.78 ± 0.28	2.91* ± 0.27
Malondialdehyde concentration, *μmol/mg of protein*	liver homogenate			
	0.27 ± 0.03	0.48* ± 0.02	0.40 ± 0.04	0.30* ± 0.02
Reduced glutathione concentration, *μmol/mg of protein*	liver homogenate			
	4.58 ± 0.33	3.25* ± 0.23	5.13 ± 0.35	6.26* ± 0.42
Glutathione peroxidase activity *μmol GSH/mg protein/min*	liver homogenate			
	4.78 ± 0.07	3.15* ± 0.03	5.13 ± 0.06	6.26* ± 0.03
	serum			
	1.39 ± 0.04	1.22* ± 0.05	1.53 ± 0.04	1.46* ± 0.05
Cholesterol concentration, *μmol/mL*	serum			
	3.00 ± 0.18	3.88* ± 0.13	2.93 ± 0.37	2.75* ± 0.33
α-Tocopherol concentration, *μg/g*	liver homogenate			
	18.3 ± 3.7	24.5* ± 4.9	5.7* ± 1.1	196.1* ± 19.2

**Variations are statistically significant at $p < 0.05$*

Glutathione peroxidase (GPX) activity reflects the level of selenocysteine accumulation and its integration into molecular structures, so it is an indicator of the body's selenium status, like the serum selenium content [11]. After 0.4 μg of selenium per 100 g of rat bodyweight was added to the daily diets of the sensitized animals, the GPX activity in their liver homogenates increased approximately 1.6-fold, and when the selenium dose was increased to 10 μg/100 g of rat bodyweight, the GPX activity in the liver homogenates increased approximately two-fold. An analysis of the enzyme activities in the sera of both animal groups showed that this indicator increased approximately 1.3-fold in both groups (Table 3). These results confirm the antioxidative effects of selenium-enriched laminaria.

An important syndrome of the damaged hepatobiliary system is cholestasis, caused by the abnormal production of bile and its abnormal outflow. The basis of its development process are inhibiting the activity of enzyme systems, or the dysfunction of bile acids and cholesterol metabolism [12]. Our experiment showed that the cholesterol concentration was up to 30% higher in the sera of the control group rats than in the sera of the intact rats (Table 3), which also confirms the toxic liver damage in the control rats. The introduction of selenium-enriched *L. japonica* into the animals' diet reduced their cholesterol levels to their initial concentrations.

Vitamin E (α-tocopherol) is considered to be the main regulator of LPO. Therefore, the concentrations of α-tocopherol were also determined in the liver homogenates and sera of the rats in this study (Table 3). The α-tocopherol levels decreased approximately four-fold in the livers of rats receiving small doses of the selenium preparation. When the selenium dose was increased five-fold in the diet, the vitamin E concentrations in the animals' livers increased approximately eight-fold. This dramatic increase in the α-tocopherol concentrations in the livers of the group II rats is consistent with the concept of a synergistic effect between selenium and vitamin E [7, 10, 8].

The results of this experiment demonstrate the positive effects of selenium-enriched *L. japonica* powder as a therapeutic treatment for rats with experimental toxic hepatitis. The increased serum selenium concentrations and GPX activities in the experimented animals demonstrate the good fixation of selenium in this product. Therefore, this kind of alga can be used to produce a selenium-enriched biomass, for the production of bioactive additives and functional foods.

References:

1. Tutelyan V.A., Knyazhev V.A., Khotimchenko S.A., Golubkina N.A., Kushlinskiy N.E., SokolovYa.A. Selenium in a human body: metabolism, antioxidant properties, role in cancerogenesis. M.: RAMS Press. – 2002. – 224 p.
2. Avanzini P., Vinceti M., Ilariucci F., Masini L., D'Incà M., Vivoli G. Serum selenium concentrations in patients with newly diagnosed lymphoid malignancies // Haematologica. 1995. Vol. 80, N. 6. - P. 505-511.
3. Badmaev V, Majeed M, Passwater R.A. Selenium: a quest for better understanding. Altern // Ther. Health.Med. 1996. Vol. 2, N. 5. - P. 101.
4. Calvin H.J., Cooper G.W., Wallace E. Evidence that selenium in rat sperm is associated with a cystein-rich structural protein of the mitochondrial capsules // Gamete Res. 1981. Vol. 4. - P. 139-149.
5. Coursin D.B., Cihla H.P. Pulmonary effects of short term selenium deficiency // Thorax. 1996. Vol. 79, Iss. 3. - P. 479-483.
6. Francescato H.D., Costa R.S., Mafalda S., Camargo R., Zanetti M.A., Lavrador M.A., Branci M.D.P. Effect of oral selenium administration on cisplatin-induced nephrotoxicity in rats // Pharmacol res. 2001. Vol. 43, N 1. - P. 77-82
7. Hoekstra W.G. Biochemical function of selenium and its relation to vitamin E // Fed. Proc. 1975. Vol. 34. - P. 2083-2089.
8. Ip C. Attenuation of the anticarcinogenic action of selenium by vitamin E deficiency // Cancer Lett. 1985. Vol. 25. - P. 325-331.
9. Jao S.W., Shen K.L., Lee W., Ho Y.S. Effect of selenium on 1,2-dimethylhydrazine-induced intestinal cancer in rats // Dis Colon Rectum. 1996. Vol. 39, N. 6. P. 628-631.
10. King M.M., McCay P.B. Anticancerogene effect of selenium and vitamin E in rats // Cancer Res. 1983. Vol. 43, Suppl. - P. 2485a.
11. Levander O., Burk R.F. Selenium // Present knowledge in nutrition / Eds. E.E. Ziegler, L.J. Filer. 7th ed. N.Y.: Acad. Press.1998. - P. 320-328.

12. Moak M.A., Christensen M.J. Promotion of lipid oxidation by selenate and selenite and indicators of lipid-peroxidation in the rat // Biol. tr. Elem. Res. 2001. Vol. 79. Iss. 3. - P. 257-269.
13. NikolayevS.M.Herbal medicines in case of damage of the hepatobiliary system. – Novosibirsk: Nauka. – 1992. – 152 p.
14. Oh S.H., Park K.K., Kim S.Y., Lee K.J., Lee Y.H. Evaluation of chemopreventive effect of dietary selenium-rich egg on mouse skin tumor induced by 2'-(4-nitrophenoxy)oxiraneand 12-O-tetradecanoylphorbol-13-acetate// Carcinogenesis. 1995. Vol. 16, N. 12. - P. 2995-2998.
15. Stone J., Hinks L.J., Beasley R., Holgate S.T., Clayton B.A. Reduced selenium status of patients with asthma // Clin. Sci. 1989.Vol. 77. Iss. 5. - P. 495-500.
16. Tutelyan V.A., Knyazhev V.A., Khotimchenko S.A., Golubkina N.A., Kushlinskii N.E., Sokolov Ya.A. Selenium in humans: metabolism, antioxidant properties, role in carcinogenesis. – Moscow: Publishing RAMS. – 2002. – 224 p.
17. Vendeland S.C., Beilstein M.A., Chen C.L. Purification and properties of selenoprotein W from rat muscle // J. Biol. Chem. 1993. Vol. 268. - P. 103-107.
18. Vitoux D., Chappuis P, Arnaud J, Bost M, Accominotti M, Roussel AM. Selenium, glutathione peroxidase, peroxides and platelet functions // Ann. Biol. Clin. (Paris). 1996. Vol. 54. Iss.5. - P. 181-187.
19. Zust J. Hrovatin B, Simundić B. Assessment of selenium and vitamin E eficiencies in dairy herds and clinical disease in calves // Vet Rec. 1996. Vol. 139. Iss.16. - P. 391-394.

Chapter 27

DEVELOPMENT OF FUNCTIONAL BURDOCK-ROOT-BASED BEVERAGES

Natalia Yu. Chesnokova, Alla A. Kuznetsova, Lyudmila V. Liovochkina, Tamara V. Levchuk
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: nchesnocova@pochta.com, kuznetsova.dvfu@mail.ru, tomarisi@rambler.ru

Abstract. Formulations for functional burdock-root-based beverages were developed. Milled burdock root was hydrolyzed with citric acid, acetic acid or ascorbic acid to split its constituent inulin to form glucose, to reduce the amount of sugar in the beverages. The hydrolyzed-burdock-root-based beverages developed had an original taste and smell, and had few calories.

Keywords: functional drinks, burdock, burdock root, inulin, fructose, ginger juice, chicory, diabetes.

Proper nutrition is an important factor in human health. An unbalanced diet results in metabolic disorders, diseases of the gastrointestinal tract, and disorders of the endocrine system. Poor nutrition can also accelerate the development of various pathological processes and cause their progression in the body.

As reported by Russian and foreign scientists, the pathologies and diseases of civilized countries are caused by the inadequate consumption by the population of vitamins, macro- and microelements, polyunsaturated fatty acids, dietary fiber, and essential amino acids rather than by the excessive consumption of animal fats.

Based on the scientific theory of balanced and adequate nutrition, different kinds of food can be considered dietetic, prophylactic, medical and prophylactic, therapeutic, healthy or optimal, or functional.

The concept of "functional" foods was first formulated in Japan in the early 1980s. "Functional" foods are products that contain natural and organic substances enriched with vitamins or microelements, which have certain useful properties (energetic, probiotic, etc.) [2]. Proper

nutrition that is adequate and safe is one of the key elements of a healthy lifestyle. Beverages are a large part of the food that people consume on a daily basis.

Beverages that can be assigned to the group of "healthy" drinks are considered in this paper. Healthy drinks are intended for mass consumption, and therefore they are the most popular functional beverages. They must be enriched with vitamins, minerals, unsaturated fatty acids, and dietary fiber, which contribute to the prevention of diseases of the cardiovascular system and gastrointestinal tract, including cancer.

Wild plants are known to be sources of functional ingredients, including dietary fiber, biologically active compounds, vitamins, and minerals. The natural habitats of these plants allow them to accumulate the highest levels of useful components. Burdock (genus *Arctium*) is one of these wild plants.

Eight species of burdock grow in Russia, and three types of them grow in the Primorye Territory: great burdock (*A. lappa*), smaller burdock (*A. minus*), and woolly burdock (*A. tomentosum*). The chemical composition of burdock is well studied. The plant roots contain 15.4% protein, 1.5% fat, 22.3% fiber, essential oils, and palmic and stearic acids. The roots of the plant also contain 45% inulin polysaccharide, which restores the function of the human digestive system. Inulin, when subjected to acid hydrolysis, is a source of fructose, which is extremely important in the diet of people with diabetes mellitus.

Great burdock (*A. lappa*) root grown in the Primorye Territory, collected in July–August when it is most succulent, was used for the experiments. To prepare the beverages, dried and roasted burdock root was ground to a fine homogeneous powder. To prepare the beverage, 8 g of burdock root powder was boiled in 200 ml of water.

Because the burdock root is rich in inulin polysaccharide, which forms fructose when split, it can be used to replace (wholly or partially) the sugar usually added to beverages. The inulin in the burdock root was acid hydrolyzed for this purpose. The dried roots were shredded before hydrolysis. The amount of inulin in the burdock root infusion was determined with a previously reported method [3]. The inulin was hydrolyzed with 6% citric acid, acetic acid or ascorbic acid at a temperature of 75 °C for 60 min. To qualitatively assess the hydrolysis of inulin, we used the naphthorezorcin Tollens' test, which characterized the presence of the fructose. The fructose content was determined as the

intensity of the solution color on a spectrophotometer (UNICO-1201) at a wavelength of 800 nm. The results are shown in Figure 1.

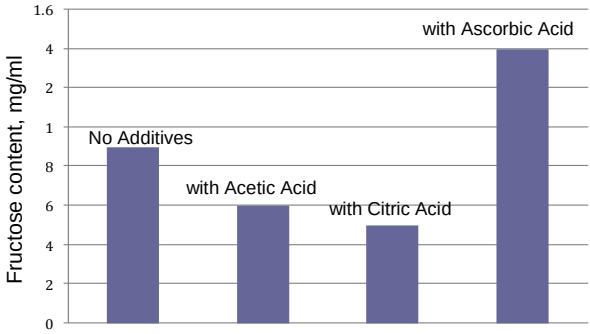


Figure 1 – Fructose content in the burdock-root-based infusions

The greatest amount of fructose (1.4 mg/ml) was present in the sample treated with ascorbic acid, which was considerably higher than that in the samples treated with acetic or citric acid. The inulin contents in these samples were 0.6 and 0.5 mg/ml, respectively. The acid strength clearly influenced the degree of inulin hydrolysis. The ascorbic acid has the greatest restoring properties of this series of acids, resulting in more complete inulin hydrolysis.

To increase the degree of inulin hydrolysis and the fructose content, the beverage was supplemented with ginger root, which contains up to 12 mg/100 g ascorbic acid. Ginger root also contains many valuable compounds, particularly asparagine, choline, linoleic, oleic, and caprylic acids, essential oils, vitamins B1, B2, and B3, and a saturated mineral complex (silicon, aluminum, zinc, sodium, phosphorus, iron, manganese, potassium, magnesium, and others).

To prepare a burdock-root-based beverage, 10% (by product volume) ginger was added as a juice - the form that is best combined with the drink. A second drink, containing chicory root as well as ginger juice, was prepared to enrich the infusion with inulin and to add a racy coffee flavor. Chicory is a source of inulin, with an inulin content of 49%–60%. Based on organoleptic indicators, the burdock-root-based drink was supplemented with 10% (by product weight) shredded chicory root. The introduction of chicory root into the beverage increased its biological value and functional focus, because chicory root contains flavonoids,

catechol tannins, glycosides, carbohydrates, unsaturated sterols, coumarin, sesquiterpene lactones, and triterpenoids [1].

The fructose contents of the prepared beverages were determined with a previously described method, and the results are shown in Figure 2.

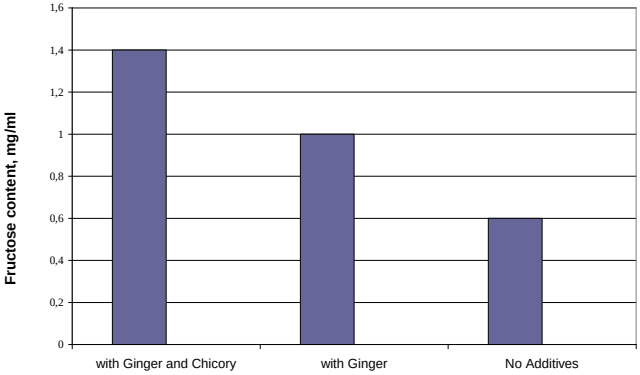


Figure 2 – Fructose contents of the burdock-root-based beverages.

The infusion supplemented with ginger juice and chicory root contained the largest amount of fructose (1.4 mg/ml). The infusion supplemented with ginger juice contained somewhat less fructose (1 mg/ml). The fructose content of the burdock-root-based beverage with no additives was 0.6 mg/ml, which was 2.5-fold less than that of the beverage containing ginger juice and chicory root and 1.5-fold less than that of the beverage containing ginger juice.

We deduced from these experiments that while preparing functional burdock-root-based beverages, it is necessary to supplement them with organic acids, such as ascorbic acid, because their contents of the acids and enzymes that catalyze hydrolysis are insufficient for the complete hydrolysis of inulin.

The burdock-root-based beverages prepared had high organoleptic properties. The optimal chemical composition was created in the beverages, giving them a wide range of flavors properties. The burdock-root-based beverage supplemented with ginger juice and chicory root was the most original according to its organoleptic indicators. The original taste and flavor of the drink were attributable to the successful combination of the grassy–nutty flavor of roasted burdock root, the pungent taste of ginger juice, and the coffee aroma and taste of chicory.

As this study shows, the addition of ginger juice to the drink formulation reduced its sugar content by as much as 5%, because it increased the degree of inulin hydrolysis.

The hydrolyzed burdock-root-based beverage developed here has few calories (51.3 kcal per 100 ml) and contains the inulin hydrolysis product, fructose. This beverage can be recommended for dietetic nutrition and for people suffering diabetes mellitus. This multicomponent burdock-root-based beverage, supplemented with ginger juice and chicory root, can be offered as an enriched functional beverage and a source of valuable biologically active substances and soluble dietary fiber.

References:

1. Useful wild plants of Russia/ Edited by A.L. Budantsev, E.E. Lesiovskaya. - St. Petersburg: SPHFA. 2001.
2. Doronin A.F. Functional foods. Introduction to the technology/ Edited by A.A. Kochetkova. - Moscow: DeLe print, 2009. – p. 288.
3. Chesnokova N.Y. Technology development for new hydrolyzed burdock root-based food products/ Chesnokova N.Yu., Liovochkina L.V., Masalova N.V. // International scientific and practical conference proceedings "Promising innovations in science, education, production and transport 2010", Engineering - Odessa. 2010. Vol. 5: P. 69-70.
4. Chesnokova N.Y., Liovochkina L.V., Masalova N.V. Investigations of the burdock root application in the food products production. Agricultural raw materials storage and processing. 2011. №1 – pp. 40-43.

Chapter 28

ANTIOXIDANT ACTIVITIES OF MANCHURIAN WALNUT-PERICARP-BASED EXTRACTS

Tamara V. Levchuk, Natalia Yu. Chesnokova, Alla A. Kuznetsova, Lyudmila V. Liovochkina
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: tomarisi@rambler.ru, nchesnocova@pochta.com, uznetsova.dvfu@mail.ru

Abstract. The feasibility of using Manchurian walnut pericarp extract in therapeutic and prophylactic products was investigated. The antioxidant activities of extracts were examined according to the maturity of the Manchurian walnut. The fresh Manchurian walnut pericarp has the highest antioxidant activity in the milk maturity stage.

Keywords**:** Manchurian walnut, Manchurian walnut pericarp, milk maturity stage, harvest maturity stage, antioxidant activity

The health status of the world population currently displays a negative trend. Both Russian and foreign scientists have attributed the pathologies and diseases of civilized countries to socioeconomic and environmental degradation and a decline in nutritional quality. The lack of nutrients in the diets of modern humans contributes to increases in diabetes mellitus, atherosclerosis, coronary heart disease, gastrointestinal tract diseases, and a variety of malignancies.

Disease prevention is the primary objective of current medicine. Healthy nutrition is important for disease prevention, and should include the complete complement of vitamins, micro- and macroelements, and substances that prevent or reduce the negative impact of radioactive elements and toxic compounds that enter the human body.

Wild plants are known sources of biologically active compounds, vitamins, and minerals. The natural habitats of these plants allow them to maximally accumulate useful constituents. One of these wild plants is the Manchurian walnut (*Juglans manshurica* Maxim), which grows in the far east of Russia, particularly in the Primorye Territory [2].

The chemical composition of the Manchurian walnut is well studied, and its pericarp is most biochemically valuable. It contains

quinones (juglone), 0.03% alkaloids, 12%–14% tannin and coloring agents, 2.6% dietary fiber, 18.4% pectin, up to 12% mineral substances, 0.8% vitamin C, and flavonoids (quercetin and isoquercitrin) [1]. The medicinal properties of the Manchurian walnut pericarp are attributed to its rich chemical composition, and its antioxidant, antibacterial, antiparasitic, and antitumor properties. Therefore, to study the antioxidant activity (AOA) of the Manchurian walnut pericarp according to its ripeness stage and storage conditions is of the utmost interest [3].

The Manchurian walnut pericarps in the milk maturity stage (harvested in June) and the harvest maturity stage (harvested in October) were examined in the study. Fruiting is seasonal in the Manchurian walnut, but the raw material for the extracts is required all year round, so we investigated its optimal mode of storage. Three ways to store Manchurian walnut pericarp have been suggested: drying at 23 °C for a month, drying at 105 °C for 6 h, and freezing at –18 °C. The extracts used to determine its AOA were prepared by extracting fresh Manchurian walnut pericarp or Manchurian walnut pericarp treated with water in a ratio of 1:5 at 60 °C for 30 min.

The AOA of the Manchurian walnut pericarp extracts was investigated by the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method.[4]. Eight samples of Manchurian walnut pericarp extract were examined according to the stage of fruit ripening and the storage conditions used; the results are shown in Table 1.

Table 1 – Antioxidant activities of Manchurian walnut-pericarp-based extracts

Maturity Stage	Storage Method	Ascorbic acid (AOA), mg/ml
Milk	Fresh	1251.67
	Dried at 23 °C	1141.18
	Dried at 105 °C	463.34
	Frozen at –18 °C	1102.97
Harvest	Fresh	543.54
	Dried at 23 °C	389.74
	Dried at 105 °C	149.36
	Frozen at –18 °C	286.52

Table 1 shows that the fresh Manchurian walnut pericarp in the milk maturity stage had the highest AOA (1251.67 mg/ml of ascorbic acid). Minor losses of AOA occurred during the process of drying at 23 °C and during freezing at –18 °C. The AOA values were 1141.18 and 1102.97 mg/ml of ascorbic acid, respectively. Significantly lower AOA values were observed during product drying at 105 °C, equivalent to

463.34 mg/ml of ascorbic acid. AOA is probably lost from the raw material with the degradation of biologically active compounds at high processing temperatures.

The AOA of the Manchurian walnut pericarp was considerably lower in the harvest maturity stage than in the milk maturity stage. Analysis of the data showed that the Manchurian walnut pericarp extracts had quite high AOA. The Manchurian walnut-pericarp-based extracts can be used in the food industry to develop a wide range of product formulations for therapeutic and prophylactic purposes.

References:

1. Berlova N.V. Manchurian walnut: characteristics and application perspectives: monograph / N.V. Berlova, S.N. Lyapustin, S.N. Avelicheva; T.K. Kalenik- Editor-in-chief; Russian Customs Academy, Vladivostok branch. - Vladivostok: WF PTA, 2008. – p.92.
2. Zemlyak K.G. Manchurian walnut as a promising raw material for food of balanced composition / G.K., A.I . Okara, T.K. Kalenik // Oils and Fats Industry. - 2009.#№5. - S.pp.34-36.
3. Yashin Ya.I., Ryzhnev V.Yu., Yashin A.Ya., Chernousova N.I. Natural antioxidants. Their content in foods and their effect on human health and aging: M - 2009. - S. pp.52-53.
4. Martysiak-Żurowska D., Wenta W., 2012. A comparison of ABTS and DPPH methods for assessing the total antioxidant capacity of human milk. Acta Sci. Pol., Technol. Aliment. 1 (11), pp.83-89.

Chapter 29

PROMISING DIETARY FOODS FROM BUCKWHEAT HUSKS

Sergey G. Yazev
Far Eastern Federal University, School of Biomedicine,
10 Ajax, Russian Island, Vladivostok, 690922, Russia;
e-mail: yazev_91sg@mail.ru, tel.:+7(908)969-90-05

Abstract. Hydrolyzed buckwheat husks have many properties that contribute to improved human health and are thus used in the food industry [1]. The replacement of potato starch with hydrolyzed buckwheat husk flour produces a low-calorie functional food useful in the nutritional therapy of patients with diabetes mellitus. Such foods are vital for the prevention of, and rehabilitation from, a number of other endocrine disorders, as well as cardiovascular and gastrointestinal diseases.

Key words: low-calorie baked foods, buckwheat husks, chemical composition of buckwheat husks, prevention of diabetes mellitus, rehabilitation of patients with diabetes mellitus.

There are significant ongoing studies to identify plant products, and byproducts of food plant processing, which may be useful in preventing disease or aiding recovery from disease. Of particular interest are foods or food byproducts effective against socially significant diseases such as cardiovascular disease, endocrine pathology such as diabetes, and gastrointestinal disease.

In addition, there is increasing interest in waste-free food processing, based on the principle of using both raw materials and waste products to the fullest extent possible.

One promising example is the use of buckwheat husks. We have studied five buck wheat cultivars: Pri 16, Pri 7, Pri 7 (Dalnerechensk), Izumrud and Pri 10.

Buckwheathusksaccountfor16%–22% of the kernel weight, are dark brown in color, and comprise rough, thick-walled cells partly filled with fagopyrin, a water-soluble brown pigment [1].

Buckwheat husks are elastic, hydrophobic, and show minimal swelling in water; consequently, they are rarely used in the food industry. When used as an ingredient in baked goods, coarsely cut buckwheat husks cannot be masticated and thus worsen the organoleptic characteristics of the baked product.

The solid content of buckwheat husks is not increased by alkaline hydrolysis, probably because the minerals cementing the microfibrils, comprising cellulose, hemicellulose, and low-molecular-weight polymeric carbohydrate fractions forming the cell walls of the initial fruit coat of buckwheat husks, pass into the hydrolysate. However, alkaline hydrolysis aids mechanical crushing of the husks, although the crushing remains incomplete.

Buckwheat husks were enzymatically hydrolyzed to destroy the compact structure of the cellulose microfibrils and thus improve the swelling properties of the husks.

The results show that enzymatic hydrolysis increases both the swelling properties and the soluble solid content of buckwheat husks.

Buckwheat husks following enzymatic hydrolysis are a light brown color with a pronounce buckwheat smell and sour flavor, and have altered organoleptic, structural, and mechanical properties. Hydrolyzed buckwheat husks ground in a coffee grinder produce a fine-grained buckwheat flour that does not leave a gritty feeling on the teeth when masticated.

The fine-grained flour produced by this two-stage processing (hydrolysis and grinding) can be used in the food industry. For example, I have developed a recipe for ‘Buckwheat biscuits’ by replacing the high-carbohydrate potato starch in the original recipe with fine-grained hydrolyzed buckwheat husks. These biscuits are useful as a functional food.

This substitution reduced the caloric value and otherwise greatly improved the biscuits, including their organoleptic, structural, and physical properties.The useofprocessed buckwheat by-products,such as thebuckwheathusk flour described here,allows the full utilization of buckwheat. In addition, this flourimproves the characteristics of baked products,has health-promoting properties,and contributes to increasing the nation’s health and lengthening the average life span. Buckwheat biscuits are low in calories and thus may be useful in rehabilitating patients suffering from socially significant diseases, particularly diabetes mellitus [2].

References:

1. The use of buckwheat husks in food production / Yazev S. G.//Scienceandmodern age – 2014: sourcebook of the XX XIV International research and practice conference – Novosibirsk: Publishing house of Scientific Cooperation Development Centre ЦРНС, 2014. – 164-165p.
2. T.N. Kholodilina. Efficiency of various technologies of buckwheat husks preparation for using in the diets of livestock and poultry. – Orenburg: All-Russian Beef Cattle Research Institute, 2006. – 245 p.

Chapter 30

THE USE OF SE-ENRICHED SEAWEEDS IN PREVENTIVE NUTRITION

Maria V. Kravchenko, Natalia E. Struppul
Far Eastern Federal University, School of Biomedicine,
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: struppul@mail.ru, tel.: +7(914)702-62-69

The seaweeds of Far Eastern seas are a valuable resource for producing food products with high nutrition value, which, in addition to everything else, is connected with the rich mineral composition of macrophytes. Selenium is one of the most valuable minerals: it is found in aminoacids and proteins, and carries out multiple functions in a human body, including the enzymic functions. A daily minimum norm of selenium in a human diet is 50-100 μg. Insufficiency of the element results in numerous health problems and pathologies connected with the endocrine system functioning, cardiovascular system, detoxication, and a total immunological status. Almost the whole territory of Russia is an area of marginal availability or deficiency of selenium. This circumstance calls for creating and introducing the food products of mass consumption, able to prevent or eliminate the selenium deficit in the population. Production of Se-enriched materials and products is one of the ways of increasing the selenium status in the population. Using local natural resources, including the sea resources, is economically attractive. Since selenium is a minor component of marine organisms, it is feasible either to concentrate or enrich their biomass with this element. Sea macroseaweeds are a convenient material for these purposes: their stocks in the Russian Far Eastern seas are practically unlimited.

We have conducted a screening study of selenium content in the dominant species of seaweeds found in the Sea of Japan. The content of selenium has been determined in thallomes of 21 species of seaweeds and seagrass collected in summer in the Posyet Bay and Vostok Bay of the Japan/East Sea. The selenium content in seaweeds mostly does not exceed 0.8 μg/g d.w.; the maximum amount has been found in Sargassaceae (*S. myabei*) – 1.06 μg/g d.w. The minimal concentration

was found in *Chondrus armatus* – 0.19, *Laminaria angustata* – 0.24, and *Ahnfeltia tobuchiensis* – 0.28 µg. The average concentration in Japanese luminaria is 0.85 µg/g d.w.

To provide a WHO-recommended daily requirement of selenium – 50-70 µg/day, it is necessary to consume about 100 g of dry seaweed daily, which is not typical of the Russian traditional diet. Therefore, the experiments have been conducted in order to study the potential of *Laminaria japonica* for accumulation of selenium and to produce a biomass enriched with selenium. The experiments have resulted in producing the luminaria biomass with 50 µg of selenium in 1 g of dry mass, which corresponds to the recommended daily requirement. Increased concentration of selenium leads to the increase in the amount of sodium and magnesium and to a substantial decrease in the amount of iodine and iron. Consequently, the elementary composition of the seaweed becomes more well-balanced for satisfying the human biological needs in minerals.

Experiments on laboratory animals have shown a positive effect of Se-enriched luminaria powder as a therapeutic agent in experimental toxic hepatitis of rats. Preventional application of the substance allows preventing the progress of immunodeficiency disease, thromboses, and anemia. The experiments also have discovered the immunomodulatory, anticoagulation, and erythropoietic effects of Se-enriched luminaria in case of immune dysfunction and poor parameters of peripheral blood.

Based on the research, the operational procedures of enriching the seaweed with selenium have been developed. The elaborated methods of cultivation can also be applied in commercial production.

Chapter 31

USE OF BUCKWHEAT HUSKS IN SPECIAL PURPOSE FOODS

Sergey G. Yazev, Yulia I. Golubeva, Lyudmila V. Levochkina
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: yazev_91sg@mail.ru, tel.: +7(908)969-90-05

Abstract. Use of secondary raw materials in foods production is of great current interest. Buckwheat husks subjected to combined hydrolysis, have a number of useful properties and can be used in production of special purpose foods.

Keywords: buckwheat husks, melanin content in buckwheat husks, antioxidant activity of buckwheat husks, prevention of diseases, structure and properties of cell walls.

Use of various anatomical parts of cereal crops and leguminous crops in food improves balance of trace elements and major nutrients, amino acids, vitamins, enzymes, carbohydrates and fats and has positive effect on human health.

One of such examples is use of buckwheat husks – a valuable secondary raw material. They contain natural biological substances, which are easier and more profitable to extract than to synthesize chemically. Study of buckwheat properties is of immediate interest as with their low cost buckwheat husks have superior culinary properties when used as a food supplement, especially in pastry. In addition to pleasant taste and flavour, the pastry is enriched with dietary fiber, which is a regulator providing for preservation of health and prevention of many human diseases (such is ischemic heart disease, obesity, diabetes mellitus, atherosclerosis, colon cancer etc.). Buckwheat husks contain a number of trace elements, and buckwheat husk ash is rich in potassium and calcium. Trace elements of buckwheat husks are particularly valuable because they form a complex with organic substances and are more easily ingested in human body [1].

Buckwheat husks are also known to contain a lot of melanin, the content and properties of which depend on agricultural features of

buckwheat growing and its grading factor. This substance participates in DNA repair, neutralizes the products of lipid peroxidation, and serves as modulator of such major systems of cellular metabolism systems as photo- and radioprotection. The mechanism of melanin's protective activity reliably protects cellular systems from mutagenic and carcinogenic factors. Melanin serves as catalyzer in many biochemical processes, deactivates free radicals resulting from exposure to ultraviolet and ionizing radiation, as well as some enzymatic processes and autooxidation reactions. Presence of melanin in foods contributes to their prolonged storage. During digestive process, a part of melanin is ingested involving intestinal microflora and another part plays the role of enterosorbent (peristalsis regulator) and normalizes the composition of intestinal microflora. Melanin is an active antidote in acute intoxication and effectively clears toxins from the gastrointestinal tract in an early stage of intoxication (prior to their absorption into blood). Melanin is also used in treatment for and prevention of liver diseases, neural disorders (such as stress, chronic fatigue syndrome), and cancers [2].

To be used in food industry, buckwheat husks are subjected to combined hydrolysis. Studies showed that enzymatic hydrolysis improves useful properties of buckwheat husks. Enzymatic processing of buckwheat husks lowers high density of intermolecular packing of substances within cell walls and makes them more susceptible to environmental exposure and activation of numerous components of buckwheat husks [3], including antioxidant activity. Total antioxidant content (TAC) in hydrolyzate obtained remained at the same level (4.2 mg/ml) as in the sample subjected to alkaline hydrolysis, while in solid residue of hydrolyzate it increased by a factor of 3 as compared to TAC in solid residue of alkaline hydrolysate and reached 69.5 mg/g. This may be due to the fact that the hydrolysis is followed by destruction of lignin-cellulose complex and disruption of silica film results in release of many heavy metals and mineral substances into hydrolyzate, thus making formerly hindered phenolic compounds available for study. Based on results obtained, the antioxidant activity of sample under study may be compared to that of green tea which is known to be connected with catechins contained in it in large amounts.

Determination of antioxidant activity of buckwheat husk samples subjected to native and combined (alkaline and enzymatic) hydrolysis is shown in Figure 1.

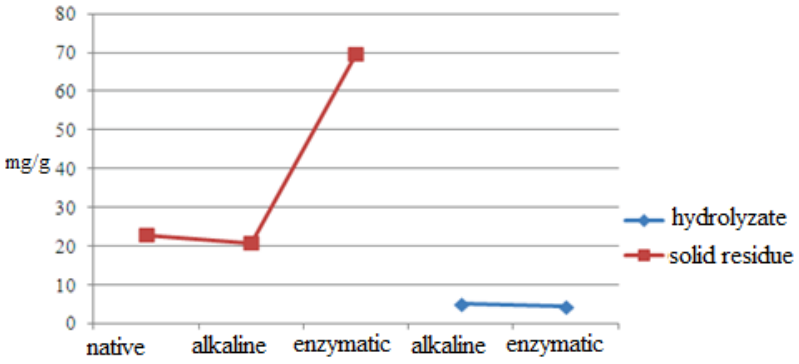


Figure 1 – Determination of antioxidant activity of buckwheat husk samples subjected to native and combined (alkaline and enzymatic) hydrolysis

Enzymatic hydrolysis of buckwheat husks increases antioxidant activity of hydrolyzate components in a way that provides for prolonged storage and improves their biological value. When enzyme preparations are used, antioxidant activity of buckwheat husks increases by a factor of 3 as compared to TAC of alkaline hydrolyzate and native sample, and this allow to treat them as a valuable raw material for pastry production.

Use of buckwheat husks in pastries allows to obtain the foods with health-promoting properties and to use them in special diets.

References:

1. Use of hydrolyzed buckwheat husk sin pastries/E.S. Voronina, S.G. Yazev // III Research and practice conference of young scientists and students: summarizing the results of research and development work in FEFU School of Biomedicine for 2014-2015.– 2015. – p. 23.
2. Use of buckwheat husks in food production /S.G. Yazev // Science and modern age – 2014: sourcebook of the XXXIV International research and practice conference. – Pp. 102-105.
3. Low-calorie pastries enriched by dietary fiber of buckwheat husks / S.G. Yazev // "The priorities of the world science: experiments and scientific debate": Proceedings of VIII International scientific conference June 17-18, 2015. – Volume 1. Natural and engineering sciences. – North Charleston, South Carolina, USA, 2015. – Pp. 106-108.

Chapter 32

STUDY OF THE ANTIOXIDANT ACTIVITY OF YOGURT WITH ADDED VEGETABLE AND FRUIT PUREE

Elena A. Guz, Ludmila V. Liovochkina
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: mandarinkalena@mail.ru, vovslev@yandex.ru, tel: +7(924)328-30-99

Abstract. Milk is a complete food containing proteins, fats, carbohydrates, and vitamins. Consequently, many Russian companies are thoroughly exploring the dairy market to expand the range of dairy products and attract new customers. Awareness of the need for a healthy diet, particularly by women, makes low-fat milk andlow-fat orskim milk dairy products such as yogurt particularly attractive.

Keywords: yogurt, dairy drink, vegetables, fruits, fruits puree, vegetable additives, vegetable purees, physalis, carrots, pumpkin, antioxidant activity, therapeutic properties, vitamins, immunity, storage life, health, healthy diet.

Yogurt is a fermented milk product obtained by fermenting milk with pure cultures of lactic acid bacteria such as *Lactobacillus bulgaricus*. Compounds produced during the growth of these bacteria accumulate in the final product and provide general health benefits. Regular consumption of yoghurt improves the immune system, thus improving the body's resistance to allergies, viral disease, and infection. Maximum therapeutic effect requires that live yogurt with a short shelf life be eaten, since such yogurts maximally preserve the live microorganisms [1, 2].

Many organic and inorganic compounds, including compounds found in yogurt, oxidize in air.Therefore, the addition to yogurt of antioxidants, which are compounds that at low concentration slow or prevent oxidative processes [5], increases the nutritional value of fermented milk beverages.

Oxidative processes occur in humans, plants, edible fats, and some food. Organic compounds are oxidized via a chain mechanism in which the superoxide radical, O2, plays a major role. Reaction with an antioxidant inactivates the O2 radical, thus decreasing or terminating oxidation.

At observance of all norms of nutrition and lifestyle in the human body, the formation of free radicals is governed by the action of the antioxidant defense system, the effect of which is based on the interaction of enzymes, serum proteins, hormones, vitamins, and low molecular weight organic acids and sulfide compounds. Even small amounts of antioxidants leads to stabilization of free radicals, considerably retarding oxidation reaction proceeding by a chain mechanism. Unfavorable factors, which gets people leads to excessive formation of free radicals, which leads to an imbalance of the antioxidant status.

Antioxidant activity determined bioavailability foods is caused by the presence of phenolic compounds, vitamins, proteins, sugars, carboxylic and amino acids, and other biologically active substances, which are contained in foods of plant origin.[7]

Oil- and fat-soluble antioxidants, including vitamin E (tocopherols, tocotrienols), carotenoids, and retinol (vitamin A and provitamins), protect the lipids in biomembranes against oxidation by free radicals [6].

Cow's milk contains provitamins which possess antioxidant activity, so yoghurt made from cow's milk likely exhibits antioxidant activity. The total content of antioxidants in yogurt prepared using different lactobacilli was examined using a "TsvetYauza" HPLC coupled with a UV detector. Figure 1 shows the total content of antioxidants in yogurts prepared using various starter cultures.

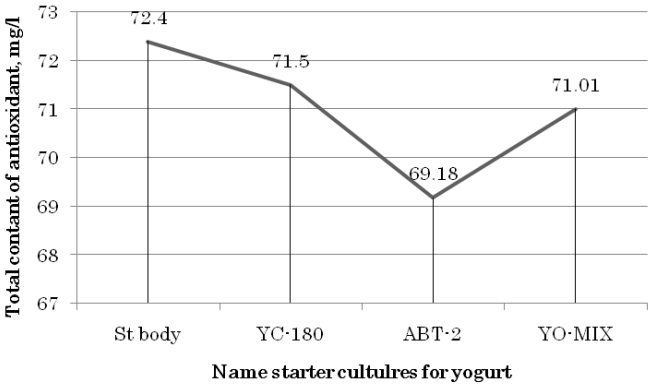


Figure 1 - Total content of antioxidants in yogurts prepared using various starter cultures

Yogurt prepared with different starter cultures showed similar concentrations of antioxidants, indicating that the type of starter has little

effect on the antioxidants. The addition of physalis puree to yoghurt increased antioxidant content by 10% (Figure 2).

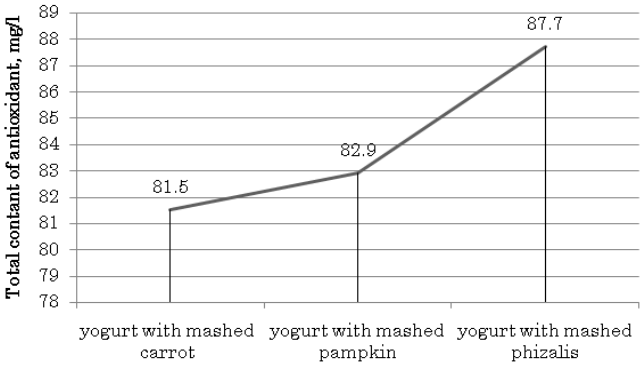


Figure 2 - Total content of antioxidants in yogurt with added vegetable or fruit puree

The increased antioxidant content of yogurt following the addition of physalis puree is due to compounds with high antioxidant activity, including bioflavonoids (natural polyphenols) and aromatic hydroxy acid, found in physalis. Natural dyes such as anthocyanins give vegetables their orange, red, purple, or blue color, and these are the most powerful antioxidants found in nature, and can penetrate the cell membrane. [3]

Changes in antioxidant content during the storage of yoghurt without additives and with added physalis puree were measured and the results are shown in Figure 3.

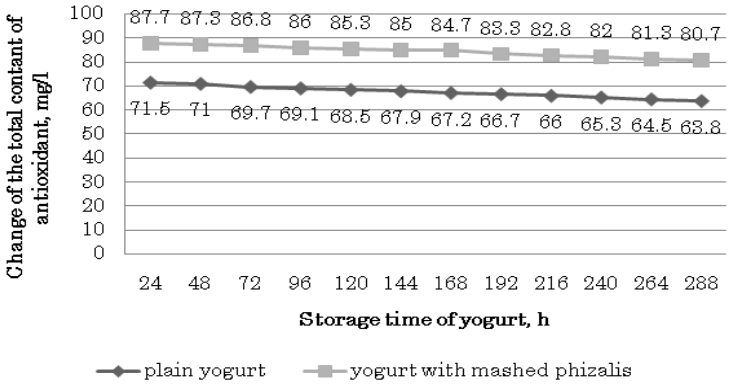


Figure 3 - Changes total content of antioxidants in plain yogurt and yogurt with added physalis puree during storage

Previous studies have shown that the storage of yogurt reduces total content of antioxidants, indicating that the concentration of natural antioxidants decreases with time due to the accumulation of active lipid secondary oxidation products [4].

The total content of antioxidants in the experimental samples of yoghurt with added physalis puree decreased during storage but remained fairly high, comparable to that observed for berries such ascranberries, blueberries, and plums, which have an antioxidant content of 73–94 mg PAS per100 grams berries [6].

We thus conclude that the addition of vegetable or fruits puree significantly increases the physiological value of yogurt.

References:

1. Federal Law of June 12, 2008 №88-FZ "Technical regulations on milk and milk products"
2. Kodentsova V.M., Vrzhesinskaya O.A. Vitamin and mineral supplements and fortified foods: their role in providing the body with vitamins and minerals // Trace Elements in Medicine, №10, 2009 - with 7-22.
3. Komov V.P., V.N. Shvedova Biochemistry, M .: Bustard, 2008 – 638
4. Tokayev E.S., Manuk'yan G.G., development of specialized products with antioxidant are of natural origin for power athletes. Abstract of dissertation for the degree of Candidate of Technical Sciences, Moscow, 2009. - 24 p.
5. Shilov A.M., Melnik M.V., M.V. Chubarov, Complex antioxidants in the prevention and treatment of diseases of the cardiovascular system, Russian medical conduct, №4. 2004
6. Yashin Frenkel, Ryzhnev V.Y., Yashin A.Y., Chernousova N.I. Natural antioxidants. Contents in foods and their influence on health and human aging. M.: Publisher "TransLit", 2009. - 212 p.
7. Khrapko N.V. The dissertation is for the degree on the topic: Defining integral antioxidant capacity of vegetable raw materials and foodstuffs. Khrapko N.V., Krasnodar, 2006 - 181 p.

Chapter 33

SEA-URCHIN ROE AS A SUPPLEMENT FOR FORTIFYING BIOCRISPS MADE FROM FISH ALBUMINOUSMASS

Victoria. A. Kharchuk, Irina. A. Suprunova
Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: ila100492@mail.ru, tel: +7(924)120-60-81, +7(423)265-24-24

Abstract: The hydrocoles have attractive taste properties and high nutritional value, and thus play an important role in human nutrition. In particular, the Pollock and sea-urchin roe have a high content of protein with a well-balanced amino acid composition, and are rich in polyunsaturated fatty acids, minerals, and vitamins, all of which contribute to the functional importance and high nutritive value of this food source. The above raw material quality can be used to create of the functional product.

Key words: fish mince, biocrisps, pumpkin, sea-urchin roe

According to the Development Strategy of the Fisheries Industry of the Russian Federation for the period until 2020, the Far Eastern region will be the primary fisheries region in Russia, providing 53.5% (3.52 million tons) of fish harvested in the Russian Federation, despite the expectation that harvests will decrease by 10.6% during this time in the Far Eastern region [11].

The share of fish yield in Primorsky Krai in the Far East has averaged 29.2% in recent years; in Russia is to 18.4%. Primorsky Krai produced over 30% by volume of the food fish products, including canned food, of the Far Eastern region, and over 17% of the food fish products in Russia. The consumption of fish and fish products per personin Primorsky Krai is 30 kg per year [4].

Yields mainly comprise fish from the gadoids family (pollock, navaga, cod), salmon, herring, and flatfish, and non-finfish (crab, squid, shrimp). The yield of harvested aquatic biological resources was 785,000 tons in Primorsky Krai in2012 and is anticipated to increase to 1,035 million tons by 2017.

This resource must be carefully managed. Accordingly, food biotechnology should focus on creating and utilizing products based on aquatic organisms.

In addition to the main species of fish in Primorsky Krai, yields include aquatic biological resources such as gray and black sea urchin, ark shell, corbicula, surf clam, luminaria, and common whelk found in specialized fishing areas.

The proportion of traditional fish in catches has been decreasing recently while that of fish of lower commercial value has been increasing, despite low demand for and limited utility of this latter category of fish for the production of traditional fish products.

It is therefore clear that the fishing industry must improve technologies for processing low-value, small fish and produce a variety of new food products with good flavor and long storage life. In addition, these products must have nutritional value [1].

These food products, which include crisps and biocrisps, should have a certain functional purpose and, as mentioned above, be prepared from fish with low commercial value. Crips are made from fish mince and biocrisps are made from fish albuminous mass [13]. The finished product is similar to crispbread, has a rectangular shape (approximately 10×5 cm), a thickness of 0.5 cm, and is fragile, brittle and crumbly, with no cracks on the surface.

Biocrisps have excellent rheological characteristics, consequently, the goal of this work is to identify aquatic organisms for producing biocrisps with increased nutritional value.

Achieving this goal requires:

- identifying raw materials that accelerate biocrisp production
- proposing an antioxidant for inclusion in biocrisps to enhance physical and mental performance after ingestion.

Biocrisps are made from fish mince. According to the Fisheries Department of Primorsky Krai, 343.2 thousand tons of Alaska pollock were harvested from internal sea waters in 2014 [3]. Alaska pollock is the least expensive fish and will thus be used in the manufacture of fish biocrisps.

Flours made from cereals, horticultural crops such as potatoes, and legumes, are used in addition to fish mince to make crisps, with 30%–40% mince being optimum. Increasing the amount of fish mince can increase friability and decrease elasticity. Therefore, making biocrisps rather than crisps would be advantageous because the main raw material

of biocrisps is albuminous fish mass, which has better structural and mechanical characteristics than conventional mince [7].

A vegetable such as pumpkin must be added to give biocrisps pleasant organoleptic characteristics and the required physico-chemical parameters. The most suitable pumpkin is "Granddaughter", grown in Primorsky Krai.

This pumpkin provides 25.7% dry matter. Its nutritional value is determined by the carbohydrate, vitamin, and protein content; these components also improve digestion with help of fibrous feeds. Dried "Granddaughter" pumpkin contains 0.99% nitrogen, 6.17% crude protein, 0.08% calcium, 0.25% phosphorus, 1.98% potassium, and 5.22% dietary fiber. This dietary fiber has a beneficial effect on the gastrointestinal tract. Pumpkin is high in sugar: this particular variety contains 3.7% sugar and up to 21.01% starch. "Granddaughter" is rich in carotene (16.3%) and so helps prevent cardiovascular disease [9, 5].

Pumpkin has a pleasant orange-yellow color that does not change upon heat treatment.

Flours made from oats, corn, or vegetables such as pumpkin are the most suitable for making biocrisps. Experiments with various biocrisp recipes shows that the amount of albuminous fish mass can be increased, thus fully utilizing and enhancing the value of albuminous fish mass [14].

Factors that determine the suitability of fish for making minced fish are the chemical composition of muscle tissue, the quality and thoroughness of the primary processing of the fish, and the storage conditions and duration prior to processing [2].

However, fish mince for the production of biocrisps will be of little value and non-functional; therefore, aquatic organisms other than Alaska pollock were considered for enriching biocrisps.

Fish traditionally harvested are often used in dietary supplements because they have a special chemical composition, are preferred as a food, or are used in traditional medicine in the Asia–Pacific region. Sea-urchin roe also has a special chemical composition [12].

An investigation by The Research Institute of Nutrition and Medical Radiological Research Center of the Russian Academy of Medical Sciences showed that sea-urchin roe stimulates physical and mental performance, reduces fatigue, is a powerful antioxidant, normalizes metabolic processes in the body, improves the overall tone of the body, significantly stimulates blood formation, regulates the hormonal system of the body, normalizes the functions of the mammary glands,

prevents the development of mastopathy, and normalizes blood pressure [15]. In addition, the regular ingestion of sea-urchin roe reduces the risk of thyroid gland diseases, is used to treat diseases of the gastrointestinal tract, aids rapid healing after injury, illness, and surgery, increases the disease resistance of organism sunder unfavorable ecological conditions, increases sexual activity, and has a rejuvenating effect [6].

All the above attributes are due to the chemical composition of sea-urchin roe. The food and biological value of this roe was investigated by The Research Institute of Nutrition and Medical Radiological Research Center of the Russian Academy of Medical Sciences (Table 1).

Table 1 – Nutritional and biological value of sea-urchin roe

№	The chemical composition of hard roe	Percentage, %
1	2	3
1	Proteins	13,8
2	Lipids	4,3
3	Carbohydrates	2,5
4	Ash	2,2
5	Water	77,2
Energy value of 100 g of the product is 104 kcal (435 kJ)		

The composition and characteristics of the lipids were also investigated (Table 2).

Table 2 – Characteristics and composition of lipids in sea-urchin roe

№	Group of lipids	Percentage, %
1	Phospholipids and monolipids, including lecithin	22,85…44,0 33,10…36,0
2	Cholesterol	24,54…31,89
3	Free fatty acid	16,27…16,8
4	Diglycerides	2,22…2,75
5	Sterol esters	3,84…4,85
6	Triglycerides	0,61…28,74

The biological value of sea-urchin protein is 112% (relative to the content in the egg), as is evident from the amino acid composition (Table 3).

Table 3 – Results of studies of sea-urchin roe, amino acid composition

Name of amino acid	Percentage of protein, %
Aspartic acid	11,05
Threonine	6,27
Serine	5
Glutaminic acid	14,23
Proline	2,56
Glycine	3,48
Alanine	5,4
Valine	5,6
Methionine	3,09
Lysine	6,78
Arginine	5,49
Tryptophan	1,05
Cystine	1,2
Isoleucine	4,49
Leucine	6,67
Tyrosine	3,66
Phenylalanine	4,49
Histidine	9,31

V.Y. Sokolov from the Institute of Marine Biology Far-Eastern Division of the Russian Academy of Science will help us develop the technology required to retain the composition and properties of the raw material in our enriched product [10]. Stabilizing and thus preserving sea-urchin roe in dry form is a promising new approach.

Conclusion: The development of biocrisps made from low-value Alaska pollock and enriched with dry sea-urchin roe is a promising technology. This dried roe may be an excellent source of scarce lipids (polyunsaturated fatty acids, phospholipids) and complete protein.

Also, the enrichment of biocrisps with dried “Granddaughter” pumpkin pulp will improve the organoleptic characteristics of the product and provide antioxidant properties.

Reference:

1. Averyanov ND Bio-based products are aquatic organisms and their functional importance / ND Averyanov, ME Tsibizova. // Herald ASTU "Fisheries". - 2008. - № 3. - P. 115-119

2. Bredikhina OV Scientific basis for the production of fishery products: a manual for schools. M .: Colossus, 2009. - 152 p.
3. Veka E.A. Enterprises Primorye caught more than 400 thousand tons of bio-resources // Official site of Primorsky Krai. - 2014 - [electronic resource] - Access. - URL: http://primorsky.ru/news/common/64435/?sphrase_id=858934 (date of treatment 05/26/2014)
4. State program of Primorsky Territory "fisheries industry development in the coastal region for 2013 - 2017": Resolution Primorsky Territory Administration on December 7, 2012 // Primorsky Krai Administration. - 2014.
5. Kalenik TK Use the coastal varieties of pumpkin in the design of functional foods / TK Kalenik, EA Kovalev, LN Stodolnik, EZ Yagubov // Food Technology and Biotechnology: a collection of the International Conference of Young Scientists. - Kazan: KSTU, 2010. - p. 63-65.
6. Kryzhanovsky SP Lipid-lowering effect of food supplements from the eggs of sea urchins in the monotherapy and combination with atorvastatin / SP Kryzhanovsky, MA Yatskova, VD Golovacheva // Pacific Medical Journal - 2012. - № 1. - p.29-31.
7. Matyukhina ZP Commodity food: a tutorial. M .: The Academy, 2013. - 352 p.
8. Minutes of the meeting of the working group of Primorye Fisheries Council on fishing of living aquatic resources and aquaculture Vladivostok: №01-2015r on January 16, 2015 Chairman - AA Front, Director of the Department of Fisheries and Aquatic Biological Resources of Primorsky Krai.
9. NP Sidorova Evaluation of varieties of pumpkin under the southern zone of the Far East Amur Region / NP Sidorova OV Schegorets, VF Kuzin // Herald MichGYaU. - 2012 - № 2. - P.35-45
10. Sokolov VY The eggs of sea urchins - a means of optimizing the functions of the body // Far Eastern Branch of the Russian Academy of Sciences. - 2013 - [electronic resource] - Access. - URL: http://www.febras.ru/ (date of treatment 30.10.2012)
11. The strategy of development of the fishery industry of the Russian Federation for the period up to 2020: Order of the

Government of the Russian Federation on March 30, 2009 // Federal Agency for Fisheries. - 2009.
12. Basic science - medicine: Sat. Art. VI scientific-practical conf., Vladivostok, 2011. 176 pp.
13. Tsibizova ME Fish protein mass - the main component of grain biokripsov / ME Tsibizova, ND Averyanov. // Herald ASTU "Fisheries". - 2009. - № 2. - p.114-120
14. Hall G.M. Surimi and fish-mince products / G.M. Hall, N.H. Ahmad // Fish Processing Technology. – 1997. – pp 74-92
15. Kryzhanovsky S.P. Effects of dietary supplement derived from sea urchin roe on biochemical indices of mice blood in case of alimentary hypercholesterolemia / S.P. Kryzhanovsky, T.A. Kuznetsova, T.S. Zaporozhets, I.D. Makarenkova // Paciic Medical Journal. – 2011 –№ 1 – p. 62–64

SECTION 5

Therapy and Rehabilitation

Chapter 34

A REVIEW ON THE WHOLE BRAIN IRRADIATION WITH PRESERVATION OF THE HIPPOCAMPUS

Kazushi Kishi
Department of Radiation Oncology, Hokuto Hospital
7-5 Kisen Inada-cho, Obihiro, Hokkaido, Japan

Rationale for hippocampal sparing

The hippocampus contains primordial neural stem cells and plays several important roles in the brain, including spatial navigation and the consolidation of new information to the fixed memory. Injury to the hippocampus due to stress, aging, toxins, chemotherapy, and radiotherapy can cause amnesia, cognitive disorder, disorientation, and a deterioration of brain function. Accordingly, sparing of the hippocampus has been a focus of recent technological advances in radiotherapy.

Whole-brain irradiation (WBI)

WBI is indicated for various clinical scenarios, which include prophylaxis for subsequent brain metastasis after complete remission of leukemia and small cell lung cancer, in the treatment of central nervous system lymphoma, and for multiple brain metastases. However, it is problematic that WBI is associated with the sequela of significant cognitive deterioration. WBI is generally performed with 30 Gy/3 Gy × 10 fractions for two weeks. In the results of the RTOG 0933 phase I trial, Gondi et al. 2014 reported there was a mean relative decline of 7.0% after WBI with hippocampal sparing between baseline and 4 months for the Verbal Learning Test–Revised Delayed Recall Score, while a historical control without hippocampal sparing demonstrated a mean relative decline of 30% ($P < .001$) following WBI. They concluded that conformal avoidance of the hippocampus during WBI is associated with preservation of memory and quality of life, as compared with historical series.

Stereotactic brain irradiation (SBI)

Individual to widespread brain metastases can be treated in single or multiple sessions using a stereotactic beam convergence technique such as Gamma Knife or Cyberknife, with a single dose of 20 Gy or fractioned doses of 50 Gy/5 Gy × 10 fractions, usually without whole brain coverage. The effectiveness of SBI is well established as a superior alternative to conventional WBI of 30 Gy/3 Gy × 10 fractions to 40 Gy/2 Gy × 20 fractions when the number of the gross metastatic lesions was small. This technique efficiently targets the gross tumors but has the drawback that it does not cover residual tumor. However, because of the risk of cumulative brain damage, additional WBI is not recommended if SBI has already been performed.

Concomitant WBI and SBI

Technically, tomotherapy enables concomitant WBI and SBI. We developed the following prescription for simultaneous delivery of SBI and WBI over two weeks: 50 Gy/5 Gy × 10 fractions to the gross tumor volume(s), and 30 Gy/3 Gy × 10 fractions to the rest of the brain as prophylactic therapy, respectively. Because there is no established clinical evidence regarding the safety and efficacy of this strategy, we have used this protocol at our institute only for selected groups of patients those with high risk of dissemination and mental deterioration. We are currently accumulating clinical cases with the aim of evaluating the availability and reliability of concomitant WBI and SBI, and presenting our clinical findings.

Reference

Gondi V et al. Preservation of Memory with Conformal Avoidance of the Hippocampal Neural Stem-cell Compartment during Whole-brain Radiotherapy for Brain Metastases (RTOG 0933): A Phase II Multi-Institutional Trial. J Clin Oncol. 2014 Oct 27.
http://www.ncbi.nlm.nih.gov/pubmed/25349290

Chapter 35

TREATMENT OPTIMIZATION OF SEVERE SPASTICITY IN PATIENTS AFTER MAJOR CEREBROSPINAL TRAUMA

Artur R. Biktimirov, Alexander S. Orlov, Tatiana F. Tubaeva, Oleg I. Pak, Ruslan I. Totorkulov, Ruslan N. Akhmadiev, Tatyana A. Gorbach
Far Eastern Federal University, Medical Center
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: Biartur2006@yandex.ru

Background. Treatment of spine and spinal cord trauma is one of the most acute issues in modern medicine. Spine and spinal cord trauma is relatively common in developed countries, with an incidence ranging from 1% to 5.3% in some reports. Unfortunately, spine and spinal cord trauma often occurs in young people at a productive age. Severe spasticity is one of the most common complications of spinal cord injury, and has been reported to affect up to 60% of patients in prior studies.

Aim. To optimize the treatment of patients who developed severe spasticity following severe spinal cord injury.

Methods and Materials. We performed a study of 18patientswho underwent surgery between April 2012 and December 2013. Spinal cord stimulators manufactured by St. Jude and Medtronic were implanted into 11 patients. The other seven patients were implanted with Codman baclofen programmable pumps. The treatment method was selected for each patient as follows. First, a diagnostic electrode was implanted into the lumbar spine for diagnostic stimulation of the spinal cord. If the tonus was reduced to a comfortable level during stimulation, a spinal cord stimulation system was implanted. If the patient did not respond to the stimuli or if the tonus was not depressed to a comfortable level, a baclofen test was performed. A baclofen pump was to be implanted if the baclofen test reduced tonus by 1 point on the Ashworth scale. The patient's proximity to the clinic and the ability for the patent to be transferred to the Federal Center of Neurosurgery within 1 day were also considered.

Results and Discussion. The treatments successfully decreased the severity of spasticity in all 18 (100%) patients. The tonus decreased by a mean of 2±0.3 points on the Ashworth scale in patients with implanted baclofen pumps. The patients with implanted stimulators experienced the decrease of spasticity as well, but unlike patients with an implanted baclofen pump they could regulate the level of spasticity depending on their physical activity. In other words, if necessary, the patients with implanted stimulators could increase their tonus up to their baseline level or decrease it by up to 1 point on the Ashworth scale.

Complications. The pump catheter was damaged because of intense physical activity in one patient with an implanted pump. Another patient experienced problems owing to pump dysfunction, which was resolved by replacing the pump. Patients with implanted stimulators experienced the following complications. In one patient, the electrode was damaged and needed to be replaced. In another patient, the impulse generator developed a fault and was replaced. In a third patient, the impulse generator discharged owing to the high stimuli parameters, and was replaced.

Based on the data obtained here and the results of prior studies, it can be concluded that chronic intrathecal therapy with baclofen and chronic spinal cord stimulation are highly effective methods for treating spasticity and improving the quality of life of patients. Therefore, it is necessary to further develop these treatments for use in the Russian Federation.

Conclusion. Although baclofen pumps are used for the treatment of severe spasticity following severe cerebrospinal trauma in patients worldwide, the results of our study indicate that spinal cord stimulation is as effective as a baclofen pump, and might be used in clinical practice together with baclofen therapy.

Chapter 36

EFFECTS OF ANTIHISTAMINES ON LYSOSOMAL MEMBRANE STABILITY IN PHAGOCYTIC CELLS FROM PATIENTS WITH DIFFERENT FORMS OF URTICARIA

[1]Igor N. Dubnyak, [1]Ekaterina V. Eliseeva, [2]Yana V. Dubnyak
[1]Pacific State Medical University
2 Ostryakova Ave., Vladivostok, 690002, Russia; tel: +7(423)245-08-65
[2]Far Eastern Federal University, School of Biomedicine
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: yana.prym@mail.ru, tel: +7(423)245-76-87

Abstract. Many drugs have a broad spectrum of effects on many organs, systems, and different parts of the immune system, including the lysosomal membrane of phagocytic cells. In this paper, we examined the effects of antihistamines on lysosomes.

Keywords: antihystamines, lysosomes, phagocytes

One of the functions of lysosomes is to maintain the stability of cells, such as phagocytic cells, a function that was first described by De Duve in 1955 [1, 6].The stability of the lysosomal membrane is a critical determinant of lysosomal enzyme efflux from cells, and is involved in the development and pathological process of a variety of diseases, and can intensify these processes. Because of the wide range of effects on a body, many drugs may affect the lysosomal membranes of cells and, ultimately, lysosomal function. The properties of some antibiotics, heparin, and statins in terms of stabilizing the lysosomal membranes of phagocytic cells have been described [2].The objective of this study was to determine the effects of antihistamines (chloropyramine, quifenadine, fexofenadine and loratadine) on the stability of the lysosome membrane by using an established method to assess the stability of the lysosomal membranes of phagocytic cells [1, 6].Previously, it was suggested that antihistamines affect components of the immune system, including phagocytic cells [3, 4, 5], by increasing their activities. Therefore, we examined the effects of these drugs on the activities of phagocytic cells obtained from rats and healthy humans. The cells were exposed to the drugs prepared in 100 ml

of physiological saline to half the therapeutic dose, the therapeutic dose, or two times the therapeutic dose. Experiments using rat peritoneal macrophages, as well as neutrophils and monocytes from healthy individuals without allergic diseases, showed that exposure to different doses of antihistamines increased the stability of the lysosomal membranes of these phagocytic cells. These results should renew our interest in these drugs, based on multidisciplinary research, including the effects of these drugs on various components of the immune system, such as phagocytosis. Antihistamines influence the stability of lysosomal membranes of cells, including phagocytic cells, and these effects should be considered when prescribing them. Accordingly, when chloropyramine and fexofenadine are prescribed for the treatment of chronic urticaria, or loratadineis prescribed for the treatmentof allergic disease, the physician may need to prescribe additional drugs to stabilizely sosomal membranes.

References:

1. Dubnyak I.N. The role of phagocytizing cells lysosomal enzymes in immunogenesis at its initial stages / I.N. Dubnyak, A.S. Sharonov // Medical Ecology. – 2003. – # 2. –pp.8-9.
2. Dubnyak I.N. Influence of drugs on the stability of phagocytizing cells lysosomal membrane / I.N. Dubnyak, E.A. Maltsev, A.S. Sharonov, N.S. Dubnyak // Allergology and Immunology. - 2006. - V.7, #3. – p. 440.
3. Goryachkina L.A. High technology antihistamines medical products for the allergic diseases treatment/ L.A. Goryachkina // Rhinology. - 2002. – # 1. – pp. 70-77.
4. Krasilova I.L. Immunotropic properties of antihistamines drugs and their combination with immune modulators: author's abstract for Cand. Med. Sc.: 14.00.25 / Krasilova I. L.; [BashkirState Med.Inst.]. - Ufa, 1996.– p.22.
5. Kuznik B.I. Immunegenesis, hemostasis and nonspecific resistance of a body / B.I. Kuznik, N.V. Vasilev, N.N. Tsybikov. - M.: Medicine, 1989. – p.320.
6. Sharonov A. Phagocytes, lysosomes, membranes / A. Sharonov, Y.I. Shilov. - Vladivostok. – Dal'nauka, 2007. – p.128.

Chapter 37

ROLE OF IMMUNOSUPPRESSING HYBRIDOMAS IN THE DEVELOPMENT OF CANCER AND METASTASES (A HYPOTHESIS)

B. M. Kovalev
Pacific State Medical University,
2 Ostryakova Ave., Vladivostok, 690002, Russia
e-mail: makarich_44@mail.ru

Abstract: In this article, I propose a hypothesis describing the role of immunosuppressive hybridomas in the development of cancer and metastases. The development of malignant tumors or cancers in humans and animals is preceded by the formation of immunosuppressive hybridomas, originating from the fusion of transformed malignant cells and cells that suppress the host's normal immune responses to abnormal cells. Physical and chemical oncogenic agents, and carcinogenic and non-carcinogenic viruses act as carcinogenic transformers and induce the fusion of these cells during the formation of hybridomas. The resulting hybridomas retain the abilities of the transformed cells to grow and divide rapidly, and suppress the host's immune system to target abnormal cells. These mechanisms underlie the pathogenesis of nonmalignant and malignant tumors, and are a major factor in cancer metastasis (Kovalev, apply for discovery No. NK-51-OT-11983, 1990).

Introduction. It is widely believed that tumor formation in humans and animals is preceded by numerous and various factors that affect the host. These physical, chemical, and biological factors promote carcinogenic transformation of cells by causing genomic mutations, DNA transcription errors, and blocking the mechanisms that control DNA replication, as well as other factors [1, 2, 3]. However, experimental studies have shown that these etiological factors only have a carcinogenic potential under specific conditions, which determine the specific effects on the host.

Thus, tumor-like processes elicited by carcinogens in the host may not have the same outcome to when these carcinogens are applied to cell/tissue cultures. Indeed, negative results have been reported when tumor cells are cultured in the presence of carcinogenic agents and

introduced to animals. This is especially true for carcinogenic viruses, which may be dormant for a long time in the host, and only exert carcinogenic effects if there are favorable conditions, such as age, concomitant diseases, and impaired immunity, for example. Therefore, the emergence of cancer is independent of the timing of exposure to an etiological factor. However, a precancerous lesion and its host represent the system in which both components are potentially of equal strength and it is the nature of their interactions that determines the final outcome: whether the cancer will emerge or not and whether the host will recover or die [4, 5, 6].

New antigens, which differ from normal ones and are recognized by the immune system as "not own" or "strange", emerge in transformed malignant cells induced by viruses or carcinogenic agents. This prompted F. Bernette to make an assumption in 1971 that the host's immune response to these antigens is involved in eliminating the transformed cells in a process known as immunosurveillance. This explains why malignant tumors and cancers only develop if the immune system's reactions are inadequate or if the tumor cells overcome immunosurveillance.

For these reasons, malignant tumors are relative common in humans and animals undergoing long-term immunosuppressive therapy, in animals that undergo thymectomy, in animals infected with oncogenic viruses or cancerous cells, in patients infected with human immunodeficiency virus, and during the neonatal and aged periods, which are generally characterized by immunological deficits and failure. Consequently, R. V. Petrov proposed that cancer only develops if transformed malignant cells resist or overcome the host's immune system via several pathways: 1) specific antitumor receptors expressed on the surface of lymphocytes are blocked by oncogenic antigens and serum blocking factors; 2) the immune responses are disrupted owing to the development of tolerance to tumor cells (immunologic silencing); 3) eliminating malignant cells expressing strong tumor antigens via immune selectivity; 4) inadequate immune responses to malignant cells expressing weak antigens; 5) activation of immunological suppressor cells inhibit the production of antitumor molecules; and 6) single immunological suppressors are produced by different tumors.

Based on these hypotheses, cancer occurs because of the development of cells transformed by carcinogens or tumor cell oncogenes, and inadequate immunosurveillance caused by suppression or dysfunction of the host's immune system. The latter seems to be the most likely

mechanism involved in the growth of immunosuppressive hybridomas in humans and animals via the fusion of tumor cells and immunological suppressor cells. We believe that this process is one of the main factors involved in overcoming immunosurveillance and leads to the development of cancer and metastases.

Proving the hypothesis. In 1960, Barski et al. cultivated two lines of malignant cells in mice. They detected a new cell type that differed from the originator cells because the chromosome set represented a sum of both parental lines. However, the frequency of cellular fusion was rather low (10^{-6} to 10^{-7}). However, in 1962, Okada et al. reported that the hybridization of malignant and non-malignant cells was increased when the cells were exposed to Japanese agglutinating myxovirus JHV. In 1965, Harris and Watkins used Sendal virus, a microvirus that resembles JHV virus, and promoted the fusion of human HeLa cells and mouse cells. In 1974, Davidson and Genatel used a chemical inducer of hybridization instead of a viral inducer, and successfully produced somatic hybridomas. In 1974, Koler and Mulstein generated a hybridoma by fusing malignant cells from myeloma P3 and antibody-forming cells from a mouse spleen. When cultivated in culture medium or in vivo, the hybridomas maintained the abilities of the malignant cells to grow continuously and the abilities of immune cells to produce monoclonal antibodies and immunosuppressive factors. In 1979, Taussing et al. generated a hybridoma by fusing T lymphoma cells and spleen cells, and the hybridoma could secrete immunosuppressive factors. In another study, a hybridoma cell line displaying normal suppressor macrophage properties was obtained by fusing myeloma cells and spleen cells [8, 9, 10].

Beyond the hybridization of animal or human somatic cells, in 1980 Crous et al. generated a hybridoma from human cells by fusing lymphocytes obtained from a patient with subacute and those obtained from a patient with panencephalitis. In 1989, human T cell hybridomas expressing immunosuppresive factors were developed [11]. The factors used in the in vitro experiment suppressed the proliferative response to mutagens in mixed lymphocyte cultures as well as antibodies produced by human mononuclear blood cells. In addition to these hybridomas and T cell lines expressing inhibitors, it has been shown that: 1) murine thymocytes and splenocytes proliferate in response to mutagens; 2) murine splenocytes proliferate in response to allogenic cells in mixed lymphocyte cultures; 3) murine splenocytes produce antibodies following exposure to sheep erythrocytes in vitro; and 4) murine splenocytes

produce antibodies in response to a T cell-free antigen, tumor necrosis factor-ficoll, in vitro [12].

In 1969, Yoshizuka et al. produced a human T cell hybridoma by fusing human peripheral blood lymphocytes with CEM-II cells, following exposure to domperidone and actinomycin D. A stable T cell hybridoma termed D 6-18 produced a factor that caused chemotaxis of guinea pig peritoneal macrophages in vitro. This factor is present in the lysate of D 6-18 hybridoma and it can induce the formation of T cell hybridoma in granule cells and vesicles, and is produced in response to stimulation by mitogens and antigens.

Taken together, the findings reported here demonstrate that forced hybridization of malignant cells and immune system cells from humans and animals with a variety of activities is possible. Unfortunately, there are currently no data on whether hybridization of these cells occurs in humans or animals in vivo. However, the appearance of a hybridoma with immunosuppressive activities is not only feasible but is known to occur. This is possible because the conditions required for the fusion of transformed malignant cells and immunosuppressive cells are similar to those in vitro, including temperature, nutrients, and the presence of factors capable of inducing hybridization. Physical and chemical carcinogens and oncogenic viruses fall into the latter category. The specific role of these cells in cellular fusion can be mimicked by several medical drugs, including emetine and actinomycin, and by non-oncogenic viruses (e.g., vaccinia virus, influenza, parainfluenza, herpes, rubella viruses, and other viruses), which not only induce tumors in mammals but also cause the fusion of multiple cells into a single multicellular mass [1]. The authors reported that the formation of this cell mass is specific to many exogenous and endogenous viruses. It is clear that the conditions (temperature, nutritional substances, and growth factors) are favorable for promoting the formation of an immunosuppressive hybridoma in humans or animals by inducing the fusion of transformed malignant cells and immunosuppressive cells.

There is some evidence to show that immunosuppressive hybridoma develop in patients with cancer or in animals, based on the results of studies examining the roles of oncogenic viruses and carcinogens in the growth of some malignant tumors. In particular, researchers found the cells that were able to suppress the humoral and cellular immune responses to tumor antigens. For example, the response of lymphocytes to phytohemagglutinin was reduced in mice with sarcoma

during tumor growth. The response to phytohemagglutinin was restored if the highly adhesive cells were removed from the lymphocyte suspension. It was also found that tumors and their waste products had immunosuppressant properties. The mixed lymphocyte reaction to normal allogenic cells was inhibited by exposing thymocytes to a homogenate of malignant cells [17]. In 1988, Toge et al. reported a 2–3-fold increase in suppressor inducer T cells (CD4 2H4) and suppressor T cells (CD8 CI11) in the spleen cell populations of 56 patients with stomach cancer [18]. The highest frequency of these cells was found in the recirculating splenocyte fraction. Concanavalin A-dependent suppressors displayed the greatest activity in this population of cells. This activity increased in the late stage of cancer. Apart from suppressor cells and malignant cells capable of inhibiting the immune reactions to cancer antigens, these activities are also typical of the serum factors present in blood samples from patients or animals with tumors [19, 20, 21]. Exposing lymphocytes to these factors in vitro inhibited their immune responses to phytohemagglutinin and pokeweed mitogens.

Splenomegaly caused by the aggregation of lymphocytes occurred during tumor growth in animals. The lymphocytes contributed to tumor growth binhibiting immune reactions. This phenomenon was eliminated by removing the primary tumor. Injectiny g animals with sensitized T lymphocytes after tumor resection prevented the death of 50% of the animals [22, 23]. In my opinion, suppressing the immune responses to malignant antigens after primary tumor resection provides convincing evidence that the development of immunosuppressive hybridomas is a major factor in the growth of a cancer and its metastasis. This is likely to hinder maximum protection of sensibilized T-lymphocytes from tumor.

Conclusion: I proposed a hypothesis that cancers grow because of the formation of an immunosuppressive hybridoma in the host through the fusion of transformed malignant cells and immunosuppressant cells. Physical and chemical carcinogens, and oncogenic and non-oncogenic viruses promote the transformation of cells and are major factors that induce the hybridization of these cells. Hybridomas maintain the ability of transformed cells to divide infinitely, thereby supporting invasive growth, and maintain the ability of immunosuppressive cells to overcome immunosurveillance. These are major factors that underlie the growth of malignant tumors and their metastasis.

This hypothesis of carcinogenesis is illustrated in Figure 1. This hypothesis not only provides a new understanding of carcinogenesis but also unites existing theories of carcinogenesis and the roles of viral and genetic factors that were proposed before the theory of transformed malignant cells overcoming immunosurveillance.

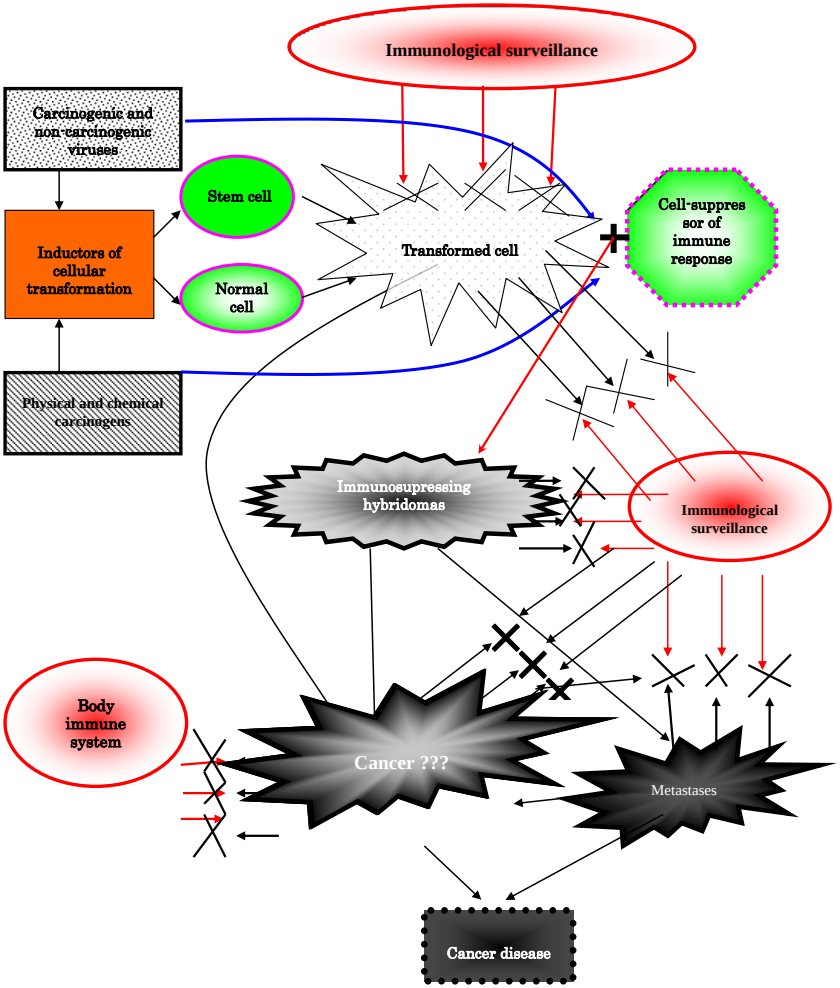


Figure 1 - Oncogenesis scheme

References:

1. Bukrinskaya A.G., Zhdanov V.M. Deproteinization of animal and human enveloped viruses by transmembrane penetrating to a cell//Discoveries in the USSR. 1987. - Pp. 35-36. (in Russian).
2. Georgiev G.P. On the mechanism of carcinogenesis: a "promoter hypothesis// Molecular Biology.1981. V. 15 (2), Pp. 261-273 (in Russian).
3. Zilber L.A., Irlin I.S., Kiselev F.L. Evolution of the virus-genetic theory for beginning tumour. 1975. Moscow: Nauka, 344 pp (in Russian).
4. Kovalev B.M. Immunosupressive hybridoma in a body as a primary condition for cancer development// Proceedings of the XIV International Congress on Allergology and Immunology. October, 1991, Kyoto, Japan.
5. Kosjakov L.N., Kosjakova N.P. Antigens of human tumors. 1985. Moscow: Medicine. Pp. 207-210 (in Russian).
6. Mazurenko N.P. Induction of mammalian tumors by non-oncogenic viruses (virus to virus co-cancerogenesis). Discoveries in USSR. 1980. Pp. 42-45 (in Russian).
7. Pashinsky V.G. On the cancer pathogenesis mechanism as the terminal stage of adaptation and pathological response// Actual Problems of Modern Oncology. 1986. Novosibirsk. V. 4. Pp. 39-45 (in Russian).
8. Petrov R.V. Immunology. 1987. Moscow: Medicine. 415 pp. (in Russian).
9. Shabad L.M. Experimental and morphological problems of cancer// Archives of Pathology. -1973. V.35 (8). P. 61 (in Russian).
10. Davidson R., Gerajd P. Improved technigues fer induction of mammalian cell hybridisation by polyathyleneglicol // Somat. Genet. -1976. V. 2. P. 165.
11. Herbrman K., Campbell D., Oldhan R., et all. Immunogenicity of tumor autigens // Proc. Intern. Confer. Immunobiology of Cancer. Academy of Scibuces. 1976. P. 276.
12. Kennet R H., McKearn T.J., Bechtol K.B. Monoclonal Antibodies. Hybridomas: A New dimension in Biological Analyses. New York: Plenum Press. 1981. 416 pp.

13. Kircher H., Holdon H., Gluser M. Et all. Suppression of in vitro limphocyte stimulation in mice bearing primeri Meloney sarcoma virus induced tumor// Cell Immunol. 1974. V. 13.P. 32.
14. Kunicka J., Calveler T., Fox F. Et all. Human suppressor factor constitutivoly produced by T-T cell hybridomas: functional and biochemical characterization // Hybridoma. 1989. V. 8 (3). P. 127-151.
15. Lilley D., Burger D., Vettj R. Tumor growth in the guinea-pig alfha globulin chages associated with lymphocyte suppression// I S. Nft. Cancer Inst. 1974. V. 53. P. 701.
16. Ocehino J., Clasgow A., Cooper S. et all. Isolation of an immunosuppressive peptide fraction from human plasma// J. Immunol. 1973. V. 110. P. 685.
17. Tanigushi M., Saito T., Tada T. Antigen-specific suppressive factor producent by a transplantable l-sbearing T-cell hybridoma// Nature. 1979. V. 278. P. 555.
18. Taussig M., Holliman A. Structure of an antigen-specific suppressor factor produced by a hybrid T-cell line// Nature. 1979. V. 277. P. 308.
19. Toge T., Kuroi K., Kuninobu H., et all. Role of the Spleen in immunosuppression of gastric cancer: Predominance of suppressor precursor and suppressor inducer T-cells in the recirculating spleen cells // Clin. Exp. Immunol. 1988. V. 74 (3). P. 409-412.
20. Treves A., Carnaud C, Trainin N., et all. Enhancing T-lymphocytes from tumor - bearing mice suppress host resistance to a syngenere tumor// Eur. J. Immuol. 1974. V.4, P. 722.
21. Treves A., Cohrn I., Feldman M. Immunotherapy of lethal metastases by lymphocytes sensitized against tumor cell in vitro// J. Nut. Cancer Inst. 1975. V. 54, P. 777.
22. Vetto P., Burger D., Lillet D. Evaluate on of immune status in tumor patients// Arch. Surg. 1974. V. 108, P. 558.

Chapter 38

REHABILITATION OF POST-STROKE PATIENTS IN AN OUTPATIENT SETTING

T.A. Kantur, E.V. Khmeleva, N.A. Doroshenko, A.V. Kudryavykh
Far Eastern Federal University Medical Center
10 Ajax, Russian Island, Vladivostok, 690922, Russia
e-mail: kanturovichi@yandex.ru

Cerebral stroke is the most severe manifestation of cerebrovascular disease. Itoccurs in up to 6 million people annually, worldwide. In Russia,stroke occurs in excess of 450,000 people every yearwith a mortality rateas high as 35% [1].Many complex issues regarding the diagnosis and treatment ofcerebral stroke have already been addressed. However, the outcomes of rehabilitation of patients are difficult to quantify, and rehabilitation is not always sufficiently effective.

The most common effects of stroke are movement disorders in the form of paralysis and paresis, typically one-sided hemiparesis with a range of severity. According to the Register of the Stroke Institute of Neurology, the acute phase of stroke hemiparesis was observed in 81.2% of survivors, and included hemiplegia in 11.2% of patients, rough and pronounced hemiparesis in 11.1%, and mild to moderate hemiparesis in 58.9% [2].

The Rehabilitation Center at Far Eastern Federal University is at the forefront of new developments in the field of stroke rehabilitation. The current paradigm forthe rehabilitation of post-stroke patients is characterized by a multidisciplinary approach delivered bya team comprising a neurologist, physical therapist, speech therapist, physiotherapist, and massage therapist.

Rehabilitation focuses on the physical therapy of movement disorders, including active and passive physical therapy and biofeedback. Additional methods include massage therapy and physiotherapy. Transcranial magnetic stimulation or transcranial direct current stimulation may also enhance the brain's ability to rewire itself after a stroke. Electrical stimulation of the nerves or muscles in the arm or leg can elicit movement of the weakened limb, and there is some evidence

that repeated treatment can partially restore movement. Partial body-weight-supported treadmill training in which the patient is held in a harness to reduce the weight exerted through the legs together with practice walking on a treadmill isalso particularly useful in the early phases of recovery, especially in patients with substantial difficulty in regaining their ability to walk.

In conclusion, the rehabilitation of post-stroke patients in a rehabilitation center should focus on physical therapy and medical gymnastics in order to improve their physical abilities.

References:

1. Kovalchuk VV, Lalayan TV, Smolko DG Functional state of patients after stroke: the possibilities of modern approaches to therapy. Effective pharmacotherapy. 2013; 15: 8-13.
2. Aziz N., Leonardi-Bee J., Walker M. et al. Therapy-based rehabilitation services for patients living at home more than one year after stroke. Cochrane Database Syst. Rev. 2008; 2: 52—9.

1st and 2nd JRIC SSD, 2014–2015

HOKUTO SOCIAL MEDICAL CORPORATION

ISBN 978-4-9908110-0-6
C3347 ¥10000E