

## MEDICAL SCIENCE

MEDICALIZATION OF  
SOCIETY 52

SPIRITUALITY AND  
MEDICINE 9

IMMUNOLOGIC  
MICROARRAYS 21

MEDICAL ETHICS 56

BIOETHICS AND  
EDUCATION 6

NEW GENERATION  
"CYTO-EXPERT" 43

COPD PHENOTYPES 25

ROLE OF FRACTALKINE 46

URINARY SYSTEM  
ORGANS PATHOLOGY 35

BABESIOSIS IN  
UKRAINE 16

## Editorial Board

### *Editor-in-Chief*

**Jean-Francois Deveny**  
President, FranceXP, Paris, France

### *Editors*

**Professor Du Hong Wei**  
Professor of Philosophy, Cultural Scholar, China

**Dr Ayesha Ahmad**  
Lecturer in Global Health, St George's University of London, Honorary lecturer in Global Health, Institute for Global Health, University College London, UK

**Dr Tharun Sathyan**  
Resident doctor, Kiev National Medical Academy, Ukraine.  
Lecturer and senior specialist in the field of dental health, clinical dentistry and health administration.  
Member of the American Academy of Implantology.  
Indian center for Hospital Administration. India / Ukraine

**Professor Iryna Sorokina**  
Head of the Department of Pathological Anatomy, Kharkiv National Medical University, Ukraine

**Professor Tetyana Ospanova**  
Head of the Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Head of the Committee on Ethics and Bioethics, Kharkiv National Medical University, Ukraine

**Dr Mykhailo Myroshnychenko**  
Associate Professor, Department of Pathological Anatomy, Kharkiv National Medical University, Ukraine

**Dr Valentyna Berezenko**  
Head of the Department of Pediatric Hepatology, National Bogomolets Medical University. Scientific Secretary of the Government Institute of Pediatrics, Obstetrics and Gynecology, National Medical Sciences Academy of Ukraine, Ukraine

**Olga Zubkova**  
Technical Director, Montenegro

**ISSN 2273-2640**

### **Regional Innovations is indexed in:**

Advance Science Index  
GIF – Global Impact Factor  
EconPapers  
Registry of Open Access Repositories  
IDEAS REPEC  
OCLC WorldCat  
RINC  
Google Scholar

### **Under evaluation:**

Ulrich's Periodicals Directory  
Index Copernicus  
Scopus

## About InterRegioNovation

**InterRegioNovation** is the International Association devoted to the transfer and exchange of knowledge and innovations at all regional levels (country, region, city, community etc.) between knowledge transfer professionals (business, research institutions, policy makers, government agencies, individuals, others) in all countries of the enlarged Europe, CIS countries and from other continents for stimulating and enhancing economic and social growth in the regions.

This is a policy and research association that brings together all knowledge transfer professionals who are interested in delivering efficient, flexible, innovative and cost-effective services across the private and public sectors. We work closely with business, research and educational institutions, government agencies, policy makers, NGOs, media, individuals and other stakeholders to promote the interests of their industries.

Our members understand the changing needs of the transfer and exchange of knowledge and innovations and through continuous professional development, marketing and networking opportunities offered in this association, we keep current with the latest knowledge trends and issues that challenge people in their work and life journey. We also offer expansive opportunities for partner connection through our networks.

Journal "Regional Innovations" is one of the Association's tools for innovators and everybody who is interested in any aspects of innovation development.



[www.irn.center](http://www.irn.center)

### **Contacts:**

E-mail: [info@irn.center](mailto:info@irn.center)  
Address: 16, rue de la Roche,  
Crégy-lès-Meaux, 77124, France  
Tel. : +33 6 48 18 86 95

## About journal

On behalf of the Editorial Board, it gives us a great pleasure to welcome you to the forth issue of 2017 of the Regional Innovations Journal. This is a thematic special issue dedicated to broad aspects of **Medical Science and other innovative research areas** from basic research to clinical and experimental work.

This particular volume provides a platform for advances in basic, translational and clinical research and includes original papers on medical and clinical research, health care innovations, reviews, medical teaching, medical law, medical ethics, spirituality and medicine, policy environmental medicine and integrative general practice. Researchers in academic and clinical settings as well as health professionals are encouraged to publish their theoretical and experimental results in this journal, which aims to integrate expertise in different medical specialties.

This is an independent, peer-reviewed, Internet-based international journal devoted to publishing original research papers of highest quality, sharing ideas and discussing innovation sector within regional dimensions. The journal welcomes to submit research papers by exceptional innovators, leading universities, globally recognized business, government agencies, policy makers and political leaders.

We intend that our readers will be exposed to the most central and significant issues in innovations development. We wish to publish papers that exemplify the highest standards of clarity, and that promise to have significant impact on existing front-line debates or to lead to new ones. The journal explores key priorities of the knowledge and innovations transfer and exchange in terms of critical aspects of human life (economy, law, science, business, health, education, culture etc.). We therefore welcome submissions not only from established areas of research, but also from new and emerging fields and those which are less well represented in existing publications, e.g. engineering studies, biomedical research etc.

We also strive to ensure that being under expert evaluation, each submission will receive developmental and supportive comments to enhance the article. Our refereeing process will involve that each submission will be reviewed by one or more specialists in the relevant field. Articles will be added to the volumes and the journal audience will receive e-mails updates to encourage them to the new articles.

We are delighted with, and immensely grateful to the large numbers of colleagues, both members of the Associations InterRegioNovation and FranceXP (France), representatives from many universities in France, Latvia, UK, Azerbaijan, China, Nigeria, Belarus, Ukraine and other institutions, who have supported the editorial process. And we are very proud of the expertise that they collectively bring, which we believe is unsurpassed by any contemporary innovative journal.

We are immensely grateful to our colleagues for their support and advice through the process of setting the journal up, and for the confidence they have placed in us in supporting this initiative at a time of economic uncertainty.

In the development of the Regional Innovations to date, we would like to enlist the support of a number of organisations who wish to promote this online journal to their experts. To ensure its sustainability, we would also like to invite other organisations, networks, conferences and meetings to associate themselves with the Regional Innovations. We therefore aim for the Regional Innovations to become the leading online forum to globally disseminate outstanding research papers on innovation sector in regional dimensions. Being an online periodical, the Regional Innovations is also a forum for exchange of imaginative ideas readers wish to share. Contributions of articles on innovations sector and your comments about this issue are very welcome.

To this end, if you lead, represent, or are a member of any such organisation, please contact us to offer your support and commit to promoting the Regional Innovations as a publication outlet for research undertaken by your experts.

We do hope you enjoy and benefit from the Regional Innovations! And many thanks for staying with us in 2017!

**Jean-François Devemy**  
**Editor-in-Chief**

## Contents

<b>BIOETHICS AS AN IMPORTANT COMPONENT IN TRAINING AND RETRAINING OF MODERN HEALTHCARE PERSONNEL</b> <i>Valery Kapustnyk</i>	6
<b>SIGNIFICANCE OF SPIRITUAL VALUE IN MODERN MEDICAL MECHANISM: THE PHILOSOPHICAL REFLECTION ON HEALTH OF MODERN PEOPLE</b> <i>Du Hongwei</i>	9
<b>REGIONAL AND CLINICAL-EPIDEMIOLOGICAL PECULIARITIES OF BABESIOSIS IN UKRAINE</b> <i>Vitaliy Tsymbaliuk</i> <i>Inna Torianyuk</i> <i>Iryna Sorokina</i>	16
<b>USING IMMUNOLOGIC MICROARRAYS FOR DIFFERENTIAL IMMUNOMORPHOLOGIC DIAGNOSTICS OF SOME LYMPHATIC TUMORS</b> <i>Aleksandr Shishkin</i> <i>Nikolay Kiryanov</i> <i>Natalia Ovchinina</i>	21
<b>COPD PHENOTYPES - THE WAY TO PERSONIFIED MEDICINE OF THE XXI CENTURY</b> <i>Tetyana Ospanova</i> <i>Zhanna Semydotska</i> <i>Ingeborg Chernyakova</i> <i>Olena Pionova</i> <i>Nataliia Tryfonova</i>	25
<b>PATHOLOGY OF THE URINARY SYSTEM ORGANS IN CHILDREN POPULATION OF UKRAINE: ITS PAST, PRESENT AND FUTURE</b> <i>Iryna Sorokina</i> <i>Mykhailo Myroshnychenko</i> <i>Nataliia Kapustnyk</i>	35

<b>CYTOANALYTICAL COMPLEX OF NEW GENERATION “CYTO-EXPERT” : ITS OPPORTUNITIES AND PROSPECTS</b>	
<i>Aleksandr Solov’ev</i>	43
<i>Aleksandr Shishkin</i>	
<i>Nikolay Kiryanov</i>	
<b>THE ROLE OF FRACTALKINE IN THE DEVELOPMENT OF INFLAMMATION IN PATIENTS WITH ASTHMA COMBINED WITH DIABETES MELLITUS TYPE 2 AND OBESITY</b>	
<i>Galyna Yeryomenko</i>	
<i>Tetyana Ospanova</i>	46
<i>Tetyana Bezditko</i>	
<i>Olena Vysotska</i>	
<i>Anna Pecherska</i>	
<b>MEDICALIZATION OF THE MODERN UKRAINIAN SOCIETY: PRO ET CONTRA</b>	
<i>Mykhailo Myroshnychenko</i>	
<i>Olha Omelchenko</i>	52
<i>Elena Lytvynenko</i>	
<i>Dmutro Molodan</i>	
<b>MEDICAL ETHICS: AN OVERVIEW</b>	
<i>Ayasha Ahmad</i>	56
<i>About authors</i>	61
<i>Requirements for papers</i>	67
<i>Call for Papers – 2018</i>	68



**Prof VALERY  
KAPUSTNYK**

*Professor, First Vice-  
Rector for Research and  
Education,  
Kharkiv National Medical  
University, Ukraine*  
prorector1@knmu.  
kharkov.ua



## BIOETHICS AS AN IMPORTANT COMPONENT IN TRAINING AND RETRAINING OF MODERN HEALTHCARE PERSONNEL

### **Abstract**

*Modern educational activity of higher medical schools must be directed at both receiving of professional knowledge, skills and habits by their students and forming of the morals, which are implanted into the students in the process of study of bioethics. Despite a wide spread of bioethical information in medical educational institutions the process of formation of a bioethical mindset in the medical community is, unfortunately, on a low level. In this article its author emphasizes the necessity of actualization of bioethical education in the process of training of modern healthcare personnel; this education must be continuous and begin in the medical educational institution at the theoretical and clinical departments, receiving its development and completion in the system of postgraduate training and professional activity of doctors.*

**Key words:** *bioethics, education, healthcare personnel.*

Scientific and technological progress as an uninterrupted and systematic process of practical application of results of the development of science and technology facilitates a rapid development of different fields of modern medicine. Innovations, as a determinative result of scientific and technological progress, stimulate increases in productivity and efficacy of using productive factors and rises in the quality and competitive capacity of the country's production [1]. It is owing to scientific and technological progress in medicine that we observe developments in transplantation of organs and tissues, cloning, assisted reproduction technology, genetic engineering and gene therapy, use of stem cells for treating diseases, a wide use of euthanasia and many other things.

Scientific and technological progress demands higher standards of professional knowledge, qualification and managerial capabilities as well as of the general cultural and intellectual level of the workers, increases the role of moral incentives and personal responsibility in work [2].

Medicine is based on moral norms, is of moral importance and full of profound moral significance. Neglect of the relation between morality and medicine

results in both disintegration of the latter and destruction of the "whole natural basis of the human society" [3]. In this connection, modern educational activity of higher medical schools must be directed at both receiving of professional knowledge, skills and habits by their students and forming of morals [4, 5].

Despite a wide spread of bioethical information in medical educational institutions the process of formation of a bioethical mindset in the medical community is, unfortunately, on a low level. The above may be caused by two facts: firstly, some medical workers believe that professionalism must prevail over everything, including culture and moral values; secondly, in some higher medical schools bioethics is taught by health professionals, who do not have any philosophical education.

The current situation in Ukraine actualizes the problem of teaching of bioethics in higher medical schools, as it was also noticed at the VI National Congress on Bioethics, which was held in Kyiv in September 27-30, 2016 [6].

Bioethics is defined as the science that studies social, legal and ethical consequences caused by appearance of new sophisticated biomedical technologies, a high cost of treatment and new rights of patients. In many

textbooks bioethics is also understood as the science about laws, principles and rules of regulation of the professional behaviour of the medical worker that in conditions of new medical technologies makes it possible not only to use achievements of science and technology to the benefit of the man but also to warn doctors about the impermissibility of causing harm to people and their progeny [7].

One of the first founders of bioethics was the American biochemist Van Rensselaer Potter, who wrote the book *Bioethics: Bridge to the Future*, published in 1971. He realized that scientific-technical achievements of the mankind, particularly in the sphere of biomedical technologies, were of both positive and negative character, since they produced their direct effect on the man's body and mentality, his nature and essence at large [7]. As he pointed out the goal of his book consisted in making a contribution into the future of the human race by formation of a new discipline named "Bioethics". If "two cultures", science and humanitarian knowledge, exist and are evidently unable to conduct a dialogue and if this is one of the reasons why the future is more doubtful than possible, then nevertheless we can construct the "bridge to the future" with help of this new discipline as a bridge between the two cultures [8].

In V. P. Potter's view, the medical scientist and practitioner of the third millennium must synthesize and organically combine knowledge with deep thinking about the humane application of this knowledge to practice in order not to harm the patient or the healthy person; he must be able to forecast the positive development of the above knowledge into the future. According to V.P. Potter's data, the highest duty of the man consists in the preservation of life on the Earth [8].

Bioethics is known to rest upon four basic principles (autonomy, harmlessness, beneficence, justice), five ethical norms (honesty, privacy, confidentiality, loyalty, competence) and resultant ethical standards in the doctor's behaviour, which can differ since it presents solutions of concrete ethical problems in concrete situations [9].

The educational process in the higher medical school is sufficiently hard and intensive; during its course it is necessary both to pay due attention to special disciplines and create organizational-methodological conditions facilitating development of the bioethical mentality of medical students [10].

In Ukraine, the formation of a biomedical mindset in students of higher medical schools is realized during the whole period of training at theoretical and clinical departments, therefore several levels of bioethics mastering are distinguished. At the first, theoretical, level a foundation of moral upbringing of future doctors in the system of philosophic education is created. Teaching of bioethics as a philosophic discipline makes it possible to demonstrate students that morality is one of the most important forms of the public conscience, which reflects the social being, while the formation of moral standards and values is a historically caused process, in which moral principles indicate key moments in the development of the mankind and produce their own effect on the course of the social evolution [5].

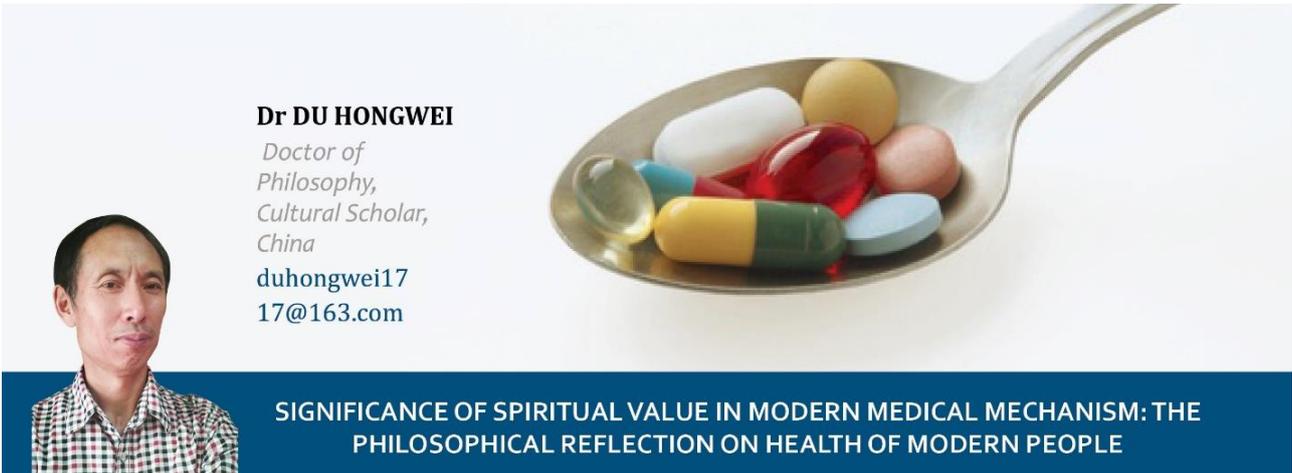
The second level of bioethics mastering is professional; this one consists in a continuous widening, deepening and concretization of knowledge in the field of bioethics while studying clinical disciplines [5], when the student contacts with experimental animals in laboratories, cadaveric material during autopsies, and with patients in the process of asking them about their complaints, taking their case histories and carrying out their objective examination.

The doctor is the person, who is continuously studying and raising his level of knowledge during all his life. The bioethical education of the doctor must not end after graduation from a higher medical school; it must receive its logical development and completion in the system of postgraduate training and professional medical activity. This is because the medical worker is a calling, which requires specific moral and spiritual qualities, rather than only a profession [11].

Conclusion. Bioethics is an important component in the educational process of healthcare personnel as it is the moral and ethical culture of the doctor that together with his professionalism and competence plays a significant part in his successful professional activity. It is necessary to actualize the problem of bioethical education in the process of the modern healthcare personnel training, which must be continuous and begin at medical educational institutions, receiving its development and completion in the system of postgraduate training and professional medical activity.

## References

1. Kovaleva T. Yu. Review of methodological approaches to evaluation of the level of scientific and technical progress: country and regional aspects / T. Yu. Kovaleva // *Vestnik of Astrakhan State Technical University. Series: Economics.* – 2015. – No. 3. – P. 20-32.
2. Kasyanov V. V. Society and a human being in terms of scientific and technical progress / V. V. Kasyanov // *Society: Sociology, Psychology, Pedagogics.* – 2012. – No. 1. – P. 11-15.
3. Characteristics of initial bioethical views of medical school students / T. G. Svetlichnaya, G. N. Chumakova, E. S. Stepanov, N. S. Larionova // *Human ecology.* – 2015. – No. 5. – P. 14-20.
4. Muzalevskaya L. V. Actualization of the problem of bioethics thinking formation in the students of medical higher schools / L. V. Muzalevskaya, N. N. Blokhina // *Siberian medical journal.* – 2011. – No. 3. – P. 141-143.
5. Ovsyannikova E. K. Teaching bioethics as a philosophical discipline / E. K. Ovsyannikova, V. M. Marukhno // *International journal of experimental education.* – 2013. – No. 4. – P. 209-211.
6. Hubenko G. Integrative pedagogical bioethics as prospect of educational discourse / G. Hubenko // *Philosophy of education.* – 2016. – No. 2 (19). – P. 271-274.
7. Begalinova K. K. The modern bioethical problems of medicine and the ways of their solving / K. K. Begalinova, A. S. Begalinov // *Professional education in the modern world.* – 2013. – No. 4 (11). – P. 65-73.
8. Gubenko A. Global biological ethic and becoming of modern appearance of science / A. Gubenko // *Contemporary picture of the world: Nature, society, people: a collection of scientific works / State Higher Educational Institution «Ukrainian Academy of Banking of the National Bank of Ukraine».* – Sumy, 2008. – P. 133-138.
9. Semenova O. A. Formation of the bases of bioethics as a component of the moral education of students of medical universities / O. A. Semenova // *Bulletin of the University of the Russian Academy of Education.* – 2010. – No. 3. – P. 143-146.
10. Sokolov V. M. Principle of bioethical responsibility in moral values continuum of modern medicine / V. M. Sokolov // *Bulletin of Siberian Medicine.* – 2006. – No. 5. – P. 147-150.
11. Kashin A. V. Modern doctor – the formation of ethical aspects of work in the modern healthcare system / A. V. Kashin // *Humanitarian expertise.* – 2012. – No. 1. – P. 261-262.



**Dr DU HONGWEI**

Doctor of  
Philosophy,  
Cultural Scholar,  
China

duhongwei17  
17@163.com

## SIGNIFICANCE OF SPIRITUAL VALUE IN MODERN MEDICAL MECHANISM: THE PHILOSOPHICAL REFLECTION ON HEALTH OF MODERN PEOPLE

### Abstract

Medical care and health is a compound issue, which does not only need to be solved from the aspect of economic input, scientific and technological progress and social security, but shall also from humanistic care, social morality as well as cultural education. In addition to genetic factors, diseases of people are also connected with personal living habit and mental state. Whether for the purpose of prevention or treatment, understanding of medical care and health issue of modern people from the perspective of spiritual value has important practical significance. Oriental culture includes health preservation wisdom, and treatment of diseases and administration of countries follow the same philosophy, thus the significance of health on success and happiness could be viewed from the perspective of life philosophy.

### 摘要

医疗与健康是个多元化问题，它的解决不仅需要从经济投入、科技进步和社会保障等方面入手，也需要从人文关怀、社会道德和文化教育等方面寻找出路。除遗传因素外，人的疾病也与个人的生活习惯、精神状态有关，无论是预防还是治疗，从精神价值角度认识现代人的医疗和健康问题有重要的现实意义。东方文化包含养生智慧，治病与治国有同样的哲学。从生命哲学角度看待健康对成功与幸福的意义。

**Key words:** medical insurance, population health, medical moral, spiritual value and health preservation philosophy.

**关键词:** 医疗保险，群体健康，医疗道德，精神价值，养生哲学，

Both the cause and proper treatment of diseases are closely related to the ideology and social morality of people. People give up their own health for success in the rapid pace of life while medical service institutes often cannot offer timely and high quality medical service for patients because of their own reason.

### 1. Medical institutions shall accept moral supervision

Although the medical skill is making progress, the morality issue of medical institutions is also serious. Taking China as an example, medical institutions have the common problem such as misuse of medicines and

疾病的产生和合理治疗都与人的思想意识、社会道德紧密相关，现代快节奏生活使人为了成功而顾不得关照身体健康，而医疗服务机构常因自身原因不能为患者提供及时和高质量的医疗服务。

### 1, 医疗机构应接受道德监督

虽然医疗手段在进步，但医疗机构的道德问题也很严峻。以中国为例，医疗机构普遍存在滥用药品、推销不必要的医疗服务等问题。对于求医的患者来

recommendation of unnecessary medical service. For patients seeking medical advice, the information got by patients and doctors is not symmetrical because of the restriction of professional knowledge and in most cases, the medical result or life of patients is mastered by doctors. Therefore, the moral cultivation of doctors will affect the interests and benefits of patients. Nowadays, there are still medical institutions taking illegal acts in the world and there is moral controversy over many new medical treatment methods. Driven by enormous economic benefit, many patients die of misuse of drugs or overtreatment. It is particular true for cancer patients, as some pathological changes resulting in the death of patients are caused by treatment of other diseases. The diseases and deaths caused by medical negligence often occur at every place across the world. For instance, many babies died in an Indian hospital lately, thousands of people are infected with AIDS in rural area of Henan and other provinces in China. Some people die as not timely treated.

Organ transplantation, gene cultivation, surrogacy and other new treatment means and medical service that have began to be used internationally still need to be evaluated by law and morality, for instance, euthanasia, test-tube baby, channel of procurement of organ needed in organ transplantation, management of medicines that can be used as drugs. The moral restriction of development of medical science and application of medical technology needs to be made from the perspective of life philosophy and spiral value. Otherwise, mankind will lose their own health guarantee and life value in the irrational medical development in future.

At present, many private capitals in China are invested into medical industry and pharmaceutical production industry. The profit-making medical behavior is getting worse. For example, the huge profit of pharmaceuticals and medical services make pharmaceutical factories and hospitals become the intuitions seeking excessive profits. When there is not sufficient legal restraint, the social morality, humanist spirit and the passion of medical workers for life of patients become very important.

## 2. Significance of medical insurance

Currently, countries in the world adopt different medical security policies and Ukraine and Russia even keep free social medical system while setting up private medical institutions. In developed societies with higher citizenship education level, medical care shall not be the low level social welfare for all the people, but shall be the paid service with high quality and efficiency. The level of social civilization is reflected in the care for the weak, but it

说，由于专业知识的限制，病人和医生所知道的信息是不对称的，大多情况下病人的医疗结果或生命是掌握在医生的手里。所以，医生的道德修养会影响到患者的利益。目前，世界上依然存在医疗机构的违法行为，许多新的医疗手段存在道德争议。为巨大经济利益驱使，很多病人死于滥用药物或过度治疗。尤其癌症病人，一些造成病人死亡的病变是治疗其它疾病时引起的。由于医疗事故引起的疾病和死亡事件在世界各地常有发生。如：前不久发生的印度医院大批婴儿死亡事件、在中国河南等地农村数千民众因输血被感染艾滋病等等。有些病人因得不到及时救治而死亡。

国际上已开始采用的器官移植、基因培植、代孕等新的治疗手段和医疗服务还有待法律和道德的讨论，如：安乐死、试管婴儿、器官移植中器官的获取渠道、可以作为毒品的药物管理，等等。需要从生命哲学和精神价值观的角度对医学的发展和医疗科技的应用做出道德约束。否则，人类会在未来不理性的医疗发展中丧失自身的健康保障和生命价值。

目前，中国有很多私人资本投向医疗行业和药品生产行业。以营利为目的的医疗行为正在加剧，如：药品和医疗服务的巨额利润使药厂和医院成为暴力机构。在缺少足够法律约束的情况下，医务工作者的社会道德、人道主义精神和对患者生命的热爱显得十分重要。

## 2, 医疗保险的意义

目前世界各国采用不同的医疗保障政策。乌克兰、俄罗斯还保留了社会免费医疗体系，同时也设有私立医疗机构。对于有较高公民教育水平的发达社会而言，医疗不该是针对所有人的低水平的社会福利，而应是高质量、高效率的有偿服务。社会的文明程度体现在对弱者的关怀上，同时也要注意，

shall be noticed that the sickness shall not be taken as a reason to get social welfare objectively or free medical care shall not be regarded as an award to sickness in economic form. Therefore, except children, disabled, retirees and people engaging in some special work that can enjoy free medical care, medical service shall be considered as a kind of personal consumption and be guaranteed through universal medical insurance.

The statistics of WHO shows 80% factors of diseases of people are connected with personal living habit and spiritual factor. From this perspective, diseases are personal life incidents, thus patients shall be responsible for their own diseases except genetic factors and social accidents. No success is worthy of being exchanged with health and life.

China does not provide free medical care for the civil and the medical burden of the public is mainly alleviated through medical insurance. At present, personal average medical burden of citizens accounts for less than 20% of total medical consumption, the rate of which is acceptable by the public. Personal average medical burden of civil servants, teachers, scientific and technical workers and other public servants accounts for less than 10% of total expenditures, and insurance premium is borne by working units or companies. The medical service of some special diseases such as AIDS, psychosis and rehabilitation of the disabled is provided by the country for free and subsidized by social charity organizations. Free medical service is provided for people in remote rural area and communities with disadvantaged groups as well as those without source of income. As medical care is a paid service, waiting and reservation are not required in China generally. In recent years, the emergence of private and international medical institutions offers more selection for patients.

### 3. Spiritual value and prevention of diseases

Excellent doctors cure diseases for people whilst great doctors prevent people from getting sick. With respect to the cause of diseases, the research of Chinese traditional medicine and modern world medicine have similar view, believing the diseases of people have close relation with their psychological state, emotional stress and living habit. The method to avoid getting sick is to keep relaxed and natural state of mind and establish good interpersonal relationship. Those factors are just the reflection of cultural accomplishment and spiritual value in nature. Due to the reason such as social environment and lack of education, some bad living habit of modern people does not only undermine the health and cause diseases but can even result in death, such as smoking, taking drugs, excessive drinking, over fatigue, drug dependence,

不该在客观上把生病变成获取社会福利的理由或者把免费医疗等同于以经济形式奖励生病。所以，除儿童、残疾人、退休人员、军人和某些特殊职业可以享有免费医疗之外，看病应视为个人的特殊消费，通过全民医疗保险获取保障。

世界卫生组织统计，人的疾病 80% 的因素与个人生活习惯和精神因素有关。从这一点说，疾病是个人的生活事故，除遗传因素和社会事故外，病人对自己的疾病应负有责任。再伟大的成功也不值得用健康和生命去换取。

中国没有全民免费医疗制度，主要通过医疗保险解决公众就医负担。目前，公民个人平均医疗负担占总医疗消费的 20% 以下。这个比例是大众可以接受的。而公务员、教师、科技工作者等公职人员个人平均医疗负担占总支出的 10% 以下。保险金由工作单位、公司负责承担。一些特殊疾病如：艾滋病、精神病、残疾人的康复等医疗服务由国家免费提供，并有社会慈善机构资助治疗。在偏远农村、贫困群体的社区和没有经济来源的人群提供普通的免费医疗服务。由于医疗是有偿服务，在中国看病一般不需要等待和预约。近年私人医疗机构和国际医疗机构的出现，给患者提供了更多的选择。

### 3， 精神价值观与疾病的预防。

优秀的医生为人治病，而伟大的医生让人避免生病。就疾病的产生，中国传统医学与现代世界医学研究有相似的看法，认为人的疾病与人的心理状态、情绪压力和生活习惯有重要关系。避免生病的方法就是保持精神轻松平和，心态自然，建立良好的人际关系。这些因素在本质上恰是文化修养和精神价值观的反映。由于社会环境和缺乏教育等原因，现代人的一些不良生活习惯不仅损害健康、引起疾病甚至直接导致死亡。如：抽烟、吸毒、酗酒、过度疲劳、药物依赖、艾滋病等等。

AIDS.

From the aspect of biological significance, the body characteristic of modern people and the physiological regularity required have a small difference with that 500 or 1000 years ago. However, the lifestyle, dietary structure, interpersonal relationship, psychological state and cultural concept of modern people are not only different from those 1000 and 500 years ago, but even different from those 100 years and 50 years ago, hence mankind does not have enough time to get used to modern society in body, mentality or soul. Such kind of physical and mental inadaptation also become the cause of diseases naturally. From the perspective of physical and mental health, it has practical significance for us to emphasize to keep traditionalism and individualism of culture; from the perspective of life philosophy, scientific development and health acquisition of mankind shall be centered on the benefit of life itself, not the other way round. While trying to change the world, mankind shall improve their ability to adapt to new life.

The humanitarianism today is reflected in the assistance and care of the society for the weak, but from an evolutionary perspective, disease is the test of nature for life and the elimination of the sick and weak is required by species evolution and the instinct for self-preservation. Thus, in ancient Greece in which only strong people can defeat enemy, Spartan follow the ethnics of abandoning sick and weak babies. Fortunately, mankind evolves to an era in which intelligence decides victory and knowledge is power. Otherwise, we would have missed Descartes and Hawking. Meanwhile, it also explains why Chinese are not physically stronger than people of other nations even China has old and developed traditional medicine and lots of knowledge about Chinese herbal medicine and method of health protection, as well-developed medicine provide chance for more patients and genes to survive and reproduce. Part of the selection mechanism of nature for the weak experienced by residents in Africa and Siberia is cancelled by well-developed Chinese traditional medicine.

From the perspective of human evolution, modern people are damaging the species quality of mankind unconsciously. Because of cultural concept, social environment and other factors, the marriage rate and fertility rate of competent people at workplace, scholars and other social elites are far lower than average social level, but the socially disadvantaged groups failing to receive sufficient education have higher marriage rate and fertility rate. In China, families in some poverty-stricken areas want to have more children and even parents with genetic defect also want to have offspring to help them make a living. The writer of this paper does not have social prejudice or ethnic discrimination, but social reality

从生物学意义上说，现代人类的机体特性和所要求的生理规律与500年前、1000年前的人类没有大的区别。但现代人类的生活方式、饮食结构、人际关系、心理状态和文化观念不仅不同于1000年、500年前，甚至不同于100年前、50年前。人类在机体上、精神上和灵魂上都来不及适应现代社会。这种生理、心理上的不适应自然也会成为疾病的原因。从身心健康角度看，我们强调要保持文化的传统性和个性化是有实际意义的，从生命哲学角度看，人类的科技发展和财富的获取都应该围绕生命本身的利益，而不是相反。在努力改变世界的同时人类更应该想到自己适应新生活的能力。

今天的人道主义体现在社会对弱者的救助和关怀上。但从进化论看，疾病是大自然对生命的考验，对病弱个体的淘汰正是物种进化的需要，也是种群自我保护的本能。因此，在身强力壮才能战胜敌人的古希腊时代，斯巴达人的伦理是丢弃病弱的婴儿。幸好人类进化到智力决定胜利、知识就是力量的时代，否则我们会错过笛卡尔，会失去霍金。但同时也说明了为什么中国有古老发达的传统医学，有丰富的中草药知识和保健方法，但中国人的体质并不强于其他民族？因为发达的医学让更多的病人和遗传基因有机会存活下来并繁殖下去。非洲和西伯利亚居民经历的大自然对弱者的淘汰机制在中国有一部分被发达的中医取消了。

从人类进化角度看，现代人正不自觉地破坏着人类的物种质量。由于文化观念和社会环境等因素，职场上的强者、学者和其他社会精英的结婚率和生育率远低于社会平均水平。而没有受到足够教育的社会弱势群体有更高的结婚率和生育率。在中国，一些贫困地区的家庭反而想要更多的孩子，甚至有遗传缺欠的父母也要生育后代，希望儿女帮自己谋生。本文作者没有社会偏见和民族歧视，但社会现实呼吁我们要关注弱势群体，全社会健康才有人类的进化。否则，大量无辜的儿童，一出生就面对贫

calls on us to pay attention to vulnerable groups and the health of the whole society is the basis of human evolution. Otherwise, lots of innocent children have to face poverty or congenital diseases or the life without cultural education right from birth. It would be hard for them, who are still a part of social population, to deal with the competitive society. The tradition of selecting babies by Spartan is cruel, but human evolution and social progress still need competition and strongers. We should not eliminate the weak, but shall improve and reduce the reason of having vulnerable children. Mankind shall also leave healthy gene for offspring in addition to material and spiritual heritages.

Hayek said, "Civilization is not designed by people's brain, but developed from the free effort made by millions of people". Although a civilized society has the obligation of providing medical care for all patients, every citizen is obliged to cherish health and try not to let the offspring have any hereditary disease. From this point, cultural accomplishment and spiritual value have great significance for improving the health quality of individuals and social groups.

#### 4. Medical philosophy is a kind of wisdom

Medical problem is also a philosophical issue. As far as treatment of diseases is concerned, the medicine in ancient China believes human body could make self-adjustment. Just like Hippocrates, a medical scientist in ancient Greek, said, "Diseases shall be cured through one's self-healing ability and doctors can only provide assistance". In fact, immunity will decline when people are down in spirit and many diseases are caused by mental factors. Some diseases even do not need to be cured by doctors. According to Chinese traditional medicine and Buddhist philosophy, ideology can change physical condition, thus both of them pay attention to improving the control of ideology for body organs through practice. The curing of some diseases is related to self-suggestion.

The psychological problems and mental diseases of modern people tend to increase, in particular, the number of patients with depression rises. Some people commit suicide because of long-term psychic pain. Some middle school students in China suffer from psychological illness or commit suicide because of study stress, some entrepreneurs commit suicide because of mental breakdown, and some stars in entertainment industry take drugs because of psychological problem. The root of and solution to social problems mentioned above can be found in spiritual value and traditional cultural concept. A person with good interpersonal relationship, ideal pursuit and spirit of self-sacrifice can come out from psychological struggle more easily.

困和先天疾病、面对缺少文化教育的生活。他们在未来难以应对充满竞争的社会，但他们将是社会人口的组成部分。斯巴达人的婴儿选择传统是残忍的，但人类的进化和社会的进步仍然需要竞争，需要强者。我们不能淘汰弱者，但应该改善和减少产生弱势儿童的原因。人类不仅要给下一代留下物质遗产和精神遗产，也要为后代留下健康的基因。

哈耶克说：“文明不是人的大脑设计出来的，而是从千百万人的自由努力中生长起来的。”虽然文明社会应该对任何一位病人尽到医疗的义务。但同时每个公民也有义务珍惜健康，尤其要努力避免将遗传疾病延续给后代。从这一点说，文化修养和精神价值观对提高个人和社会群体的健康质量都有重要意义

#### 4. 医疗哲学是一种智慧。

医疗问题也是哲学问题，就治病而言，中国古代医学认为人体有自调功能。正如古希腊医学家希波克拉底所说：“疾病的痊愈是要通过自身的自愈力，医师只是在旁协助而已。”事实上，情绪低落时免疫力会下降，很多疾病是精神因素造成的。也有一些疾病是不需要看医生的。中国传统医学和佛教哲学认为思想意识会改变身体状态，因此都重视通过修炼提高意识对人体器官的控制力。有些疾病的治愈与人的自我暗示有关。

现代人的心理问题、精神疾病有增加的趋势，尤其抑郁症患者增多。有些人因长期精神痛苦而导致自杀。在中国的中学生中出现因学习压力而患心理疾病或自杀的例子。有些企业家因精神崩溃而自杀。一些演艺界明星因心理问题而吸毒。上述这些社会问题都可以在精神价值观和传统文化观念中找到根源和化解的出路。一个有良好人际关系、有理想追求和忘我精神的人更容易从心理纠结中走出。

Some traditional Chinese culture can relieve anxiety and emotional stress and cultivate the mind and improve the character, for instance, Chinese painting and calligraphy art, Tai Chi, Buddhist meditation and tea culture. As the calmness, serenity and selflessness realm pursued by those traditional cultures are conducive to relieve anxious psychology and emotional fluctuation of people, and then alleviate the pain brought by diseases.

We could view the world with health preservation philosophy in reverse. The administration of a country is just like preservation of health of human body and government decision-making organization is the brain. Once the mind of people has any problem, the society will become instable. If the organ of authority of a country and the thinking of politicians could be kept rational and sober, and principle of peaceful co-existence in the world could be insisted, a country could make less error in action and public interest and social body will not be seriously damaged.

In 2017, 3 Nobel Prize programs are directly related to people's life, spirit and social behavior, including (Physiology) study of biological rhythm, (literature) revelation of the deeper part of human nature and (economics) analysis of the relation between cognitive psychology and economic behavior of people. These scientific research deepen the understanding of mankind for itself and also explains that economical behavior of mankind is returning to a rational and human era from a craze times lacking spiritual value. We believe in this trend, the health and medical care issue as well as survival and happiness of mankind will be solved in a better way along with the improvement of humanistic consciousness.

中国一些传统文化具有解除焦虑和情绪压力的因素，有修心养性的功能。如：中国书画艺术、太极拳、佛教冥想、茶道等等。因为这些传统文化追求的平静、安详和忘我的境界有助于解除人的焦虑心理和情感波动，由此达到缓解疾病痛苦的目的。

借用养生哲学反观我们的世界，治理国家如同人体保健，政府决策机构正是大脑器官。一旦人类思想出问题，社会就动荡。如果国家权力机构和政治家的思想能保持理性、清醒，坚持世界和平相处的原则，国家行为可以减少出错，避免民众利益和社会机体受到严重伤害。

2017年，有3个诺贝尔奖项目是直接关于人的生命、精神和社会行为的：（生理学）关于生物节律的研究，（文学）对人性深处的揭示，（经济学）分析了人的认知心理和经济行为的关系。这些科学研究加深了人类对自身的认识。也说明人类经济行为正由缺少精神价值观的疯狂时代向理性和人文时代回归。相信，在这一趋势中，人类的健康和医疗问题，人的生存与幸福问题也将随着人文意识的提升得到更好的解决。

## References

1. The Road to Serfdom, Friedrich Hayek
2. Leap from Ideal to Humanity, Ding Jianfeng, 2017, Caixin Cultural Magazine
3. Gao Yaojie, an anti-AIDS fighter, Baidu baike
4. Status of Chinese health insurance, Baidu baike

## 参考资料

- 1, 《通往奴役之路》，弗里德利西·哈耶克。
- 2, 《从理想到人性的跨越》，丁建峰，2017，财新文化杂志
- 3, 防艾滋病斗士高耀洁，百度百科
- 4, 中国医疗保险现状，百度百科



## REGIONAL AND CLINICAL-EPIDEMIOLOGICAL PECULIARITIES OF BABESIOSIS IN UKRAINE



**Prof VITALIY  
TSYBALIUK**

*Professor,  
Academician,  
President of  
National Academy  
of Medical Sciences  
of Ukraine,  
State Institution  
“Romodanov  
Neurosurgery  
Institute of  
National Academy  
of Medical Sciences  
of Ukraine”,  
Ukraine*  
[tsymbaliuk@  
neuro.kiev.ua](mailto:tsymbaliuk@neuro.kiev.ua)



**Dr INNA  
TORIANYK**

*Associate  
Professor,  
Laboratory of a  
New and Little-  
Studied Infectious,  
State Institution  
“Mechnikov  
Institute of  
Microbiology and  
Immunology of  
National Academy  
of Medical Sciences  
of Ukraine”,  
Ukraine*  
[kamysh\\_in@ukr.  
net](mailto:kamysh_in@ukr.net)



**Prof IRYNA  
SOROKINA**

*Professor, Head of  
the Department  
of Pathological  
Anatomy,  
Kharkiv National  
Medical University,  
Ukraine*  
[soririna@gmail.  
com](mailto:soririna@gmail.com)

### **Abstract**

*In this article the authors presented generalized data about the regional, clinical and epidemiological features of babesiosis in Ukraine. The authors of the article substantiated the factors of danger of this parasitosis, which are related to the geo-climatic features of the prevalence of pathogens of the disease and their carriers in Ukrainian regions, the high susceptibility of the human organism to this parasitic invasion, certain clinical polymorphism of the disease. On the example of the detection of new types of Babesia the analysis of the resources, capabilities and prospects of modern diagnostic methods taking into account regional specifics were carried out. The material about the clinical and epidemiological features of the babesiosis development was described in detail, the conclusions were confirmed by digital material.*

**Key words:** babesiosis, Ukraine, clinical and epidemiological features.

**Introduction.** Human babesiosis (B60.0 Babesiosis, Babesia invasion – BI, ICD-10) is an emergent obligate transmissible protozoan disease caused by protozoans of the genus *Babesia*. The causative agents of babesiosis are characterized by their ability to invade and parasitize in erythrocytes and haemopoietic organs and initiate an infectious process whose clinical course may vary from asymptomatic subclinical mild flu-like forms to a severe flash-like progressing disease (the fulminant form) with lethal outcomes.

Babesiae are a group of protozoan unicellular haemoparasites united into the genus *Babesia*, which together with the genera *Piroplasma* and *Fransaiella* are included into the family Babesiidae, the order Piroplasmida, the type Apicomplexa (or Sporozoa), the superphylum Alveolata, the subkingdom Animalia, the domain Eukaryota [4]. By today they have been recognized as the blood parasites, which are the most widespread in the world and dangerous for people, by the number of cases of their invasion these parasites being inferior only to trypanosomes (causative agents of African trypanosomiasis and Chagas disease). Specialists point out that babesiae are characterized by certain epidemiological and epizootic specificity, unpredictability of the clinical course and some difficulties in the ways of their diagnosis and prevention [14]. It is in view of the last feature and clear urgency of in-depth studies of the regional specificity of babesiosis spreading in Ukraine and its clinical-epidemic aspects of development that the present research began [1; 4].

**Problem statement.** The danger of babesiosis is based on the spread of causative agents of this disease, their carriers and, as it is known now, a rather high vulnerability of the human organism to parasitic invasions. Today we know more than 100 species of the genus *Babesia*, which infect many varieties of mammals and a number of birds [1; 4; 10; 15]. The number of *Babesia* species is continuously increasing owing to discovery of their new representatives. The use of resources of the molecular-biological (phylogenetic) classification of *Babesia* species in Ukraine and their grouping by evolutionary relationship [4; 6] have made it possible to confirm existence of 5 different groups (clades) of the causative agents. The 1<sup>st</sup> group consists of *B. microti*, including such species as *B. rodhaini*, *B. felis*, *B. leo*, the species *B. microti* itself and *B. microti*-like parasites, before KO-1, ovine Babesia-like. By the way, this group is characterized by a broad spectrum of warm-blooded hosts (small rodents, the Felidae, the Canidae, birds). The 2<sup>nd</sup> group unites such species as *B. duncani* (WA-1,2, the causative agent of babesiosis in dogs), *B. duncani*-like (before CA1-6, its natural reservoir is unknown), *B. conradae* (the aetiological factor of the disease of dogs in southern regions of the State of California, the USA). The 3<sup>rd</sup> group is made up of Theileria, which cause invasions in cattle. The 4<sup>th</sup>

group is formed by the “true” (*sensu stricto*) *Babesia* spp. with the species *B. canis* and *B. gibsoni* (isolated from representatives of the genus Canidae), as well as *B. divergens*, *B. divergens*-like (before MO-1), *B. venatorum* (before EU-1) and *B. odocoilei* (haemoparasites of domestic and wild artiodactyles, cattle, deer, roe deer). The 5<sup>th</sup> group, also of the “true” *Babesia* spp., unites a considerable number of haemoparasites, mostly causative agents of invasions in hoofed animals: *B. caballi* (horses), *B. ovis* (sheep), *B. bovis* and *B. bigemina* (cattle).

Geographical specificity of causative agents and carriers. Different geographical territories, which have natural foci of spreading of certain varieties of babesiae, are associated with the habitat of absolutely concrete species of ixodid tics. In Ukraine, *Ixodes ricinus*, *Dermacentor reticulatus* and *Ixodes persulcatus* are definitive hosts of *Babesia* spp. [11; 12]. Recent large-scale researches have shown that the *Babesia* invasiveness level reaches 4.6 % (including the parasite species *B. microti*, *B. venatorum* and *B. divergens*, which are pathogenic for people – 2.8, 1.2 and 0.2 % respectively) for the tics *I. ricinus* and 2.7 % for the tics *D. reticulatus* (*B. microti* were revealed in 2.1 % of this species of tics) [12]. Currently in Ukraine the contamination of the tics *I. ricinus* and *D. reticulatus* with *B. microti* reaches, respectively, 7.1 % and 7.8 %, and with other species of babesiae 18.9 % and 17.9 % [3; 4]. Vertebrate (chiefly warm-blooded) animals, whose list today includes more than 30 species of mammals and 10 species of birds, act as the intermediate host of babesiae [3; 6]. Earlier a viewpoint prevailed among scientists that there were strict borders of the “specific linkage” of each species of babesiae to the concrete species of their intermediate host. But, as results of researches conducted during past decades showed, typical for many representatives of this group of haemoparasites is their rather high plasticity in adaptation for existence in different species of intermediate hosts (e.g. *B. microti* are able to cause invasions in 10 species of mammals and 4 species of birds).

Usually people are an accidental intermediate link in the life cycle of the development of these parasites, while the main natural intermediate hosts of *Babesia* species pathogenic for people are as follows: small myomorph rodents (for *B. microti* and *B. microti*-like – voles, shrews, wood mice, etc.), domestic and wild hoofed animals (for *B. divergens*, *B. venatorum* and *B. divergens*-like – cattle, deer, roe deer, etc.) as well as maybe the Canidae (for *B. duncani* and *B. duncani*-like) [13]. The level of contamination of myomorph rodents with babesiae in Ukraine remains unclear, while on Poland territories adjacent to Ukraine the contamination of voles with *B. microti* ranges from 7.7 % to 50.0 % (depending upon the species of animals and their

habitat), that of other varieties of myomorphic rodents being about 2.0 %. By the level of contamination of cattle with babesiae the enzootic foci include territories of Volyn, Zhytomyr, Kyiv, Cherkasy and Chernigiv Regions, where contamination of cattle with causative agents of babesiosis is within 2.8-55.5 %, while other areas of Ukraine are recognized as menacing foci (with irregular sporadic cases of the disease or where no purposeful studies were conducted) [3]. As for other domestic hoofed animals, significant outbreaks of babesiosis are observed in sheep of the Autonomous Republic of Crimea, Kherson and Zaporizhzhya Regions as well as the steppe area of Kharkiv Region, where the infection rate among the livestock ranges from 2.0 % to over 20.0 %. Besides, cases of babesiosis in domestic dogs are constantly registered actually on the whole territory of Ukraine (annually about 6.0 % of animals fall ill), the peaks of the disease incidence (up to 30.0 % of the whole number of dogs) occurring in May-June and September-October [12].

Unfortunately, almost all researches in diagnosis of babesiosis in animals conducted in Ukraine were not accompanied with an exact identification of causative agents with help of modern molecular-biological methods, thereby making it impossible to reveal the spread of the species of Babesia that are pathogenic for people. Nevertheless the above scientific data completely substantiate the conclusion about presence and intense cooperation of some definitive and intermediate hosts of these haemoparasites on the territory of Ukraine, thereby providing reproduction of the life cycle of these parasites and spread of Babesia invasions.

Clinical-epidemiological regularities of babesiosis. The main epidemiological regularities of human babesiosis in Ukraine in general are similar to those described in Europe and the USA. The principal differences of these diseases are as follows: an overwhelming majority of cases (about 80.0 %) was diagnosed in asplenic patients and cases with other types of the pronounced immunocompromised state; severe forms of the disease course dominate with the lethality level among the patients (even hospitalized in due time and treated in compliance with proper protocols for giving medical aid) reaching 50.0 %; *B. divergens* is the chief species of the causative agent (more than 70.0 %) [7; 9]. It is important to note that for a long period of time the species *B. divergens* was regarded as the only causative agent of human babesiosis in Ukraine (according to our data, in countries of the Old World too). But beginning from 2003 it became clear that a considerable number of cases of the disease in people were caused by the species *B. microti* and *B. venatorum*. The latter species of babesiae is characterized by a substantial level of similarity to *B. divergens*, therefore at the initial stage of study *B. venatorum* was regarded as a representative

of the variety *B. divergens*-like with the previous name *Babesia* sp. EU1 [6].

Results of our studies, carried out in 2015 on blood serum samples from people and animals that suffered from tick bites, confirmed the presence of invasions on the territory of Ukraine, these invasions being caused by different species of *Babesia* pathogenic for people: *B. microti* in 2.3 %, *B. divergens* and similar babesiae in 5.4 %. Clinical manifestations of babesiosis develop in people, when the level of erythrocytes infected with the causative agent reaches 3.0-5.0 %, severe forms in the course of the disease are registered after achievement of parasitaemia > 10.0 %, while levels of parasitaemia up to 1.0-2.0 % reveal, as a rule, asymptomatic invasion [7; 11].

The clinical picture of babesiosis is characterized by a broad spectrum of manifestations and varies from asymptomatic to severe and fulminant forms; the above depends upon the immune status and genetically caused patient's predisposition to the disease, the species of the causative agent and the infecting dose, the mechanism of contamination, the presence of concomitant diseases and other factors [2; 5; 11].

The incubation period lasts: most frequently 1-4 weeks (more seldom up to 6 weeks) after a tick bite and 1-9 weeks (sometimes up to 3-6 months) after transfusion of infected blood or its components. Neonatal babesiosis results from transfusive (about 60.0 %), tick transmissive (about 20.0 %) and transplacental (about 20.0 %) transmission of the causative agent. In the latter case manifestations of babesiosis can be revealed as early as during the prenatal period (spleno- and hepatomegaly, haemolytic anaemia, hyperbilirubinaemia, etc.) and in newborns immediately after the birth or during the first two weeks of their life [11].

According to conclusions of the specialists, who carried out long-term observations of patients with detected babesiosis, the clinical course of the above disease manifests itself in three leading forms: asymptomatic parasitic invasion, mild/moderate and severe invasion (in some cases – fulminant manifestation with a flash-like course, development of a chronic recurrent disease or even the lethal outcome) [11].

Asymptomatic forms of babesiosis are diagnosed in about 30.0-40.0 % of the population (in 19.0-25.0 % of adults and 40.0-50.0 % of children) that lives in endemic regions and almost in 6.0 % of the people who live in the regions which are "safe" as for this parasitosis [9; 11]. Scientists consider even the above high values of detection of *Babesia* invasion lowered and its real level of spread significantly higher. Asymptomatic parasitaemia in people can last for several months and even years. During all this time the

invaded persons feel clinically healthy, but preserve an increased risk of activation and development of the disease in case of a reduced resistance of their organism as well as can be the source of infection in cases of provision of donor blood and transmission of pathogens to other people and animals by means of subsequent tick bites [11].

Most cases of human babesiosis, diagnosed in the world, are attributed to mild and moderately severe forms. These are characterized by a gradual onset of indisposition and one or several following signs and symptoms, which are revealed in patients with different frequency: intermittent fever (from 85.0 to 91.0 %), tiredness (from 79.0 to 91.0 %), chills (from 63.0 to 77.0 %), hidrosis (from 53.0 to 69.0 %), headache (in 39.0 %), myalgia (in 33.0 %), anorexia (in 24.0 %), coughing (in 22.0 %), arthralgia (in 18.0 %), nausea (in 16.0 %) [5; 7; 11]. More seldom the patients pay attention to pains in their throat and abdomen, suffer from vomiting, loss of their body weight, congestion of the conjunctiva and photophobia, paleness of the facial skin and eruptions on the body (fingers, hands, region of the abdomen and waist), skin hyperesthesiae, emotional impatience and depression [8; 11].

An objective examination of the patients often reveals only minimum manifestations of the disease in the form of fever with an elevated body temperature from 37.5 to 39.5° C. Moderately manifested splenomegaly and/or hepatomegaly are observed in 10.0-25.0 % of patients; erythema of the pharynx, skin icterus, retinopathies with punctate haemorrhages and retinal infarctions, petechial eruptions on the body (extensive eruptions and haemorrhages are more typical for severe forms of babesiosis) occur less often [11]. The duration of the disease, as a rule, is from a few weeks to several months with gradual recovery and restoration of the organism that may last up to one year and more. In such cases parasitaemia quite often persists even if the patient feels well. A severe, including fulminant (flash-like with the lethal outcome), chronic recurrent (lasting for three months and more, and sometimes up to one year) course of babesiosis is observed in patients with immunocompromised states, which are most commonly caused by: splenectomy (asplenia/hyposplenia), HIV infection, malignant tumours, taking of immunosuppressive drugs [8]. It should be noted that the first case of babesiosis, revealed in Ukraine in a 6-year-old boy (Kyiv, 2011), proved to be endemic. The fact of the disease was diagnosed posthumously by specialists from the USA. This tragic case was covered in media resources (“The first case of babesiosis is

registered in Ukraine”: Topmost news of ICTV channel, FACTS OF THE WEEK, 2013-05-19; “The killer tick”: The Observer, May 17, 2013). Also, patients at the age of 50 and over are more inclined to a severe course of babesiosis, though such data are still more frequently attributed to genetically determined higher sensitivity of certain people to haemoparasites [11].

Besides, a more severe course of the disease can be caused by mixed tick infections, when babesiosis is combined in 10.0-30.0 % of diagnosed cases with boreliosis (Lyme disease) and/or human granulocytic anaplasmosis, monocytic ehrlichiosis, bartonellosis, rickettsioses, haemorrhagic fevers, leptospirosis and other diseases, the above combination being a rule rather than an exception for this group of infections [8; 11].

**Conclusions.** The danger of babesiosis is based on the spread of causative agents of this disease, their carriers and a rather high vulnerability of the human organism to parasitic invasions. The number of *Babesia* species is continuously increasing owing to discovery of their new representatives. The use of resources of the molecular-biological (phylogenetic) classification of *Babesia* species in Ukraine and their grouping by evolutionary relationship have made it possible to confirm existence of 5 different groups (clades) of the causative agents. Scientific data completely substantiate the conclusion about presence and intense cooperation of some definitive and intermediate hosts of these haemoparasites on the territory of Ukraine, thereby providing reproduction of the life cycle of these parasites and spread of *Babesia* invasions.

The main epidemiological regularities of human babesiosis in Ukraine in general are similar to those described in Europe and the USA. The principal differences of these diseases are as follows: an overwhelming majority of cases (about 80.0 %) was diagnosed in asplenic patients and cases with other types of the pronounced immunocompromised state. Results of our studies, confirmed the presence of invasions on the territory of Ukraine, these invasions being caused by different species of *Babesia* pathogenic for people: *B. microti* in 2.3 %, *B. divergens* and similar babesiae in 5.4 %. Clinical manifestations of babesiosis develop in people, when the level of erythrocytes infected with the causative agent reaches 3.0-5.0 %, severe forms in the course of the disease are registered after achievement of parasitaemia > 10.0 %, while levels of parasitaemia up to 1.0-2.0 % reveal, as a rule, asymptomatic invasion.

## References

1. Bajer A. *Babesia behnkei* sp. nov., a novel *Babesia* species infecting isolated populations of Wagner's gerbil, *Dipodillus dasyurus*, from the Sinai Mountains, Egypt / A. Bajer, M. Alsarraf, M. Bednarska [et al.] // *Parasit Vectors*. – 2014. – Vol. 7. – P. 572.
2. Fang D. C. Transfusion-Transmitted *Babesia microti* / D. C. Fang, J. McCullough // *Transfus Med Rev*. – 2016. – Vol. 30, No. 3. – P. 132-138.
3. Hersh M. H. Reservoir competence of wildlife host species for *Babesia microti* / M. H. Hersh, M. Tibbetts, M. Strauss [et al.] // *Emerg Infect Dis*. – 2012. – Vol. 18, No. 12. – P. 1951-1957.
4. Gray J. S. *Babesia microti*. In: Khan, N. (Ed.), *Emerging Protozoan Pathogens* / J. S. Gray, L. M. Weiss // Taylor and Francis, Abingdon, UK. – 2008. – P. 303-349.
5. Kostyria I. A. Cytological analysis of blood of domestic dogs with babesia infection / I. A. Kostyria, S. I. Pokhyl, I. I. Torianik, O. M. Tymchenko // «Topical issues of new drugs development». - Kharkov, 2015. – P. 450.
6. Laha R. Morphology, epidemiology, and phylogeny of *Babesia*: An overview / R. Laha, M. Das, A. Sen // *Symposium*. – 2015. – Vol. 5, No. 2. – P. 94-100.
7. Mørch K. Severe human *Babesia divergens* infection in Norway / K. Mørch, G. Holmaas, P. S. Frolander [et al.] // *Inter. J. Infect. Dis*. – 2015. – Vol. 33. – P. 37-38.
8. Pantchev N. Tick-borne Diseases (Borreliosis, Anaplasmosis, Babesiosis) in German and Austrian Dogs: Status quo and Review of Distribution, Transmission, Clinical Findings, Diagnostics and Prophylaxis / N. Pantchev, S. Pluta, E. Huisinga [et al.] // *Parasitology research*. – 2015. – Vol. 114, Suppl. 1(1). – P. 13-48.
9. Shah J. S. Human babesiosis and ehrlichiosis – current status / J. S. Shah, R. Horowitz, N. S. Harris // *Eur. Infect. dis*. – 2012. – Vol. 6, No. 1. – P. 49-56.
10. Solano-Gallego L. A review of canine babesiosis: the European perspective / L. Solano-Gallego, Á. Sainz, X. Roura [et al.] // *Parasites Vectors*. – 2016. – Vol. 9. – P. 336.
11. Vannier E. Human Babesiosis / E. Vannier, P. J. Krause // *N. Engl. J. Med*. – 2012. – Vol. 366, No. 25. – P. 2397-2407.
12. Wojcik-Fatla A. *Babesia microti* in adult *Dermacentor reticulatus* ticks from eastern Poland / A. Wójcik-Fatla, K. Bartosik, A. Buczek, J. Dutkiewicz // *Vector Borne Zoonotic Dis*. – 2012. – Vol. 12. – P. 841-843.
13. Wong S. S. Y. Detection of *Babesia hongkongensis* sp. nov. in a Free-Roaming *Felis catus* Cat in Hong Kong / S. S. Y. Wong, R. W. S. Poon, J. J. Y. Hui [et al.] // *J. Clin. Microbiol*. – 2012. – Vol. 50, No. 8. – P. 2799-2803.
14. Yabsley. M. J. Natural history of zoonotic babesia: role of wildlife reservoirs [Electronic resource] / M. J. Yabsley, B. C. Shock // *Intern. J. Parasitol.: Parasites and Wildlife*. – 2013. – Vol. 2. – P. 18-31. – Mode of access: [www.elsevier.com/locate/ijppaw](http://www.elsevier.com/locate/ijppaw)
15. Zhou. X. Human babesiosis, an emerging tick-borne disease in the People's Republic of China / X. Zhou, S. Xia, J. L. Huang [et al.] // *Parasites and Vectors*. – 2014. – Vol. 7, No. 1. – P. 509.



USING IMMUNOLOGIC MICROARRAYS FOR DIFFERENTIAL IMMUNOMORPHOLOGIC DIAGNOSTICS OF SOME LYMPHATIC TUMORS



**Prof ALEKSANDR SHISHKIN**

Professor,  
Department of  
Physiology,  
Izhevsk State  
Agricultural  
Academy, Russia  
shishkinlab@  
yandex.ru



**Prof NIKOLAY KIRYANOV**

Professor, Head of  
the Department of  
Pathology,  
Izhevsk State  
Medical Academy,  
Russia  
kirnik@list.ru



**Dr NATALIA OVCHININA**

Associate  
Professor,  
Department of  
Pathological  
Physiology,  
Izhevsk State  
Medical Academy,  
Russia  
shishkinlab@  
yandex.ru

**Abstract**

*The article presents the data showing the possibility of effective application of original immunologic microarrays which allow making combined immunomorphologic study of cells. The microarrays were made by applying the drops of antibody solutions onto fixed test sites of plastic substrates. Immobilization of the molecules of antibodies occurred due to adsorption. Mononuclear leukocytes were separated from peripheral blood of patient with lymphatic tumors by centrifugation in density gradient (ficoll - urographin). The suspension of cells was incubated on the surface of the microarray. We have studied the cells of 100 patients suffering from different lymphatic tumors. The results show that using the created microarrays for analysis allows making differential diagnosis of these diseases.*

**Key words:** immunologic microarrays, cell surface antigens, lymphatic tumors.

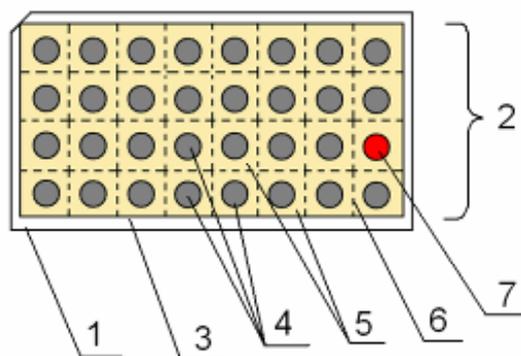
**Introduction.** Definition of an immunophenotype of cells is one of the most important conditions of diagnosis in a hematology. Immunophenotyping plays a large role also in diagnostics of the diseases bound to disturbance of cellular immunity. Immunologic microarrays are a new fast developing class of

diagnostic (analytical) test systems for an immunoassay that allow carrying on a set of homotypic studies simultaneously. Different researchers [1-7] have created immunologic microarrays that contain immobilized antigens and enable us to detect multiple surface antigens on different cells simultaneously. Using

microarrays permits reducing considerably the cost of cell immunophenotyping due to very low antigen expenditure. Nevertheless, microarrays of this class and analysis techniques continue to improve. Due to the use of transparent chemical-resistant substrate it became possible to additionally perform cell staining and carry on microscopic study of cells in transmitted light. It enabled us to combine antigen detection with morphological study of the same cells.

The aim of this work is to show applicability of the developed microarrays for making differential immunomorphological diagnosis of various mature lymphatic tumors the cells of which have considerable morphological resemblance.

**Materials and methods.** 75 patients with chronic lymphocytic leukemia (CLL) and 25 patients with various non-Hodgkin lymphomas have been included in this work. A microarray is a substrate on which the molecules of antibodies specific to cell surface antigens are immobilized at fixed test sites (“spots”). The microarrays were made by applying the drops of antibody solutions onto fixed test sites of plastic substrates (fig.1). Immobilization of the molecules of antibodies occurred due to adsorption. Microarrays were used for the study of mononuclear leukocytes separated from peripheral blood by centrifugation in density gradient (ficoll - urographin 1077 g/l). The separated cells were washed 3 times and resuspended in the solution containing 0.1% of BSA, 20% (in volume) of inactivated human serum and 1.5 mmol/l EDTA in PBS.



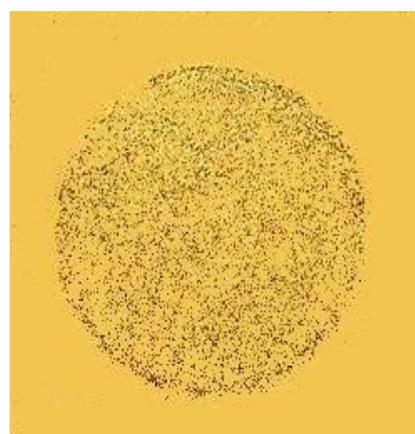
**Fig. 1.** The photo of a surface of the biochip manufactured by method of microcontact drawing. 1 – substrate; 2 – working (functional) region of the biochip; 3 – edge of the substrate; 4 – test areas (spots) with immobilized antibodies; 5 – background areas of the substrate without immobilized antibodies; 6 – dividing lines; 7 – control spot.

Each sample a microarray was incubated (without mixing) with the suspension of cells which settled on the surface of the microarray during this process. If detectable surface antigens were present on the cells, their firm specific binding occurred in the “spots” of the

microarray (fig. 2). After that the microarray was washed with PBS to remove unbound cells. Next, the microarray was fixed with methanol for 12 minutes and was dried; the cells that remained bound were stained by Romanowsky-Giemsa technique (fig. 3).



a.



b.

**Fig 2.** Density of binding of the cells in the test sites of the biochip is different. Magnification  $\times 75$ .

While examining the cells of the patients with hairy cell leukemia were used additional microarrays on which the bound cells were fixed with the mixture of ethanol and formaldehyde and cytochemical examinations were performed to detect acid phosphatase when inhibiting with sodium tartrate.

Morphological examination of the cells bound in each “spot” was done and the density of the cell binding (the number of cells bound on a definite area) was assessed. The density of the cell binding in the area of the biochip “spots” under the given conditions of analysis making was directly proportional to the number of the cells expressing appropriate antigens in the studied sample.

**Results.** Using microarrays we studied the cells of 75 patients with CLL and 25 patients with various non-Hodgkin lymphomas in whom neoplastic leukocytosis was noted in peripheral blood. Among the patients there were 12 with follicular lymphomas, 7 with spleen marginal zone B-cell lymphomas, 4 with mantle-zone lymphomas, and 2 with hairy cell leukemia. In all the examined patients the initial diagnosis was made on the basis of generally accepted clinical and laboratory criteria and guidelines of WHO.

Diagnostic decisions made as a result of the examination with microarrays were compared with clinical diagnoses. The examinations were necessary to demonstrate the possibility of using the microarrays created by us for differential diagnosis of the above-mentioned diseases.

While examining the cells with the help of the microarrays was made conclusions on the basis of the findings about the expression of differential diagnostic antigens by the cells and morphologic characteristics of the bound cells (fig. 3). However due to morphological

resemblance between the cells of the tumours of this group the main differential sign was their immunophenotype.

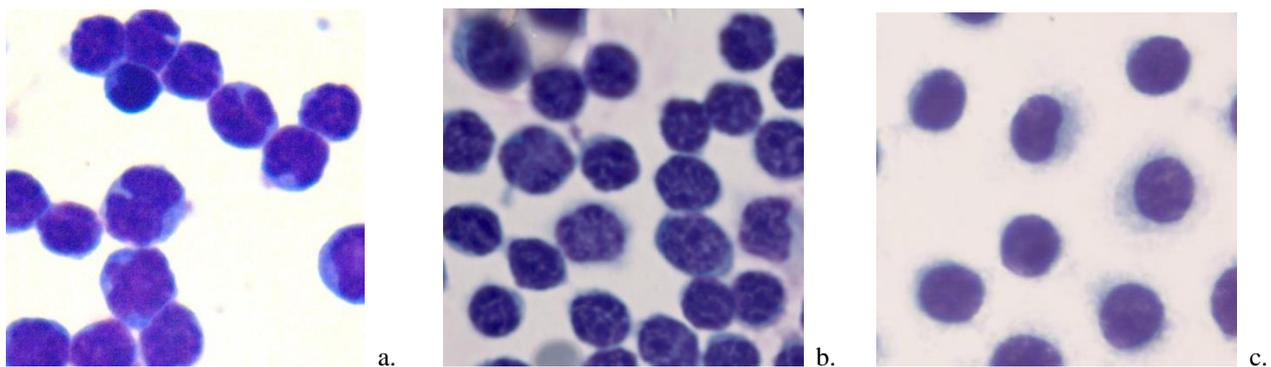
When studying 75 samples of clinical material we determined the high density of the cell binding in the area of the microarray “spots” with the antibodies specific to antigens CD5, CD19, CD23, CD20 and low density of the cell binding in the area of the microarray “spots” with the antibodies specific to antigens IgM and CD10. The density of the cell binding in the area of the “spots” with the anti- CD22 antibodies varied, but was low in the majority of cases. Thus the cells had immunophenotype CD5+, CD19+, CD23+, CD10-, CD20+, CD22+/-, IgM-. Morphological examination showed that these cells were small lymphocytes. The above is characteristic of CLL.

The cells of 4 patients had the morphology of small lymphocytes and immunophenotype CD5+, CD10-, CD19+, CD20+, CD22+, CD23-, IgM+ that is characteristic of mantle-zone lymphoma.

In 12 patients some of the lymphocytes had split or irregular nuclei (fig. 3a). Immunophenotype stated as CD5-, CD10+, CD19+, CD20+, CD22+, CD23-, IgM+ allowed us to verify follicular lymphoma.

In 7 patients many of the cells were larger than ordinary small lymphocytes. Some of them had irregular nuclei (fig. 3b). Immunophenotype was as follows: CD5-, CD10-, CD19+, CD20+, CD22+, CD23-, sIgM+, it confirmed spleen marginal zone B-cell lymphoma.

In 2 patients cells larger than small lymphocytes prevailed, their immunophenotype was CD5-, CD10-, CD19+, CD20+, CD22+, CD23-, sIgM+. Many of them had marked “villosity” (fig. 3c). These factors suggested that the patients suffered from hairy cell leukemia. Tartrate resistant acid phosphatase was detected in the bound cells, which confirmed the diagnosis.



**Fig.3. Micrographs of the cells bound with microarrays that were taken from patients with different lymphatic tumors. Romanowsky-Giemsa staining, magnification  $\times 1000$ : a) Cells of the patient with follicular lymphoma, the cells are bound with anti-CD38 antibodies in the “spot” area. b) Cells of the patient with spleen marginal zone B-cell lymphoma, the cells are bound with anti-CD19 antibodies in the “spot” area. c) Cells of the patient with hairy cell leukemia, the cells are bound with anti-CD19 antibodies in the “spot” area.**

**Discussion.** Despite strong morphologic resemblance between the cells of these tumors, they have a number of morphologic differences. Using the microarrays make it possible to detect these differences. There is no doubt that immunophenotype is of the greatest significance in differential laboratory diagnosis of these tumors, but morphological examination of the same cells increase validity of the results obtained.

In this work were compared the findings of detecting only those antigens which are important for differential immunodiagnosics, although the microarrays used for

detecting a significantly larger number of antigens. The detection of other antigens will be important for assessing individual features of tumors cell immunophenotype in a particular patient. However studying this issue requires carrying out much more research into each disease.

**Conclusion.** Diagnostic decisions reached during the conducted investigations coincided with the clinical diagnoses made earlier. Thus using the microarrays for analysis allows making differential diagnosis of these diseases.

## References

1. Immunodiagnosis of chronic lymphocytic leukemia using immunological chips / N. G. Ovchinina, A. V. Shishkin, E. N. Nikitin [et al.] // *Bull Exp Biol Med.* – 2010. – Vol. 149, № 2. – P. 223-225.
2. Ko I.K. Antibody microarray for correlating cell phenotype with surface marker / I.K. Ko, K. Kato, H. Iwata // *Biomaterials.* – 2005. – № 26 (6). – P. 687-696.
3. Profiling CD antigens on leukaemias with an antibody microarray / N. Barber, S. Gez, L. Belov [et al.] // *FEBS Lett.* – 2009. – № 583 (11). – P. 1785-1791.
4. Screening microarrays of novel monoclonal antibodies for binding to T-, B- and myeloid leukaemia cells / L. Belov, P. Huang, J. S. Chrisp [et al.] // *J Immunol Methods.* – 2005. – № 305 (1). – P. 10-19.
5. Surface antigen profiling of colorectal cancer using antibody microarrays with fluorescence multiplexing / J. Zhou, L. Belov, P.Y. Huang [et al.] // *J Immunol Methods.* – 2010. – № 355 (1-2). – P. 40-51.
6. Surface profiles of live colorectal cancer cells and tumor infiltrating lymphocytes from surgical samples correspond to prognostic categories / J. Zhou, L. Belov, P. Chapuis [et al.] // *J Immunol Methods.* – 2015. – № 416. – P. 59-68.
7. Surface profiling of extracellular vesicles from plasma or ascites fluid using dot scan antibody microarrays / L. Belov, S. Hallal, K. Matic [et al.] // *Methods Mol Biol.* – 2017. – № 1619. – P. 263-301.



COPD PHENOTYPES - THE WAY TO PERSONIFIED MEDICINE OF THE XXI CENTURY



**Prof TETYANA  
OSPANOVA**

*Professor, Head of the Department of Propaedeutics of Internal Medicine No.2 and Nursing, Kharkiv National Medical University, Ukraine*

t.ospanova1@gmail.com



**Prof ZHANNA  
SEMYDOTSKA**

*Professor, Department of Propaedeutics of Internal Medicine No.2 and Nursing, Kharkiv National Medical University, Ukraine*

vade\_mecum2001@yahoo.com



**Dr INGEBORG  
CHERNYAKOVA**

*Associate Professor, Department of Propaedeutics of Internal Medicine No.2 and Nursing, Kharkiv National Medical University, Ukraine*

irinakaramazina805@gmail.com



**Dr OLENA  
PIONOVA**

*Assistant Professor, Department of Propaedeutics of Internal Medicine No.2 and Nursing, Kharkiv National Medical University, Ukraine*

olena\_pion@meta.ua



**Dr NATALIA  
TRYFONOVA**

*Assistant Professor, Department of Propaedeutics of Internal Medicine No.2 and Nursing, Kharkiv National Medical University, Ukraine*

energyna1@ukr.net

**Abstract**

*This article is proposed to isolate the phenotype (subphenotype) of chronic obstructive pulmonary disease, taking into account the kidneys functional state to minimize the risk of developing chronic kidney disease. According to our data, in patients with COPD and comorbid pathology, inverse correlations between GFR and remodeling of the right heart as well as direct connections between GFR and left ventricular remodeling were detected indicating the effect of myocardial remodeling on GFR. Along with that found a direct correlation between CRP and PASP ( $R=0.49$ ,  $p<0.05$ ) and negative correlations between CRP and FEV1 ( $R=-0.51$ ,  $p<0.05$ ), SpO2 ( $R=-0.51$ ,  $p<0.05$ ), underlines the role of CRP in the development of systemic inflammation in case of COPD and the role of hypoxia in its development. The following clusters are distinguished by clustering the obtained data: the first one constitutes GFR, SpO2, FVC and FEV1, the second made up CRP, the Tiffno index, the frequency of exacerbations and the duration of COPD. The studies allow allocating a clinical subphenotype COPD: the level of GFR less than 90 ml/min., over the age of 60 years, the incidence of exacerbations more than 2 per year, the severity of comorbid conditions.*

**Key words:** phenotype, chronic obstructive pulmonary disease, glomerular filtration rate, personified medicine.

Chronic obstructive pulmonary disease (COPD) has been gaining interest of the medical community, doctors of various specialties, such as internists, pulmonologists, microbiologists, epidemiologists for the last 20 years [1]. This concern is associated with a rapid rise of morbidity, disability and mortality rates, which doubles every 10 years [2, 3], as well as with pronounced comorbidity in COPD: the most frequent lesions are the organs of the cardiovascular, digestive, genitourinary and musculoskeletal systems [4-9]. In COPD with coronary heart disease (CHD) is described a disadaptive remodeling of the heart muscle [10, 11]. Genetic factors are currently recognized as one of the causes of comorbidity: the AC/AG alleles of the CB A138C/A186G genotypes, the TT/CT alleles of IL-33 G308A/C3953T genotypes, the heterozygous DI genotype of ACE in chronic cardiorespiratory pathology and the homozygous DD genotype of ACE in patients with aggravated respiratory anamnesis, even without concomitant cardiac pathology [11].

Development of systemic inflammation, oxidative stress, protease-antiprotease imbalance, endothelial dysfunction, immune response is given a significant role [1, 12]. It is discussed the role of accelerated aging, the development of autophagy in acute and chronic lung diseases [13-15], and numerous biomarkers are proposed for clinical use in COPD [16-18], which in combination with indicators of the pulmonary tissue state will allow to make new steps in phenotyping. It is worthwhile noting that majority of the currently existing biomarkers are not specific for COPD [19], and today their investigation oftentimes is not available for practicing physicians.

In 2010, the international expert team recognized the main priority of respiratory medicine to study phenotypes of COPD with a view for maximum individualization approaches to prevention, treatment, rehabilitation, and improving the quality of life [20, 21]. However, despite a large quantity of research devoted to numerous aspects of COPD, undoubted advances in the diagnosis and treatment of this complex heterogeneous disease, its progression mechanisms, many problems of COPD remain unresolved. In particular, the condition of the kidney to predict the course of COPD, the detection of concomitant chronic kidney disease (CKD), acute renal injury (AKI) is not taken into account. Meanwhile, known pulmorenal syndromes based on the affinity of the antigenic structures of the kidneys and lungs, the renal response to hypoxia, and metabolic disorders. The development of CKD and AKI in COPD can also be associated with comorbid conditions: cardiorenal syndrome in essential hypertension (EH), CHD, diabetic nephropathy in diabetes mellitus (DM).

**The goal:** To study the effect of external respiratory function, myocardial remodeling, systemic

inflammation on renal functional state with a view to allocating the phenotypes of COPD to optimize diagnosis and treatment.

Materials and methods of study: 34 patients suffering from COPD were examined: 14 women and 20 men admitted to the pulmo-allergological department of the Kharkiv Regional Clinical Hospital in the exacerbation of the disease. The diagnosis of COPD was established according to GOLD criteria [22] and orders of the Ministry of Health of Ukraine No. 128 from 29.03.2007 and No. 555 from 27.06.2013 [23, 24]. The age of the examined patients ranged from 42 to 82 years, in average 60.00 [54.00-67.00] years. Group B included 11 patients, group C - 14 and group D - 9 patients. Smoking was denied by 6 patients, smoker's experience was up to 10 pack-years in 12 patients, up to 20 packs-years also in 12 patients. Duration of COPD up to 5 years was noted in 8 patients, up to 10 years - in 10, up to 20 years and more - in 16, on average 7.00 [5.00-15.00] years. The frequency of exacerbations was 1 times per year in 13 patients, twice per year - 7, 3 times per year - 5, and 4 times per year - 8 and up to 5 times a year - in 1 patient. On average, this figure was 2.00 [1.00-5.00]. Signs of an infectious exacerbation were present in 28 patients to whom prescribed antibiotics (respiratory fluoroquinolones, 3<sup>d</sup> generations of cephalosporins, and macrolides). The treatment was performed according to recommendations [22, 25]: short course of systemic glucocorticosteroids (SCS), inhaled glucocorticosteroids (ICS), short- and long-acting beta2-agonists and M-cholinolytics, methylxanthines, oxygen therapy through oxygen concentrator. Inhalation introduction of drugs was carried out using the nebulizer.

Diagnosis and treatment of concomitant pathology were implemented according to the recommendations of experts (cardiologist, endocrinologist, gastroenterologist, etc.). Patients were examined upon admission to the hospital and the 14th day of treatment. EH was noted - in 22 patients, aortocardiosclerosis - in 25, angina - in 3, post-infarction cardiosclerosis - in 3 patients. 11 patients were suffered from DM 2 type.

Objective examination revealed BMI ranged from 18 to 24 kg/m<sup>2</sup> in 24 patients, from 30 to 40 kg/m<sup>2</sup> - in 9 and more than 40 kg/m<sup>2</sup> - in 1 patient. Cyanotic skin and mucous was noted in all patients, moderate ankle and feet edema - in 16 patients. Breathing frequency (BH) on admission to the hospital ranged from 18 to 30 per minute, on average of 24.02 per minute. Lungs auscultation revealed weakened breathing in 13 patients, harsh breathing - in 21 patients, wheezing - in 30 patients, buzzing - in 3 patients and silent bubbly wet rales - in 3 patients. Moderate hypertension was noted in 9 patients, subfebrile body temperature in 10 patients. Exercise tolerance was assessed using with 6 - minute

walk test according to the standard protocol and at admission was 373 m. Leukocytosis (from 10.1 to 22.5 g/l, an average of 19.0 g/l) was detected in 17 patients, a moderate amount of leukocytes in sputum was found in 28 patients. The level of C-reactive protein (CRP) was 5.28 [2.1-7.5], oxygen saturation of arterial blood (SpO<sub>2</sub>) in 18 patients ranged from 90% to 95%, in 10 - from 85% to 89%, in 3 - from 75% to 79%, an average of 92.00 [75.00-96.00]. Proteinuria from 0.2 to 0.87% was found in 4 patients, the urine sediment was unremarkable. The glomerular filtration rate (GFR) was calculated according to the Cockcroft-Gault formula and averaged 81.65 [58.60-129.00] ml/min: in 9 patients the GFR was more than 90 ml/min, in 20 patients - 60 - 89 ml/min and in 1 patient - 58.6 ml/min. Hyperfiltration (120.00 - 126.4 ml/min) was found in 4 patients.

ECG pathology was not found in 6 patients, sinus tachycardia was noted in 18 patients, signs of right atrial overload in 15 patients, right ventricular hypertrophy in 12 patients, and left ventricular hypertrophy in 11 patients. X-ray examination showed no changes in 3 patients, in 25 - signs of bronchitis, in combination with pneumosclerosis - in 22 and with emphysema - in 2 examined. Evaluation of pulmonary ventilation function was carried out on the basis of registration relationships flow-volume forced expiratory maneuver using a computer spirograph. The results of the post-bronchodilation test were analyzed: FEV<sub>1</sub> was 46.5 [29.00-63.00]%, FVC 58.94 [43.00-66.00]%, FEV<sub>1</sub>/FVC index 0.68 [0.63-0.71], reversibility of airway obstruction 5.00 [4.00-8.00]% over the baseline value.

Standard ultrasound examinations was performed to assess morpho-functional condition of myocardium. The following morphological parameters were studied: linear dimensions of the left ventricle (end-diastolic volume (LVEDV), terminal diastolic size (left ventricular dyskinesia), terminal systolic size (LVDd), posterior left ventricular wall thickness and interventricular septum Left ventricular myocardial mass (LVMI) In addition, the final systolic diameter of the right atrium (CDC PP) and the final diastolic size of the right ventricle (CD of the prostate cancer) were also analyzed Functional indices: Left ventricle (PV) and mean pressure in the pulmonary artery (PASP).

The statistical processing of the results was done using the Statistica 10 package using nonparametric methods. Data are expressed by a median with an interquartile range (Me [25% -75%]), unless otherwise indicated. To determine the differences between independent groups, the Mann-Whitney test (U) was used. The dependence between the variables was estimated using the Spearman correlation coefficient (R). A cluster analysis of the obtained data was also carried out, dendrograms

(trees of variable) were constructed for graphical display of the results.

**Study results:** The patients were divided into 2 groups using cut-off value GFR 90 ml/min. The average age of the patients group 1 (GFR<90 ml/min, n=25) was 61.8 [42-82] years, group 2 (GFR > 90 ml/min, n = 9) - 50.7 [42-68] years. Exacerbation frequency in 1<sup>st</sup> group was 2.56 [2.00-4.00] per year, in 2<sup>nd</sup> group - 1.66 [1.00-4.00] exacerbations per year (p=0.046). The duration of COPD in 1<sup>st</sup> group was 7.00 [5.00-15.00], in 2<sup>nd</sup> group - 10.00 [5.00-18.00], p=0.66.

In 1<sup>st</sup> group the comorbid pathology was more often observed: DM type 2 - in 8 patients (38%) in group 1 and in 2 patients (22%) of 2<sup>nd</sup> groups; CHD (angina pectoris, aortocardiosclerosis) - in 20 patients of 1<sup>st</sup> group, (3 (95.2%) of them was post-infarction cardiosclerosis) and in 5 (55.5%) patients of 2<sup>nd</sup> group stable angina. EH was diagnosed in 16 patients of 1<sup>st</sup> group (76%) and 2 patients of 2<sup>nd</sup> group (22%).

Patients' conditions improved after treatment in both groups: decreased dyspnea, exercise tolerance increased (6-minute walking test after treatment was 495.8 m); and body temperature, BF, CBC and SpO<sub>2</sub> normalized; wheezing disappeared, minor edema of the feet persisted in 4 patients.

The results of the CAT and mMRS questionnaires also improved. However, EBF parameters changed insignificantly: FEV<sub>1</sub> 52 [36-65]%, FEV<sub>1</sub>/FVC - 0.69 [0.66-0.71]. There were no significant differences in the response to therapy in both groups. It is most likely that reduction of the clinical symptoms of bronchial obstruction was associated with the effect of systemic CS and antibiotic therapy.

The study of the morphofunctional characteristics of the myocardium showed the following: LVEDV was 16.9 [13.8-19.5] cm, LVDd was 5.85 [4.8-6.2] cm, LVPWth was 1.3 [1.2-1.4] cm, IVST was 1.3 [1.0-1.4] cm, LVMI was 86 [76-96], LVEF was 64.0 [58.0-65.0] %. PASP was 32.00 [26.00-38.00] mmHg., RVDd was 2.90 [2.4-23.6] cm, RAESP - 3.9 [3.4-4.3] cm. Thus, signs of remodeling of the right atrium, right and left ventricles, and signs of pulmonary hypertension were found.

Correlation analysis of the relationship between GFR and EchoCG indicates a negative moderate strength of the relationship between GFR and LVDd (R=-0.38), RAESP (R =-0.48), RVDd (R=-0.46). A positive strong relationship between RAESP and RVDd (R = 0.85) was found. There is a direct moderate dependence between the Tiffno index and GFR (R = 0.43). Along with this, there are a direct moderate relationship between CRP and SDLA (R = 0.49), negative mean force dependence between PASP and FEV<sub>1</sub> (R=-0.69), FVC (R=-0.61),

CRP and FEV<sub>1</sub> (R=-0.51), CRP and SpO<sub>2</sub> (R=-0.51) were found. Reliable values of the interrelations of indicators in the form of correlation galaxies in Fig. 1 and Fig. 2. are reflected.

Two clusters were formed by using clustering analyze of obtained data, (Fig. 3): the first formed GFR, SpO<sub>2</sub>, which merged with FVC and FEV<sub>1</sub>, and the second, located at a large inter-cluster distance from the first. In the second cluster, a strong pair relationship between CRP, the Tiffno index and exacerbations frequency was revealed.

This supplements the results of the correlation analysis, which also revealed the presence of two independent galaxies that are formed by GFR and CRP. The combination of GFR and SpO<sub>2</sub> in one cluster indicates a paired relationship between these indicators and with indicators FVD through them. Apparently, COPD ventilation violation causes hypoxia that affects GFR. The second cluster emphasizes the connection between the frequency of exacerbations, CRP and FER, and also, to a lesser degree, the duration of COPD. A large intercluster distance indicates a fairly autonomous regulation of changes in these variables and their management by different subsystems of the body.

**Discussion of results.** Despite the avalanche-like increase in the number of studies devoted to COPD the understanding of the nature of the disease, the causes of its progression, the importance of molecular and cellular mechanisms of the development of the COPD [14, 26], the allocation of markers of systemic inflammation [16, 17, 27], the pathogenesis of exacerbations [18, 28], of the comorbidity and the principles of phenotyping [28, 29] remain a matter of debate and require further study. The study of the relationship of renal function in COPD with other clinical parameters was in the focus of our attention. Using of general clinical indicators that are available not only to pulmonologists, but also to internists and family doctors seemed to us useful in choosing the design of the study.

The severity of the bronchial obstructive syndrome and the frequency of the infectious - dependent exacerbation (fever, leukocytosis, peripheral blood leukocytes in the sputum in 28 patients) were the features of the course of COPD in the examined patient population, which required the appointment of the systemic glucocorticosteroids, inhaled corticosteroids and antibiotics. Increase in blood levels of CRP - a popular biomarker of systemic inflammation was also not detected.

A correlation analysis of the relationship between GFR, FVD, EchoCG, which indicate that GFR decreases with increasing load on the right heart and increasing airway obstruction. In contrast, left ventricular hypertrophy is

accompanied by an increase in GFR level, which may be due to increasing of cardiac output, minute volume. These data underscore the effect of myocardial remodeling on renal function (Fig. 2).

A moderate direct correlation between CRP and PASP (the possibility of vasculopathy) was detected. Negative links between CRP, FEV<sub>1</sub>, confirming the importance of CRP as an indicator of the systemic nature of the inflammatory process in COPD, were also found [30]. The negative relationship between CRP and SpO<sub>2</sub>, which indicates the role of hypoxia in the development of systemic inflammation was identified (Fig. 2).

Clustering complements the results of the correlation analysis with the observed similarity between GFR and SpO<sub>2</sub>, that indicates the role of hypoxia in renal dysfunction in COPD. The similarity of CRP, the frequency of exacerbations, FER, duration of the disease underscores the impact of CRP as an indicator of systemic inflammation on COPD (Fig. 3.) It should be noted that in carrying out the correlation analysis, two galaxies have also been singled out, one of which included GFR, into another CRP. Modern science assigns more and more importance to the classification of the objects under study, revealing the differences and similarities of clusters, which can contribute to an in-depth knowledge of the pathogenesis of various symptoms and syndromes. To comparison of the results of different types of analysis an important role is given.

According to the principles of modern personalized medicine [21, 28, 29, 31, 32] clinical phenotypes in the treatment of patients should be considered. Phenotyping can help a practitioner predict the patient's response to a pharmacological intervention and is the beginning of a pathway to a patient-specific medicine [33]. Currently, the efforts of pharmacologists are aimed at creating of the new combinations of fixed doses of the long-acting  $\beta_2$ - agonists (LABA) with inhaled GCS, LABA with long-acting muscarinic antagonists (LAMA), "triple" inhalers are being developed, as well as double functional compounds, Which have the effects of muscarinic antagonist and  $\beta_2$ - agonist (MABA), new inhibitors of phosphodiesterase 4, "targeted" anti-inflammatory and immunotropic drugs. The effects of these drugs largely depend on the phenotype of COPD [32-34].

The opinion that modern methods of treatment are not able to eliminate inflammation, prevent the progression of the disease or reduce mortality is expressed [32]. In the future, the use of nanoparticles for the delivery of drugs to a specific location, stem cell therapy, tissue engineering of the respiratory tract, bronchoscopic therapy based on ablation of parasympathetic nerves and many other new, often unexpected approaches to the treatment of COPD (like as statins, vitamin D,

acupuncture, yoga using), individual choice of which will be determined by the phenotype of the disease [1].

January 27, 2017, the Report of the working group on the global strategy for the diagnosis, treatment and prevention of COPD was published, reflecting the results of the planned large revision of the approaches to the diagnosis and treatment of COPD: separation of symptoms from a spirometric assessment of the patient's condition, taking into account the threshold values of the spirogram for the choice of non-pharmacological treatment, in particular, reduction of lung volume, lung transplantation, assessment of the risk of exacerbations, the degree of influence of symptoms on the overall health. The strategies of de-escalation of drug therapy, non-drug treatment (vaccination, smoking - cessation, programs of pulmonological rehabilitation, physical training, self-learning, correction of the patient's behavior in order to improve the physical and psychological state, increase adherence to therapy) is proposing. The doctors' attention is drawn to the provision of palliative care, a worthy end to life, a strategy for controlling symptoms that reduce the quality of life (sleep apnea, shortness of breath, pain, anxiety, depression, eating disorders). These recommendations are based on a personalized approach to the diagnosis and treatment of a patient suffering from COPD, the isolation of phenotypes [25].

Based on the results that were obtained by us, the phenotype (subphenotype) of COPD is distinguished, taking into account the level of GFR: GFR less than 90 ml / min, age over 60 years, frequency of exacerbations more than 2 per year, severity of comorbid conditions. Isolation of this phenotype seems actual because it will draw the attention of practicing physicians to the functional state of the kidneys in COPD, will allow predicting the risks of CKD and AKI, will serve as a basis for monitoring the course of COPD of microalbuminuria (MAU), serum creatinine level.

Reduction of GFR in COPD can be promoted by hypoxia, which causes spasm of small arteries, including kidneys', ischemia of nephrons, and also aggravates the severity of comorbid conditions. There is evidence that in chronic heart failure, the level of lethality is inversely proportional to GFR and in AH a moderate decrease in GFR is accompanied by a doubling risk of cardiac death. The dose-dependent factor in reducing GFR and the emergence of UIA in COPD is smoking, especially in individuals with hypertension, as well as a BMI greater than 25 kg/m<sup>2</sup> in young people.

The proposed phenotype is based on an assessment of the anamnesis, "a simple intuitive assessment of the

severity of the disease" (GOLD 2016), results of general clinical studies and it can help to personify therapy with regarding the statement of the kidneys. Monograph on "New shades of the COPD problem" [17], suggests that most of the published papers represent the results of small studies that should be further evaluated in large cohorts of patients.

In order to reduce the risk of developing CKD in patients with COPD, it is necessary to develop a strategy for reducing the frequency of exacerbations individually for each patient, to stimulate the patient's adherence to the treatment of comorbid pathology. In 2010, as one of the priority areas of respiratory medicine, the study of clinical nosological units of COPD and the development of definitions that allow them to be identified were recognized [21]. The future will show how promising this direction is in case of COPD.

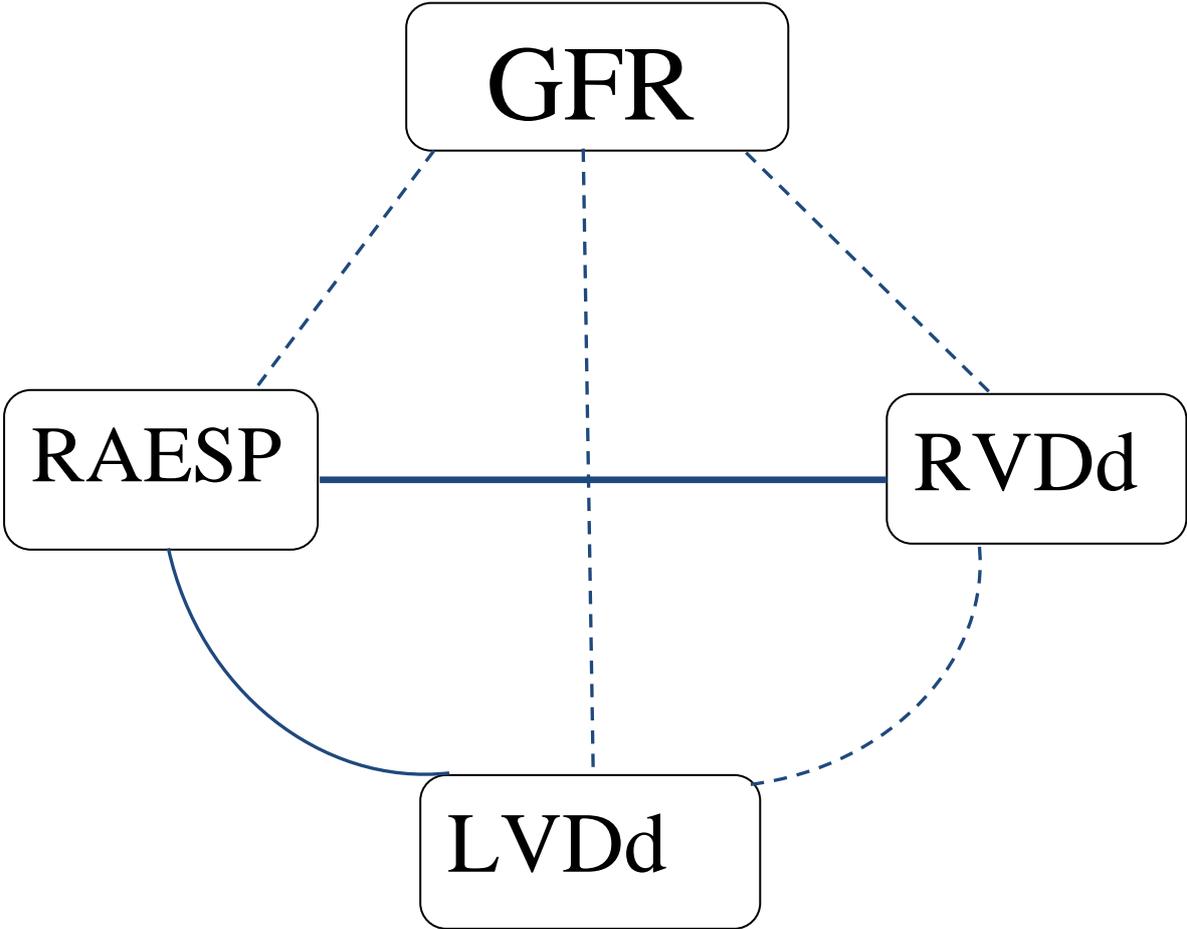
## Conclusions

1. In patients with COPD, inverse correlations between GFR and remodeling of the right heart as well as direct connections between GFR and left ventricular remodeling were detected, that indicates the effect of myocardial remodeling on GFR.
2. There are a direct correlation between CRP and PASP and negative correlations between CRP, FEV<sub>1</sub>, SpO<sub>2</sub>, underlines the role of CRP in the development of systemic inflammation in case of COPD, the role of hypoxia in its development.
3. Clustering of the received data indicates to the presence of two clusters: the first one includes GFR, SpO<sub>2</sub>, FVC and FEV<sub>1</sub>, and the second was the CRP, the Tiffno index, the frequency of exacerbations and the duration of COPD.
4. The carried out researches allow to allocate a clinical phenotype (subphenotype) of COPD taking into account the level of GFR (GFR less than 90 ml / min, age over 60 years, frequency of exacerbations more than 2 per year, severity of comorbid conditions. Isolation of the phenotype of COPD depending on the functional state of the kidneys will allow personifying diagnostic, therapeutic, preventive strategies in COPD, direct them to reduce the frequency of exacerbations, adequate therapy of comorbid conditions in order to minimize the risks of development of CKD.

## References

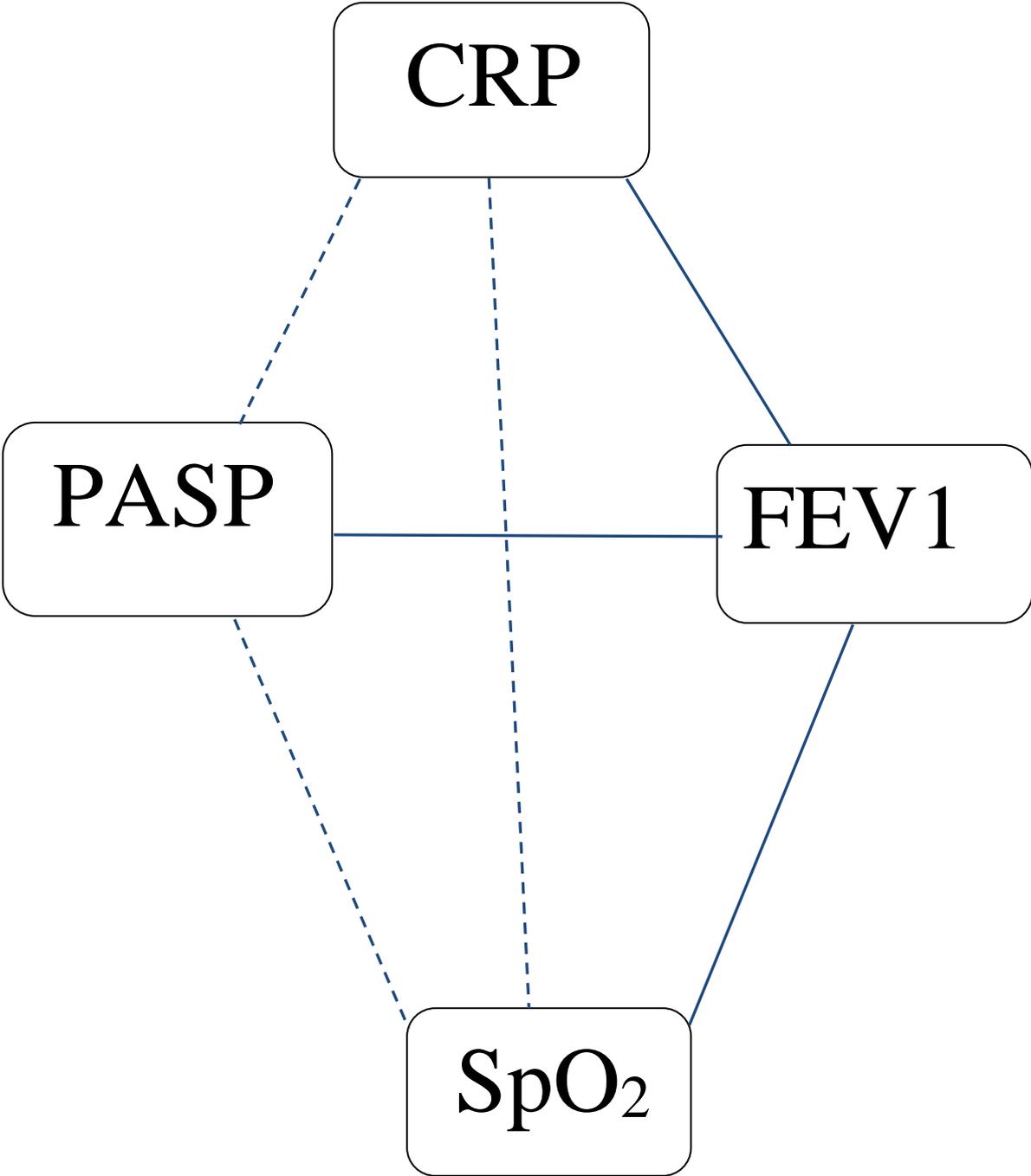
1. Feshchenko YuI, Tchaikovskiy JB, Ostrovskiy MN, Dyeltsova OI, Gerashchenko SV, Kulinich- Mis'kiv MO, Savelihina IA. Chronic obstructive pulmonary disease. SIMYK 2016. 400p.
2. Feshchenko YuI. Chronic obstructive pulmonary disease: a medical and social challenge. *Ukrainskyi pulmonolohichnyi zhurnal - Ukrainian pulmonology journal* 2011; 2: 6 (in Russ).
3. Mathers CD, Loncar D Projections of global mortality and burden of disease from 2002 to 2030. *PLOS. Med.* 2006; 3 (11): e442.
4. Avdeev SN, Baymakanova GE. COPD and cardiovascular diseases: mechanisms of association. *Pul'monolohyja – Pulmonology* 2008; 1: 5-13 (in Russ).
5. Klester EB. COPD is association with cardiovascular diseases, organs of digestive system, Urogenital System. Clinical features, course, optimization of comprehensive treatment – dissertation synopsis for the degree of MD, Barnaul 2009: 46p.
6. Trishina VV, Bychkova LV, Fedorenko MG. Role of chronic obstructive pulmonary disease in the development of kidney pathology. *Vestnyk Rossyjskoho unyversyteta družby narodov - Bulletin of peoples' friendship university of Russia, medical series* 2011; 2: 37-39 (in Russ).
7. Chronic obstructive pulmonary disease. The federal program, review and supplemented, 2nd addition. Edited by Chuchalin AG. – Moscow; 2004: 61s (in Russ).
8. Chuchalin AG. Chronic obstructive pulmonary disease and comorbidities. *Zdorovia Ukrainy - Health of Ukraine* 2010; 2 (231): 26-27 (in Russ).
9. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: role of comorbidities. *Eur. Respir. J.* 2006; 28: 1245 – 1257.
10. Boev SS, Dotsenko NYa, Shekhunova IA, Dedov VO. Combination of chronic obstructive pulmonary disease and ischemic heart disease. Issues of rational therapy. *Therapia. Ukrainskyi medychnyi visnyk - Therapia. Ukrainian Medical Bulletin* 2005; 2: 95-96 (in Ukr).
11. Kalmykov AA Mechanisms for implementation of cardiorespiratory disorders, of chronic occupational diseases of bronchopulmonary system accompanying with coronary heart disease: diagnostic and preventive aspects – dissertation synopsis for the degree of MD, Kharkov 2016: 39p.
12. Fischer MB, Pavlisko E, Voynow JA. Pathogenic triad in COPD: oxidative stress, protease – antiprotease imbalance, and inflammation. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2011; 6: 413-21.
13. Dyeltsova OI, Genyk SM. Autophagy - the fundamental mechanisms and the problems. *Svit medytsyny ta biolohii - The world of medicine and biology* 2009; 4: 161-166 (in Ukr).
14. Boyer L, Savale L, Boczkowski J, Adnot S. Cellular senescence and pulmonary disease: COPD as an example. *Rev. Mal. Respir.* 2014 Dec; 31(10): 893-902.
15. Ryter SW, Choi AM. Autophagy in lung disease pathogenesis and therapeutics. *Redox Biol.* 2015; 4: 215-25.
16. Konopkina LI. Diagnostic significance of some markers of systemic inflammation in infectious exacerbation of chronic obstructive pulmonary disease. *Ukrainskyi pulmonolohichnyi zhurnal - Ukrainian pulmonological Journal* 2008; 3 (suppl): 136-137 (in Ukr).
17. Agusti A, Sin DD. Biomarkers in COPD. *Clin. Chest. Med.* 2014 Mar; 35(1): 131-41.
18. Brightling C. E. Biomarkers that predict and guide therapy for exacerbations of chronic obstructive pulmonary disease. *Ann. Am. Thorac. Soc.* 2013 Dec; 10 Suppl: S214-9.
19. Ambade VN, Sontakke AN, Barthwal MS, Tyagi R, Basannar DR. Diagnostic utility of biomarkers in COPD. *Respir. Care* 2015 Dec; 60(12): 1729-42.
20. Padyganova A.V. Phenotype of chronic obstructive pulmonary disease at women with arterial hypertension: features of the functional condition of kidneys. *Kardjosomatyka - Cardiosomatics.* 2015; 6 (2): 40–46 (in Russ).
21. Han M.K, Agusti A, Calverley PM, Celli BR, Criner G, Curtis JL, Fabbri LM, Goldin JG, Jones PW, Macnee W, Make BJ, Rabe KF, Rennard SI, Sciurba FC, Silverman EK, Vestbo J, Washko GR, Wouters EF, Martinez FJ. Chronic obstructive pulmonary disease phenotypes: the future of COPD. *Am. J. Respir. Crit. Care Med.* 2010 Sep 1; 182(5): 598-604.
22. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease, 2013-2016. Available at: [http:// www.goldcopd.org](http://www.goldcopd.org).
23. On approval of clinical protocols of medical care in the specialty pulmonology: the Order Ministry of Health of Ukraine № 128 from 19 Mar 2007.
24. Unified clinical protocol of primary, secondary (specialized), tertiary (highly specialized) care and rehabilitation «Chronic obstructive pulmonary disease», approved by order of Ministry of Health of Ukraine № 555 from 27 Jun 2013 «On approval and implementation of medical and technological documents for standardization of medical care in chronic obstructive pulmonary disease»

25. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, 2017. Report Available from [http:// goldcopd.org](http://goldcopd.org) // accessed November 2016.
26. Kadushkin AH, Tahanovich AD. Molecular and cellular mechanisms of the development of chronic obstructive pulmonary disease. Zhurnal «Voennaia medytsyna» - Journal «Military Medicine». 2012; 1: 132 – 138 (in Russ).
27. Krakhmalova OO, Voyeykova LS, Talalay IV. Systemic inflammation as a factor in the development of extrapulmonary complications of COPD. Ukrainskyi terapevtychnyi zhurnal - Ukrainian Therapeutical Journal. 2011; 2: 79-83 (in Ukr).
28. Ostrovsky MM, Stovban MP. Phenotype COPD with frequent exacerbations: the impact on the rate of disease progression and prognosis for the patient. Zdorovia Ukrainy - Health Ukraine. 2013; Thematic issue: 29-30.
29. Burgel P.R. From COPD definition to COPD phenotypes. Presse Med. 2014; 43(12 Pt1): 1337 – 1343.
30. Velkov VV. Procalcitonin and C-reactive protein in modern laboratory diagnostics. Laboratornaia dyahnostyka - Laboratory diagnostics 2010; 2 (52): 39-76 (in Russ).
31. Tolokh OS, Rudnitska ND, Chulovska UB, Volnitzka HI. Optimization of treatment of COPD based clinical phenotype. Klinichna imunolohiia. Alerholohiia. Infektolohiia - Clinical Immunology. Allergology. Infectology 2015; 9; 10 (88-89): 12- 16 (in Ukr).
32. Barnes P.J. Identifying molecular targets for new drug development for chronic obstructive pulmonary disease: what does the future hold? Semin. Respir. Crit. Care Med. 2015 Aug; 36(4): 508-22.
33. Lopez – Campos JL, Bustamante V, Muñoz X, Barreiro E. Moving towards patient-medicine for COPD management: multidimensional approaches versus phenotype - based medicine – a critical view. COPD. 2014 Sep; 11(5): 591-602.
34. Miyazaki M, Nakamura H, Takahashi S, Chubachi S, Sasaki M, Haraguchi M, Terai H, Ishii M, Fukunaga K, Tasaka S, Soejima K, Asano K, Betsuyaku T; Keio COPD Comorbidity Research (K-CCR) group. The reasons for triple therapy in stable COPD patients in Japanese clinical practice. Int. J. Chron. Obstruct. Pulmon. Dis. 2015 Jun 4; 10: 1053-9.



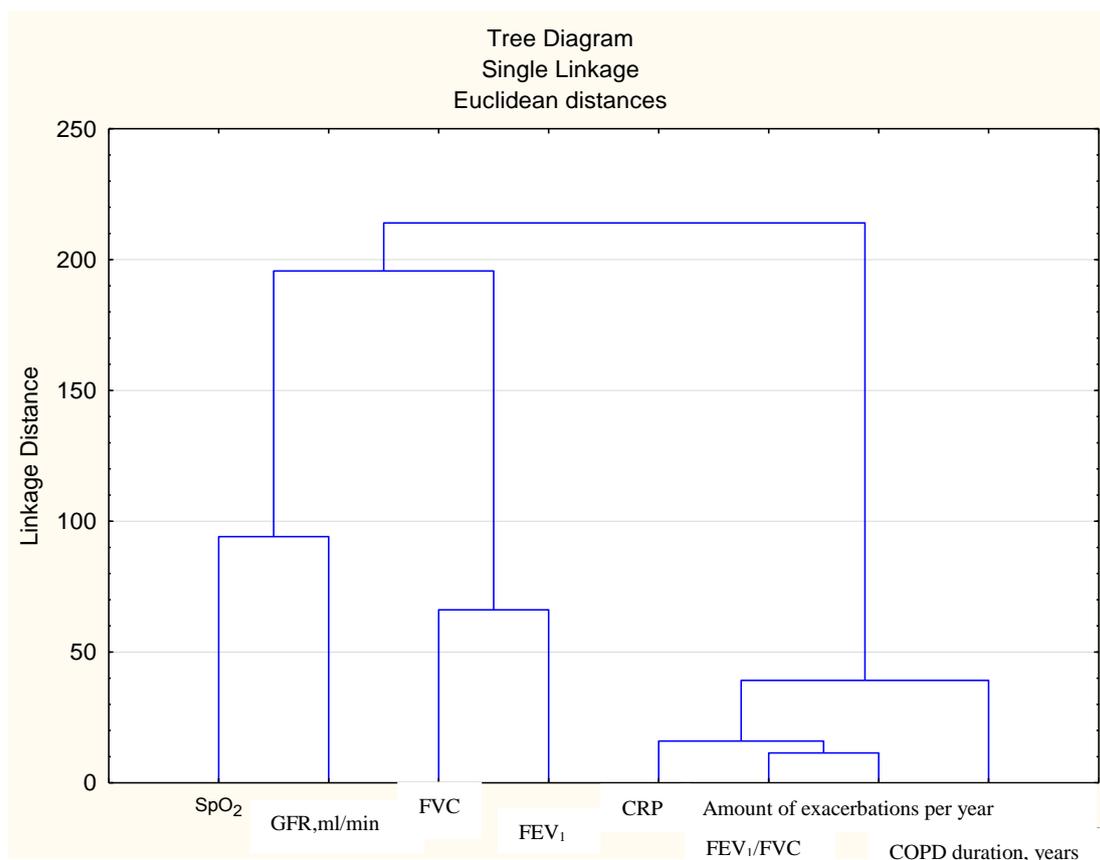
- - - negative dependence with moderate strength
- direct moderate dependence
- positive strong dependence

Fig. 1. A correlation of GFR interrelations with echocardiogram indicators

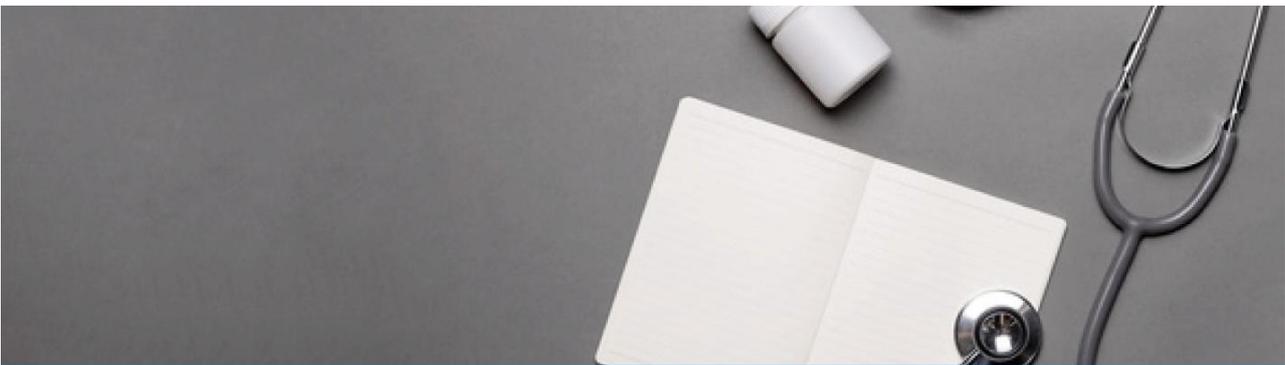


----- negative mean force dependence  
————— direct moderate dependence

Fig. 2. A correlation of CRP interrelations with indicators of FEV<sub>1</sub>, PASP, SpO<sub>2</sub>



**Fig. 3. Cluster analysis of the studied parameters in patients with COPD**



**PATHOLOGY OF THE URINARY SYSTEM ORGANS IN CHILDREN POPULATION OF  
UKRAINE: ITS PAST, PRESENT AND FUTURE**



**Prof IRYNA  
SOROKINA**

*Professor, Head of  
the Department  
of Pathological  
Anatomy,  
Kharkiv National  
Medical University,  
Ukraine*  
[soririna@gmail.com](mailto:soririna@gmail.com)



**Dr MYKHAILO  
MYROSHNY-  
CHENKO**

*Associate  
Professor,  
Department of  
Pathological  
Anatomy,  
Kharkiv National  
Medical University,  
Ukraine*  
[mmyroshnychenko@ukr.net](mailto:mmyroshnychenko@ukr.net)



**Dr NATALIYA  
KAPUSTNYK**

*Associate  
Professor,  
Department of  
Obstetrics and  
Gynaecology No. 1,  
Kharkiv National  
Medical University,  
Ukraine*  
[naukapathomorphology@ukr.net](mailto:naukapathomorphology@ukr.net)

**Abstract**

*In order to create a healthy society people must pay due attention to its child population, since children are the future of any nation and no state, which aspires to a rightful place in Europe, will have its future without preservation and strengthening of their health. Pathology of the urinary system organs in children is an urgent problem for the modern Ukrainian society. An important part in the development of pathology of this system in children is played by a damaging effect of maternal pathology, as it was revealed during complex morphological researches conducted at the Pathological Anatomy Department of Kharkiv National Medical University. In order to receive new data about the urinary system organs pathology in children it is absolutely necessary to carry out combined researches using classical morphological methods of investigation and modern molecular-genetic methods, because any conducted research must, firstly, be of practical value and, secondly, have its evolutionary significance.*

**Key words:** children, maternal health, pathology, Ukraine, urinary system organs.

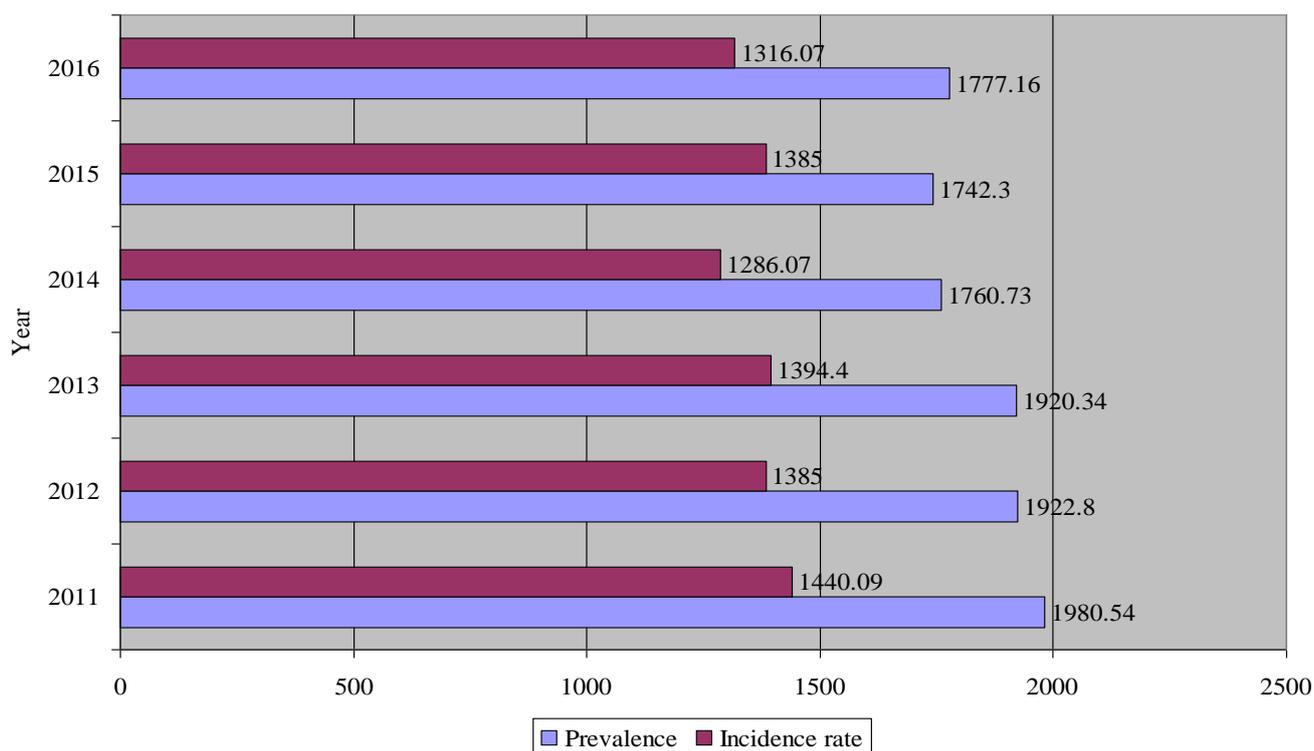
Human health is the highest value, a necessary component of the development and social-economic prosperity of any country, including Ukraine. Today the state of the Ukrainian population health is assessed, unfortunately, as unsatisfactory. This fact is caused, for example, by high levels of mortality and morbidity, low levels of the mean expectedness of life duration and healthy life duration, etc. [1].

In order to create a healthy society people must pay due attention to its child population [2], since children are the future of any nation and no state, which aspires to a rightful place in Europe, will have its future without preservation and strengthening of their health [3]. According to the data of the Global Strategy for Women's, Children's and Adolescents' Health (2016-2030) of the World Health Organization it is clear that investments in children's health have a high economic efficiency and provide the best guarantee to receive a productive workforce in future [4].

The incidence rate and prevalence of diseases are the most important criteria, which characterize the state of health in all age periods [5]. In Ukraine, against a background of a reducing number of its child population

(8003281 children aged 0-17 years in 2011 versus 7614006 children in 2016) the levels of incidence rate and prevalence of diseases remain high: the prevalence of diseases was 198054 in 2011 and 177716 in 2016 per 1000 children of the above age, and the incidence rate was, respectively, 144009 and 131607 [1, 4] (fig. 1). Our analysis of the prevalence of diseases revealed a decrease of this index from 2011 to 2015 and its increase from 2015 to 2016. Having analyzed the incidence rate, we found out its decrease from 2011 to 2012, an increase from 2012 to 2013, a decrease from 2013 to 2014, an increase from 2014 to 2015, and a decrease from 2015 to 2016 (fig. 1).

Our analysis of the incidence rate and prevalence patterns of different diseases in the child population of Ukraine during the period from 2011 to 2016 showed that the urinary system organs pathology within the above period accounted for 2.0-5.0 % [1, 4]. According to the data of the World Health Organization, diseases of the urinary system organs in the incidence rate and mortality patterns of the child population in economically developed countries amount to 2.5-3.0 % [6].

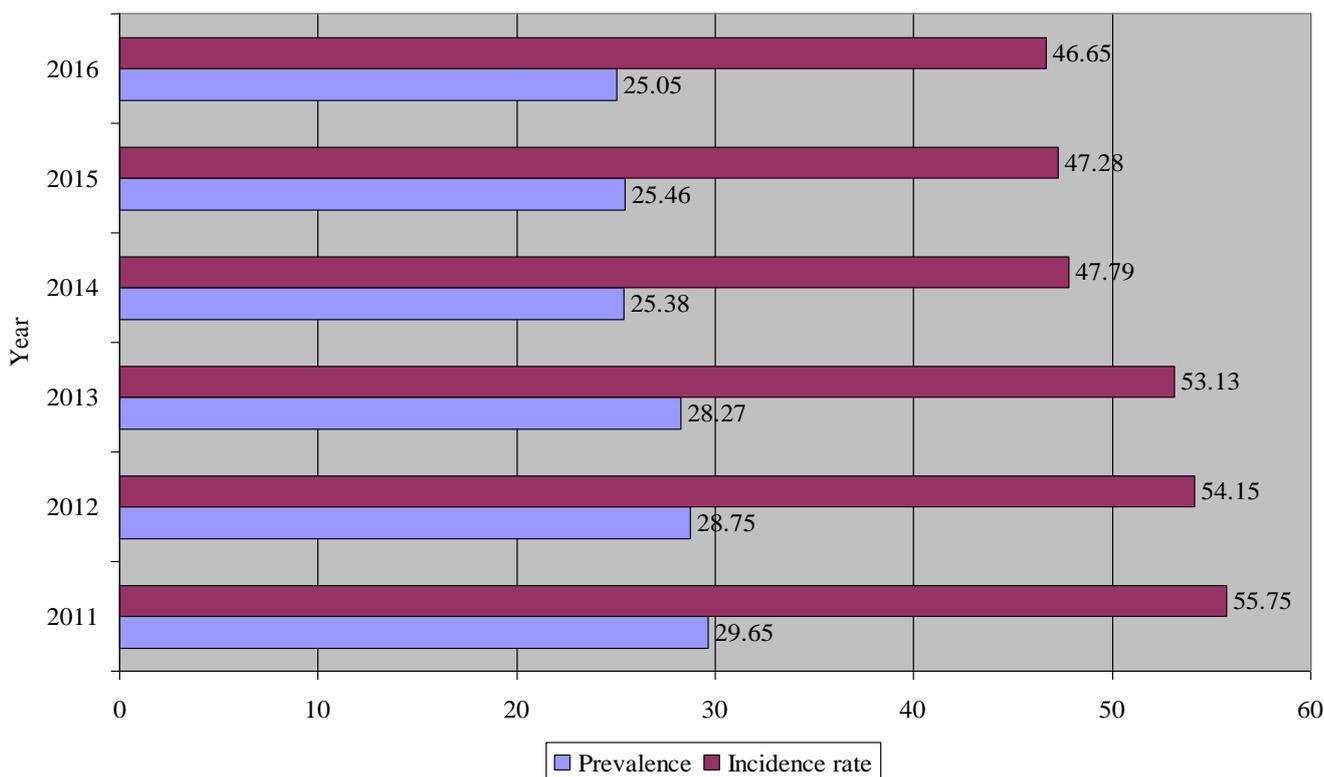


**Fig. 1. The dynamics of the incidence rate and prevalence of diseases in children aged 0-17 years in Ukraine within the period from 2011 to 2016 (per 1000 of the above population)**

Having analyzed the dynamics of changes in the index of incidence rate of the urinary system organs diseases in Ukrainian children aged 0-17 years, we revealed its decrease from 2011 to 2014, an increase from 2014 to 2015 and a decrease from 2015 to 2016. Our analysis of the index of prevalence of the urinary system organs diseases in the child population of Ukraine showed its decrease from 2011 to 2016 (fig. 2).

The pattern of diseases of the urinary system organs in children of the Kharkiv Region remains virtually

constant during many years. A significant number of cases in the total pathology of the urinary system organs in the child population of the Kharkiv Region within the period from 2007 to 2015 accounted for infections of the urinary system organs (interstitial nephritis, acute and chronic pyelonephritis, infection of the urinary system organs without identification of its localization, acute cystitis), dysmetabolic nephropathy, congenital malformations of the urinary system organs, glomerulonephritis, vesicoureteral reflux and neurogenic dysfunction of the bladder [7] (table 1).



**Fig. 2. The dynamics of the incidence rate and prevalence of the urinary system organs diseases in Ukrainian children aged 0-17 years during the period from 2011 to 2016 (per 1000 of the above population)**

Pathology of the urinary system organs in children is known to be of a polyetiologycal character. Owing to a rapid development of science the range of damaging factors, which form the basis for development of different pathology of the above system in children, widens from year to year, thereby resulting in a change of our conceptions about the essence of the diseases. The main etiopathogenetic factors, which cause the development of the urinary system organs pathology in children, include bacterial and viral infections, drug damages, bad habits, metabolic disturbances, hereditary and environmental factors, and many others [6].

It is generally recognized at present that the foundation of human health is laid during the intrauterine period, the cause-effect relationship between the morbidity of pregnant women and their children is undoubtful. Many diseases of the urinary system organs in children appear during the antenatal, intranatal or postnatal periods of their development. It is known that damages of the urinary system organs, which developed antenatally, can become evident some years or even decades later rather than immediately after the birth [8].

**The proportion (%) of different diseases in the total pathology of the urinary system organs in children of the Kharkiv Region within the period from 2007 to 2015**

Name of the pathology	Year								
	2007	2008	2009	2010	2011	2012	2013	2014	2015
Urinary system organs infections	46.39	38.25	41.50	49.17	43.21	48.79	48.79	29.06	31.33
Congenital malformations of the urinary system organs	7.03	19.97	18.70	7.86	6.87	10.11	11.27	31.14	28.43
Dysmetabolic nephropathy	26.94	27.30	16.18	22.94	25.61	15.52	15.48	16.32	18.34
Glomerulonephritis	6.89	4.66	7.24	7.62	7.88	9.33	7.46	9.98	10.03
Vesicoureteral reflux	8.28	6.96	9.57	6.43	6.97	6.14	5.22	4.33	4.09
Neurogenic dysfunction of the bladder	2.42	1.62	3.15	3.36	2.71	2.71	3.53	3.34	2.91
Chronic renal insufficiency	1.12	0.75	1.90	1.54	2.71	4.27	4.88	2.94	3.32
Urolithiasis	0.33	0.08	0.82	0.28	2.82	2.35	2.57	1.85	1.19
Acquired renal cysts	0.60	0.41	0.94	0.80	1.12	0.54	0.46	0.29	0.06
Lupus nephritis	–	–	–	–	0.05	0.24	0.34	0.46	0.12
Hemolytic uremic syndrome	–	–	–	–	0.05	–	–	0.17	0.12
Wilms tumor	–	–	–	–	–	–	–	0.12	0.06

Very important for prevention of health problems in children is development of methods of prognosis and early diagnosis of these disorders [9]. We have singled out such risk factors for the development of pathology of the urinary system organs in children of the Kharkiv Region as a reduced body weight and length of the baby at birth, a late initiation of sex by the mother, the female sex of the baby, smoking of its parents, presence of abortions in the mother's case history, complications during pregnancy (placental insufficiency and preeclampsia) and delivery (placental abruption and abnormal labour activity), presence of genital and extragenital pathology in the mother (diseases of the urinary system) [10, 11]. On the basis of the above risk factors we derived the formulae, with whose help it is possible to prognosticate both the development of pathology of the urinary system organs in children and its character (congenital or acquired).

An important part in the establishment of concepts concerning the morphofunctional basis of diseases of the urinary system organs in children is paid by pathological anatomy. As it is known, practical and scientific pathological anatomy has passed three main stages of its development, during which the main methods of the morphological perception of pathological processes were successively improved: macromorphological (XVI-XVIII centuries), microscopic (the end of XVIII – the first half of XX

century) and molecular-genetic (since 1970s of XX century) [12].

Despite the appearance of new morphological methods of research the concept of a damaging effect of the mother's pathology on the urinary system organs of her foetus and newborn has not lost its urgency; it is supplemented with more and more new confirming facts, which we revealed as a result of our morphological studies on clinical and experimental materials.

Preeclampsia (PE) belongs to serious complications of pregnancy. Our macroscopic examination of the kidneys of foetuses and newborns from the mothers, whose pregnancy was complicated with severe PE, revealed a more marked lobulation. Mild and moderate degrees of PE severity in mothers do not produce any effect on the degree of expression of embryonic lobulation of the kidneys in foetuses and newborns.

Our organometric study showed that in foetuses and newborns from the mothers, whose pregnancy was complicated with a mild degree of PE severity, the mass of the left kidney significantly prevailed over that of the right one; the same fact was also observed in foetuses and newborns from mothers with physiological pregnancy. In case of development of moderate and severe degrees of PE severity in the mothers we did not reveal any significant differences between the mass of

the left and right kidneys in the foetuses and newborns. The length, width and thickness of the right and left kidneys both in the foetuses and newborns did not differ significantly in case of development of different degrees of PE severity in their mothers.

The revealed organometric indices of the kidneys (their mass, length, width and thickness) were significantly larger in the newborns versus the foetuses in cases, when their mothers' pregnancy was complicated with mild and moderate degrees of PE severity. In case of development of severe PE in mothers the organometric indices of the kidneys of their foetuses and newborns did not differ significantly.

In the course of our research we made a conclusion that PE with a moderate degree of severity and especially severe PE in the mothers inhibit the growth of the kidneys in their foetuses and newborns, as it is demonstrated by significant decreases of the mass, length, width and thickness of these organs. PE with a mild degree of severity in the mothers does not produce any effect on the organometric indices of the kidneys in their foetuses and newborns.

Our publications mentioned such structural changes in the ureters and bladder of the foetuses and newborns from the mothers, whose pregnancy was complicated with PE, as: pronounced dystrophy of urotheliocytes; damaged myoarchitectonics in the form of thinning of the muscular layer, separation of muscle bundles with connective tissue fibers, sclerosis development; haemodynamic and ischaemic changes [23].

Iron deficiency anaemia (IDA) is a common complication of pregnancy; according to the data of the World Health Organization its rate in different countries of the world ranges from 21 % to 80 % if assessed by the level of haemoglobin and from 49 % to 99 % if assessed by the level of serum iron [13].

In the course of our studies on autopsy material we revealed that IDA, which complicated the course of pregnancy in the mothers, was a damaging factor with resultant structural changes in the ureters of the foetuses and newborns, the degree of manifestation of the above changes increasing from the foetus to the newborn as well as in case of an increasing degree of IDA severity. Structural changes in the ureters of foetuses and newborns, caused by the presence of IDA in their mothers, developed in all layers of the organ walls. The epithelial layer revealed its "loosening" with disordered layer-by-layer structuredness and development of dystrophic, desquamate and atrophic changes resulting in a decrease of its thickness. But against a background of the above changes the foetuses, whose mothers had IDA with a mild degree of severity, developed focal compensatory intensification of proliferative activity in

their epithelium and, as a total result, its thickness increased. Dyscirculatory and sclerotic changes developed in the in the lamina propria of the mucous membrane, submucosa and adventitia, thereby causing an increased thickness of these structural components of the ureter. There were haemodynamic disturbances and atrophic-sclerotic changes in the muscular layer, whose thickness increased. We drew a conclusion that the revealed structural changes in the ureter could result in its functional inferiority [14].

Oxygen deficit (hypoxia) is the most important damaging factor, which affects even the further development of the child rather than the state of health of the foetus and newborn only. Hypoxia develops as a result of genital and extragenital pathologies in mother and accompanies the majority of obstetric complications [15].

During our experimental studies with modelling of chronic intrauterine hypoxia (CIH), acute postnatal hypoxia (APH) and mixed hypoxia (MH) in WAG rats we saw that APH caused a moderately pronounced, while CIH and MH caused pronounced capillary congestion, microfocal haemorrhages in the renal corpuscles, epithelial desquamation in the parietal layer of the capsule, the above changes increasing from the foetus to the newborn in the case of CIH modelling. Morphometric study revealed that CIH and MH caused a decreased number of glomeruli in the kidneys of foetuses and newborns as well as slower rates of maturation of renal corpuscles; APH did not affect quantitative indices of the glomerular apparatus of the foetuses and newborns kidneys [16].

Our previous immunohistochemical study revealed that experimental hypoxia induced apoptotic processes in the kidneys, ureters and bladder of foetuses and newborns, whose degree of expression was moderate in the case of APH modelling, marked in CIH modelling and severe in MH modelling. Under the influence of APH, CIH and MH in the ureters and bladder of the foetuses and newborns p53-positive cells were evenly located in all wall layers of these organs, whereas in the kidney cells expressing p53 prevailed in the tubular component. We also observed that in the case of CIH apoptotic processes in the kidneys, ureters and bladder increased in newborns versus foetuses, while in intact animals the apoptotic activity decreased from the foetus to the newborn [17].

We showed that CIH and MH in newborns resulted in a significant decrease of the index of the mean value of the muscle fiber thickness in the muscular layer of the ureter and bladder as well as in an uneven expression of smooth muscle actin by cells of the muscular layer in these organs. APH did not produce any damaging effect on qualitative and quantitative characteristics of the

muscular layer of the ureter and bladder in newborns. In newborns APH did not affect indices of the mean value of the muscle fiber thickness in arterioles and venules of the kidneys, ureters and bladder, while CIH and MH resulted in a significant decrease of the above indices. CIH and MH increased the degree of manifestation of smooth muscle actin expression by myofibroblasts in the kidneys, ureters and bladder, by mesangiocytes and epithelial cells of glomeruli as well as by epithelial cells in renal tubules that later can develop sclerotic changes in these organs in such children at different stages of ontogenesis [18].

It is known that kidney diseases in children can be accompanied with evident symptoms or pass with minimal clinical manifestations. Some renal diseases in children may be asymptomatic for a long period of time. In modern nephrology, renal biopsy is the “gold” standard that makes it possible to receive material for a histological study of the renal tissue and, using histological, histochemical, immunohistochemical, morphometric methods and electron microscopy, make a morphological diagnosis, which will enable the clinician to take correct therapeutic measures [19].

Nevertheless the morphological methods of research, used in Ukraine, sometimes become insufficient for verifying different variants in the course of renal pathology in children. As the way out of the current situation it is important to put into practice molecular-genetic methods of research [22], without which it is impossible in some cases to make the correct morphological and, consequently, clinical diagnosis and hence to treat the patient. A better diagnosis of nephrotic syndrome in children owing to molecular-genetic methods of research is a convincing example.

The study of causes for development of nephrotic syndrome is associated with researches that assess the state of proteins in the slit membrane of podocytes, namely reveal mutations in the genes, which encode these proteins. For example, nephrin is one of the important protein of the slit membrane. Mutations in the

family of nephrin proteins – NEPH1, NEPH2, NEPH3 – develop to congenital nephrotic syndrome, which is characterized by resistance to steroid therapy. Another important role in the development of nephrotic syndrome is played by the membrane protein podocin, which is encoded by the NPHS2 gene located in chromosome 1 on 1q25-q31 region. Histological studies of renal biopsies in such patients diagnose, as a rule, focal segmental glomerulosclerosis [20].

Improvement of methods for diagnosing any pathology in the human organism, including pathology of the urinary system organs, results from the modern development of different sciences. As far as the well-known theory of formation of diseases, the theory of pathology, is concerned, it was formulated in 1849 in works by Carl von Rokitansky and Rudolph Virchow. They created this theory at the time, when there were not so many methods of research as now. Is it not for this reason that the information, which can be received by modern methods of study, is sometimes perceived in the clinical practice so aloof? Therefore a discussion was aroused in the medical community about a necessity to form a new theory of pathology, the theory of XXI century [21].

Thus, pathology of the urinary system organs in children is an urgent problem for the modern Ukrainian society. An important part in the development of pathology of this system in children is played by a damaging effect of maternal pathology, as it was revealed during complex morphological researches conducted at the Pathological Anatomy Department of Kharkiv National Medical University.

In order to receive new data about the pathology of the urinary system organs in children it is absolutely necessary to carry out combined researches using classical morphological methods of investigation and modern molecular-genetic methods, because any conducted research must, firstly, be of practical value and, secondly, have its evolutionary significance.

## References

1. The annual report about the state of the population's health, sanitary-epidemiological situation and operating results of the system of health protection in Ukraine. 2015 / Ed. by Shafransky V.V.; Ministry of Health of Ukraine, Government Agency "Ukrainian Institute for Strategic Studies". – Kyiv, 2016. – 452 p.
2. Mashina N.S. Health status of infants and its determining factors / N.S. Mashina, M.Yu. Galaktionova // *Siberian Medical Review*. – 2015. – No 2. – P. 26-31.
3. Indices and social context in the formation of adolescents' health: A monograph / O.M. Balakireva, T.V. Bondar, D.M. Pavlova et al. ; ed. by O.M. Balakireva. – K. : UNISEF, Ukrainian Institute for Social Research after Oleksandr Yaremenko. – K., 2014. – 156 p.
4. The annual report about the state of the population's health, sanitary-epidemiological situation and operating results of the system of health protection in Ukraine. 2016 / Ministry of Health of Ukraine, Government Agency "Ukrainian Institute for Strategic Studies". – Kyiv, 2017. – 516 p.
5. Panchyshyn N.Ya. Morbidity of the child population of Ukraine and the factors, which produce their effects on children's health / N.Ya. Panchyshyn, V.L. Smirnova, O.Ya. Halytska-Kharkhalis // *Urgent Problems of Paediatrics, Obstetrics and Gynaecology*. – 2011. – No. 2. – P. 131-132.
6. Inogamova V.V. Risk factors of diseases of the kidneys and urinary tract in modern conditions / V.V. Inogamova, Z.Sh. Giyasova // *Young Scientist*. – 2016. – No. 10 (114). – P. 486-490.
7. The nosological pattern of pathology of the urinary system organs in the child population of the Kharkiv Region / G.R. Muratov, T.F. Kolibaeva, M.A. Gonchar, I.V. Sorokina, M.S. Myroshnychenko // *Problems of Continuous Medical Education and Science*. – 2016. – No. 3 (23). – P. 22-28.
8. Ignatova M.S. Urgent problems of paediatric nephrology in the beginning of XXI century / M.S. Ignatova // *Paediatrics*. – 2007. – Vol. 86, No. 6. – P. 6-13
9. Lukyanova Ye.M. Medcial and pedagogical aspects in the problem of preservation of children's health / Ye.M. Lukyanova // *International Medical Journal*. – 2003. – No. 3. – P. 6-9.
10. Risk factors of the development of the urinary system organs in the child population of the Kharkiv Region / I.V. Sorokina, M.S. Myroshnychenko, N.V. Kapustnyk, A.V. Arsenyev // *Congress "Prevention. Anti-Aging. Ukraine"*. Congress materials. – Kharkiv. – September 28-29, 2017. – P. 12-13.
11. Peculiarities in the course of pregnancy in the mothers, whose children had pathology of organs of their urinary tract system / M.A. Gonchar, G.R. Muratov, T.F. Kolibaeva, I.V. Sorokina, M.S. Myroshnychenko // *West Kazakhstan Medical Journal*. – 2016. – 3 (51). – P. 56-61.
12. *Pathomorphology: The national textbook* / V.D. Markovskiy, V.O. Tumansky, I.V. Sorokina et al.; ed. by V.D. Markovskiy, V.O. Tumansky. – K. : All-Ukraine Special-Purpose Publishing House "Medicine", 2015. – 936 p.
13. Kulakov V.I. Iron deficiency anaemia and pregnancy / V.I. Kulakov, V.N. Serov // *Women's Health*. – 2015. – No. 9 (105). – P. 21-24.
14. Iron deficiency anaemia in the mother, complicating the course of pregnancy, as the factor that results in structural changes in the ureters of her offspring / I.V. Sorokina, M.S. Myroshnychenko, N.V. Kapustnyk, S.A. Sherstiuk, S.A. Nakonechna // *Development and modernization of medical science and practice: experience of Poland and prospects of Ukraine: Collective monograph. Vol. 3. Lublin: Izdevnieciba "Baltija Publishing", 2017. – P. 209-223.*
15. Andreeva A.A. Nitric oxide production in the newborns, who survived intrauterine hypoxia / A.A. Andreeva, T.I. Oparina // *Journal of Obstetrics and Gynaecological Diseases*. – 2010. – No. 26. – P. 30-34.
16. Morphological peculiarities in the renal glomerular apparatus of fetuses and newborns in modelling different hypoxias / I.V. Sorokina, V.D. Markovskiy, I.V. Borzenkova, M.S. Myroshnychenko, O.N. Pliten // *Morphology*. – 2016. – Vol. 10, No. 3. – P. 267-272.
17. Pathogenically induced apoptosis, caused by hypoxic influence, in organs of the urinary system of fetuses and newborns (an experimental research) / M.S. Myroshnychenko, S.A. Sherstiuk, Ye.O. Zubova, S.A. Nakonechna // *Georgian Medical News*. – 2017. – No. 9 (270). – P. 94-99.
18. Sorokina I.V. The features of smooth muscle actin expression in the kidneys, ureters and bladder of the newborns exposed to chronic intrauterine, acute postnatal and mixed hypoxia / I.V. Sorokina, M.S. Myroshnychenko, I.V. Korneyko // *The New Armenian Medical Journal*. – 2017. – Vol. 11, No. 2. – P. 33-39.
19. Snigur G.L. Significance of modern methods of pathohistological study in diagnosing renal diseases / G.L. Snigur, A.V. Smirnov, M.V. Schmidt // *Volgograd Scientific Medical Journal*. – 2014. – No. 4. – P. 43-47.
20. Molecular nephropathology: new abilities for diagnosing renal diseases / S.L. Morozov, V.V. Dlin,

- V.S. Sukhorukov, A.S. Voronkova // Russian Herald of Perinatology and Paediatrics. – 2017. – No. 62 (3). – P. 32-36.
21. Titov V.N. One and half century after C. Rokitansky's humoral theory and R. Virchow's cell theory: the phylogenetic theory of pathology / V.N. Titov // Nephrology. – 2012. – Vol. 16, No. 4. – P. 11-27.
  22. Ignatova M.S. The role of genetics in the development of paediatric nephrology / M.S. Ignatova, V.V. Dlin // Russian Herald of Perinatology and Paediatrics. – 2015. – No. 3. – P. 6-9.
  23. Myroshnychenko M.S. Pathomorphological peculiarities of the ureter and bladder in foetuses and newborns from mothers with complicated pregnancy / M.S. Myroshnychenko, D.A. Feldman // V International Youth Medical Congress "St. Petersburg Scientific Readings – 2013". Congress materials. – St. Petersburg. – December 4-6, 2013. – P. 203.



**Dr ALEKSANDR SOLOV'EV**

Associate Professor,  
Department of Histology,  
Izhevsk State Medical Academy,  
Russia  
histolog@igma.udm.ru



**Prof ALEKSANDR SHISHKIN**

Professor,  
Department of Physiology,  
Izhevsk State Agricultural Academy,  
Russia  
shishkinlab@yandex.ru



**Prof NIKOLAY KIRYANOV**

Professor, Head of the Department of Pathology,  
Izhevsk State Medical Academy,  
Russia  
kirnik@list.ru

**Abstract**

*Electric charge of living cells and zeta-potential of a cell membrane are included into a number of most significant indices which determine hemostasis of any living organism, its tissues and organs at the cellular level. The most comfortable, accurate and reliable method is considered to be cell electrophoresis. A serial instrument complex for cell electrophoresis performance which differs from foreign models by using alternating current and an original electrophoretic chamber is described in the article. Duration of a single analysis is 5-6 min.; the volume of cell suspension is 400mcl; the number of cells analyzed is 100-300; voltage on electrodes in the chamber is 10-30 V. The device can be used for solving a wide choice of research and practical tasks. In particular, its usage is effective in express estimation of therapy efficacy in advanced conditions accompanied by intoxication (which causes changes of cell electric charge).*

**Key words:** cell analysis, microelectrophoresis, electrokinetic indices, express diagnostics.

Elaboration of express diagnostic methods in disturbances of morphofunctional conditions of cells of a human in various pathologic processes is an actual problem of modern medicine. It has been proved that electrophoretic mobility of erythrocytes (EPHME) which shows not only the condition of surface charge of

red blood cells but its organism in a whole is an effective criterion of both stress reaction expression and adaptive processes of the body in extreme influences [1, 2, 3]. In connection with it, the study of surface membranes using the method of cytoelectrophoresis which shows the state of electric charge system on

external surface of blood cells has a great significance for medicine. Wherein, electric charge of the surface membrane of a cell is directly connected with physico-chemical processes occurring in cell membranes. Blood cells carry negative electric charge on their surface. Complicated physiological body functions, such as cells interactions, exchange of gases, adsorption on entire surface of antigens, toxins and so on are impossible to occur without electric charge of erythrocytes. The magnitude of negative charge of red blood cell membrane changes in pathologic conditions. Therefore, stability of this magnitude can be used as a diagnostic criterion in various critical conditions such as, sepsis, peritonitis, pneumonias, and disturbances of cerebral blood circulation and so on [4, 5, 6, 7].

To establish the electric potential of erythrocytes various devices have been proposed. For example, spectrofluometre Hitachi, LTD (MPF- 400) with a positively charged probe for estimating the charge of erythrocytes, « Parmakvant» and cytoferrometre worked out by OPTON (Germany) for estimating electrophoretic mobility of red blood cells were run in production. However, the methods mentioned above deal with creation of constant electric fields where cells move from anode to cathode. This became the reason to work out a new device which will be lacking of those disadvantages. The device is aimed to obtain information on electric charge of surface membrane of erythrocytes circulating in blood by using multi- vector microelectrophoresis (MEPh) which does not require big material and temporal costs. The advantages of the method of multi-vector MEPh during which an alternative electric field is created in comparison with

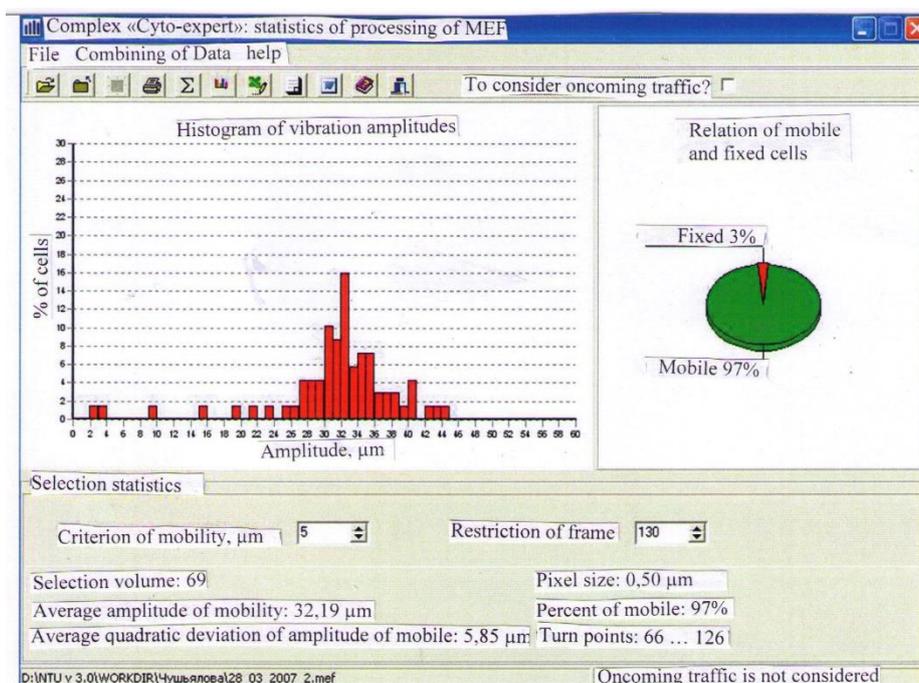
typical MEPh (with a constant electric field and a cell moves from anode to cathode) allow: a) to analyze thoroughly cell reactions on the action of electric fields, taking into consideration relationship of bioelectric reactions of cells with their cytoskeleton and the level of permeability; b) to avoid errors connected with inhibition of a cell movement from anode to cathode; c) to study a great number of cells for a short period of time; d) to study various types' cells, this broadens the opportunities of using the method for diagnosing diseases and determining the efficacy of treatment.

The preparation of the medicinal product includes: making a suspension with a small number of cells being studied, in a buffer and placement of 3-4 drops of this solution into a working zone of an electrophoretic cell. Exposing cells by the influence of sign-alternative electric field with the magnitude of current not less than 2.0mA, the rate of the sign change being 0.25 Hertz, the living cells which have their own electric charge move co-directly with a field phase. An operator in a computerized or semicomputerized regimen using original software determines the characteristics of this movement under the microscope after its video recording with an ocular camcorder. The programme forms automatically a report basing on the results of processing. The duration of an analysis (including a sample preparation) is no longer than 5-6 minutes.

The technique worked out is an operating method for determining androgenic intoxication. Such instrumental complex in comparison with foreign analogues, such as Parmakvant and Opton is more informative, simple in usage and economical in operation and service.



**Fig.1 The instrument complex for signalternative microelectrophoresis «Cyto-expert»**



**Fig.2 The results of processing with the kit of programmes NTU Complex**

## References

1. Baskurt OK, Tugral E, Neu B, Meiselman HJ. Particle electrophoresis as a tool to understand the aggregation behavior of red blood cells. *Electrophoresis*. 2002 Jul;23(13):2103-9.
2. Cook GM. Glycobiology of the cell surface: Its debt to cell electrophoresis 1940-65. *Electrophoresis*. 2016 Jun;37(11):1399-406. doi: 10.1002/elps.201500476. Epub 2016 Feb 1.
3. Sukhonenko EP, Lisitsin NB, Palagin VA, Solov'ev AA, Kir'ianov NA. The electrophoretic cell analysis applying the instrument complex "Cito-expert". *Klin Lab Diagn*. 2011 Nov;(11):35-8.
4. Golovetsky I. Ya., Popova O.V., Kozinets G.I. Determination of the electrophoretic mobility of red blood cells in patients with peritonitis of various etiology. *Klin Lab Diagn*. 2005 Oct;(10):53a.
5. Deryugina A.V., Martusevich A.A., Khlamova Yu.N., Kuvaeva S.S., Martusevich A.K., Rumyantseva T.N. Electrophoretic mobility of erythrocytes in inflammation. [Article in Russian]. *Medical newsletter of Vyatka*. 2016; 52 (4): 57-60.
6. Deryugina AV, Krylov VN, Shumilova AV, Filippenko ES, Boyarinova LV, Solov'eva OD. Using mexicor to correct the functional parameters of red blood cells in rats with traumatic brain injury model. [Article in Russian]. *Eksp Klin Farmakol*. 2015;78(8):14-7.
7. Fedin AI, Vasilenko IA, Badalyan KR. The effect of cholesterol on the electrokinetic properties of erythrocyte membranes in chronic cerebral ischemi. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2015;115(9 Pt 2):30-37. doi: 10.17116/jnevro20151159230-37.



## THE ROLE OF FRACTALKINE IN THE DEVELOPMENT OF INFLAMMATION IN PATIENTS WITH ASTHMA COMBINED WITH DIABETES MELLITUS TYPE 2 AND OBESITY



**Dr GALYNA  
YERYOMENKO**

Associate  
Professor,  
Department of  
Internal Medicine  
Propedeutics No.2  
and Nursing,  
Kharkiv National  
Medical University,  
Ukraine  
galyna0512@ukr.  
net



**Prof TETYANA  
OSpanova**

Professor, Head of  
the Department of  
Propaedeutics of  
Internal Medicine  
#.2 and Nursing,  
Kharkiv National  
Medical University,  
Ukraine  
t.ospanova1@  
gmail.com



**Prof TETYANA  
BEZDITKO**

Professor,  
Department of  
Propaedeutics of  
Internal Medicine  
#.2 and Nursing,  
Kharkiv National  
Medical University,  
Ukraine  
tvbezdetko@  
gmail.com



**Dr OLENA  
VYSOTSKA**

Associate  
Professor,  
Professor of  
Biomedical  
Engineering  
Department,  
Kharkiv National  
University of  
Radio Electronics,  
Ukraine  
olena.vysotska@  
nure.ua



**Dr ANNA  
PECHERSKA**

Senior Research  
Associate of  
Biomedical  
Engineering  
Department,  
Kharkiv National  
University of  
Radio Electronics,  
Ukraine  
anna.pecherska@  
nure.ua

### **Abstract**

*Asthma, obesity, diabetes mellitus type 2 often coexist. A steady tendency to aggravation of the disease course and increase of the number of patients requiring urgent hospitalization is observed. An important pathogenetic role of chemokines, in particular fractalkine (CX3CL1). We study the level of plasma fractalkine in groups of patients with asthma and in cases of its combination with diabetes mellitus type 2 and obesity. The levels of plasma CX3CL1 in patients with asthma statistically significantly ( $p < 0.001$ ) exceed the same indices in the group of somatically healthy people. A progressing increase of the plasma level of fractalkine with addition of comorbidity in the group of patients with accompanying diabetes mellitus by 2.2 times and with obesity by 1.8 times versus the control group was revealed. Patients with asthma demonstrated a direct dependence of the level of plasma CX3CL1 upon the duration of their disease.*

**Key words:** asthma, obesity, diabetes mellitus type 2, fractalkine.

At present, asthma remains an urgent problem of the world medical practice rather than of the national one only. The last decade witnesses an incremental increase of BA incidence both in Ukraine and in the whole world.

A steady tendency to aggravation of the disease course and increase of the number of patients requiring urgent hospitalization is observed [4]. Achievement of the control over asthma and an effective prevention of exacerbations are urgent problems of the modern medicine [8]. Regardless of the degree of the disease severity, extremely high incidence of asthma in combination with comorbid states, diabetes mellitus type 2 and obesity being some of them. Disorders in the immune system, microcirculatory disturbances and a reduced diffusion capacity of lungs, which develop in diabetes mellitus, predispose to chronic inflammatory diseases including those of the bronchopulmonary apparatus [1, 3, 10, 11]. Obesity, even in the absence of asthma, results in physiological changes of the pulmonary function including reduction of lung volumes, chest rigidity and increase of oxygen respiration cost with formation of dyspnea [6]. Fundamental researches during last years made it possible to specify the risk factors of asthma and pathogenetic mechanisms in the disease development as well as to realize standardization and unification of ways for diagnosing and treating this disease [7]. The modern stage of the study of asthma is characterized by search for sensitive and specific biomarkers, which make it possible to perform diagnosis of early stages of the disease complications and optimize the treatment.

According to modern views, an inflammation of the respiratory tract is the main morphological sign of asthma [5].

The inflammation is realized by means of humoral immunological mechanisms with participation of a broad range of cytokines, which are responsible for activation, proliferation and chemotaxis of different cells. Here among all the cytokines a group of small (8-10 kD) proteins is isolated; these are able to induce directed chemotaxis of surrounding cells and are called “chemokines” [14]. The group of proteins CX3C, where three amino acids are present between three cysteine groups, was discovered later than others. At present this family includes only one chemokine, fractalkine (CX3CL1), which is a unique chemokine consisting of 373 amino acids. The soluble form of CX3CL1 demonstrates chemotactic activity for monocytes, NK and T cells. Besides, CX3CL1 acts as a molecule of adhesion to leukocytes [2, 17]. Findings of the performed researches make it possible to suppose that CX3CL1 plays an unclear part in the process of inflammation. Really, it is not only in case of inflammation but even during its absence that CX3CL1 and its receptor are detected in different organs and on different cells (for example, macrophages and dendrite cells). The statement that its effect on the activity of an inflammatory reaction is

always stimulating at least in some cases does not correspond to the received findings [21].

An important pathogenetic role of CX3CL1 and its receptor has already been demonstrated on the example of some diseases: rheumatoid arthritis [18], lupus nephritis [22], inflammatory lesions of intestines [17], diabetic nephropathy [15, 20], oncopathology [12], septic lesions [13], neurological diseases [9].

Consequently, one can suppose that CX3CL1 is an immune response regulator and the direction of its effect depends upon the concentration of this chemokine in blood. At present, facts are being accumulated in evidence of the considerable role of CX3CL1 – the only chemokine, which exists in its soluble and fixed forms – in the pathogenesis of different diseases. The above makes it possible to regard CX3CL1 as an important marker of activation of an inflammatory process associated with chemotaxis of different leukocytes (first of all monocytes and lymphocytes) into the area of inflammation. Taking into account literature data one can draw a conclusion about significance of CX3CL1 as an activity marker of an inflammatory process and an important factor, which participates in the pathogenesis of asthma. Further active studies of the part of CX3CL1 and its relationships with other chemokines are necessary for both understanding the pathogenesis and developing pathogenetic methods of treatment of this pathology on the basis of the data obtained.

**Objective:** to study the level of plasma fractalkine, to carry on a comparative analysis of hyperfractalkinaemia in groups of patients with asthma and in cases of its combination with diabetes mellitus type 2 and obesity, thereby making it possible to optimize the diagnosis and prognosis of the course of asthma.

**Materials and methods:** Patients with asthma, diabetes mellitus (DM) type 2 and obesity.

The diagnosis of asthma was made according to the international consensus paper GINA 2014 [7]. The diagnosis of DM was verified in compliance with international protocols [8, 19]. The level of fractalkine was detected in blood plasma with help of a kit of reagents “RayBioHumanFractalkine (CX3CL1) ELISA Kit” (USA) by the immunoenzyme method. This test is based on the technique of enzymeimmunoassay and designed for detecting fractalkine immediately in human biological fluids (plasma, urine, cell culture supernatant). All in all the examination involved 78 cases with asthma – the whole group of patients. Three groups of cases were singled out: group 1 – patients with asthma (asthma, n = 20); group 2 – patients with asthma and DM type 2 (n = 29); group 3 – patients with asthma and obesity (n = 29). The control group included 21 somatically healthy persons. The patients’ age

averaged  $43.1 \pm 2.7$  years. The average age in the control group was  $48.1 \pm 1.4$  years.

All patients underwent a complex examination, which included collection of patients' complaints, study of their case histories, physical examination with study of their body mass index, additional examination with clinical and biochemical studies, ECG and computed spirometry.

The findings were statistically treated with help of SPSS 19 (IBM, USA) software tool. Medians and interquartile intervals were computed. The significance of median differences was assessed on the basis of the Mann-Whitney U test and the Kruskal-Wallis H test. The relation between the signs was assessed with the Spearman's rank correlation coefficient. The Shapiro-Wilk test was used for analysing the normality of data distribution.

## Results

At the first stage of the research the distribution of CX3CL1 index in the examined groups was compared versus the normal one. According to the findings of the Shapiro-Wilk test, the distribution of CX3CL1 index in the examined groups significantly differs from the normal one. The medians and interquartile range of CX3CL1 values in each group of patients and in the control group are shown on Fig. 1.

Pair-wise comparison resulted in revealing of significant differences of CX3CL1 values between all examined groups ( $p = 0.0001$ ).

In the group of asthma patients the median value of the CX3CL1 level was 46.00 ng/ml, in the group of patients with asthma+DMT2 it was 97.60 ng/ml and in patients with asthma+obesity – 79.14 ng/ml. The value of the 25<sup>th</sup> percentile was 44.6 ng/ml in the group of patients with asthma, 77.02 ng/ml in patients with asthma+obesity and 94.97 ng/ml in patients with asthma+DMT2 versus 42.06 ng/ml in the control group. The value of the 75<sup>th</sup> percentile of CX3CL1 in the control group was 45.27 ng/ml versus 81.44 ng/ml in the group of patients with asthma+obesity and 99.25 ng/ml in the group of patients with asthma+DMT2. All

the examined groups revealed a reliable difference of the CX3CL1 level ( $p = 0.0001$ ).

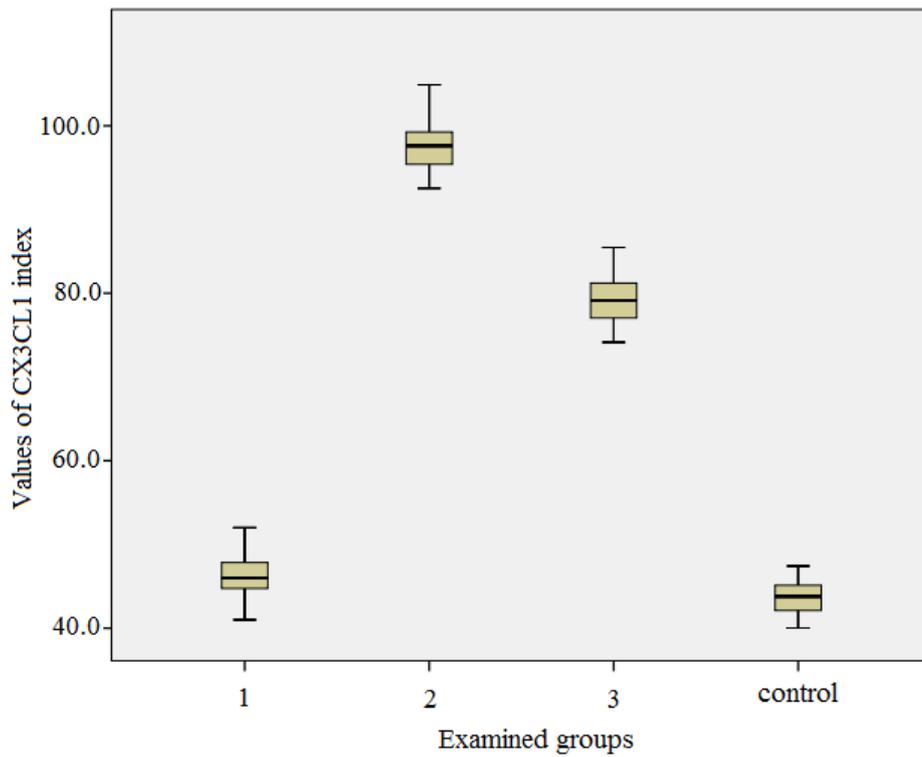
## Discussion

The obtained results confirm literature data about participation of CX3CL1 in the development of inflammation in patients both with asthma and DM as well as obesity [6, 7, 10]. In our study, asthma patients with comorbid states revealed the highest levels of CX3CL1, which exceeded its values versus the control group 2.2 times in the group with asthma+DMT2 and 1.8 times in the group with asthma+obesity.

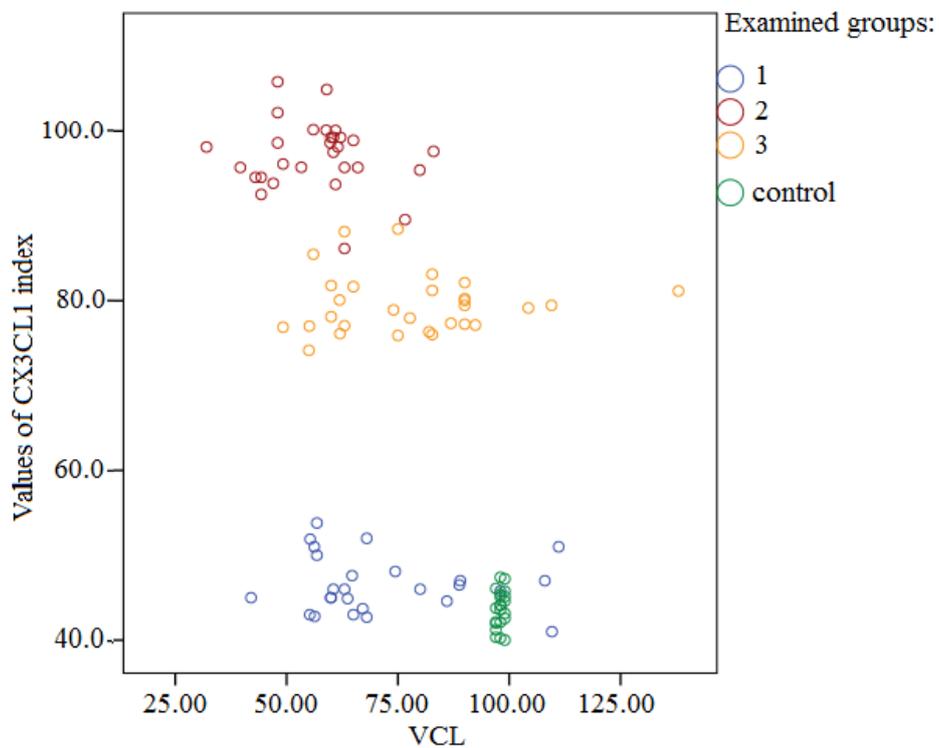
The whole group of examined patients with asthma underwent a correlation analysis between RF-VCL and RF-FEV1 values that revealed reliable negative relationships between: CX3CL1 and VCL ( $r = -0.53$ ,  $p = 0.001$ ) (Fig. 2.); CX3CL1 and FEV1 ( $r = -0.496$ ,  $p = 0.001$ ) (Fig. 3). Also, a positive correlation was received between CX3CL1 and duration of the disease ( $r = 0.766$ ,  $p = 0.001$ ) (Fig. 4). An analysis of CX3CL1 with VCL and FEV1 by groups with comorbidity revealed a relationship only in the group of asthma+DMT2, which was  $r = -0.45$  ( $p = 0.015$ ).

## Conclusions

1. The levels of plasma CX3CL1 in patients with asthma statistically significantly ( $p < 0.001$ ) exceed the same indices in the group of somatically healthy people. A progressing increase of the plasma level of fractalkine with addition of comorbidity in the group of patients with accompanying diabetes mellitus by 2.2 times and with obesity by 1.8 times versus the control group was revealed.
2. Patients with asthma demonstrated a direct dependence of the level of plasma CX3CL1 upon the duration of their disease.
3. More detailed studies on the basis of populations are necessary in order to assess the clinical and diagnostic significance of CX3CL1 in the pathogenesis of asthma combined with diabetes mellitus type 2 and obesity.



**Fig.1. Values of CX3CL1 index in the examined groups**



**Fig. 2. Correlations between the level of CX3CL1 and VCL in the examined groups**

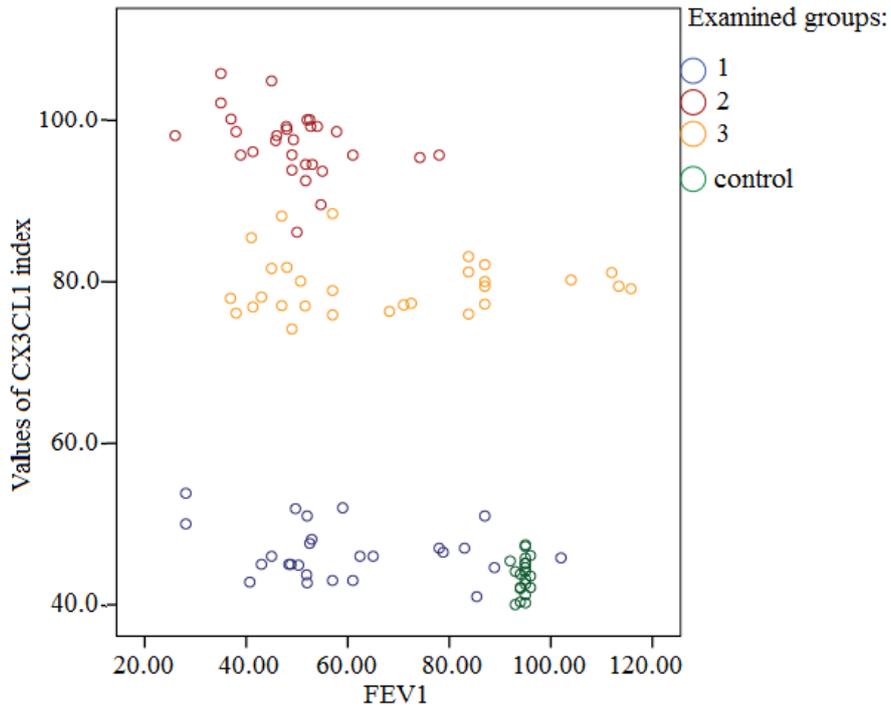


Fig. 3. Correlations between the level of CX3CL1 and FEV1 in the examined groups

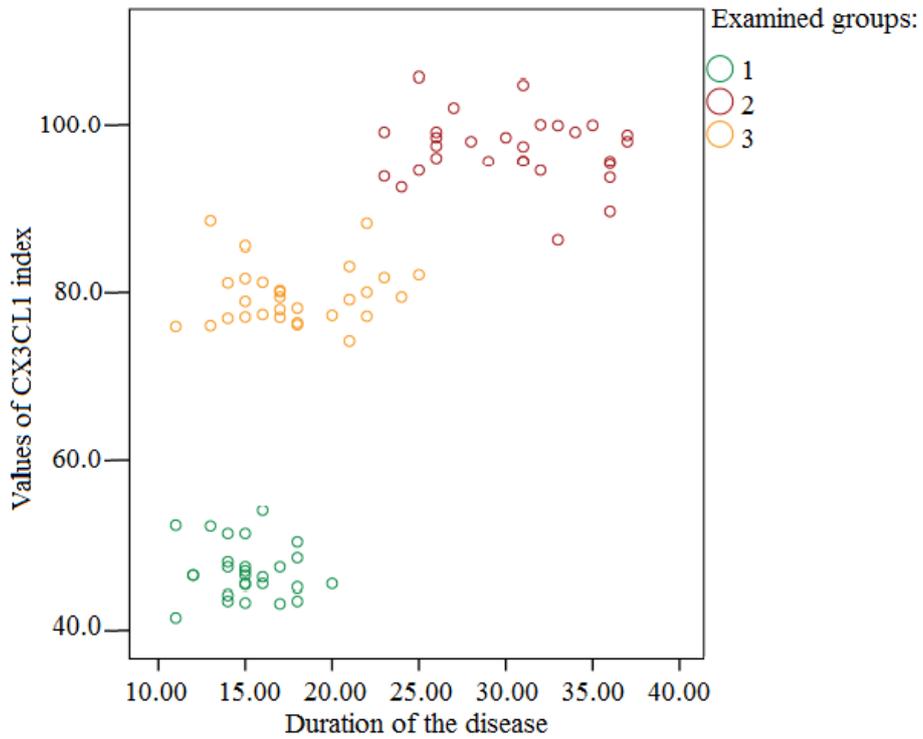


Fig. 4. Correlations between the level of CX3CL1 and duration of the disease in the examined groups of patients

## References

1. V.A. Vakhlamov, G.N. Varvarina, A.A. Eriskina, Yu.A. Orlova (2012) Carbohydrate metabolism status in patients with bronchial asthma depending on the character of glucocorticosteroid baseline therapy. *Sovremennyye tekhnologii v meditsine*. [Modern technologies in medicine.] Vol.1 P.129-132
2. Sevostyanova I.V., Polunina O.S., Voronina L.P., Perova N.Yu., Belyakova I.S., Polunina E.A. (2014) The influence of cytokines with chemotactic properties on the condition of vascular endothelium in bronchial asthma. *Astrakhanskiy meditsinskiy zhurnal*. [Astrakhan Medical Journal]. Vol9. № 3. P. 56-62.
3. A.L.Chernyayev, M.V.Samsonova. (2001) Pathological anatomy of chronic bronchitis and bronchial asthma. *Consilium medicum*. Vol. 3. № 3. P. 3-10.
4. Barnes PJ. Scientific rationale for inhaled combination therapy with long-acting beta2-agonists and corticosteroids/ PJ Barnes // *Eur Respir J*. - 2002 Jan; 19(1):182-91.
5. Beuther, D.A. Obesity and pulmonary function testing / D.A. Beuther, E.R. Sutherland // *J Allergy Clin Immunol*. – 2005. – Vol. 115. – P. 1100-1101.
6. Chang PJ. Corticosteroid insensitivity of chemokine expression in airway smooth muscle of patients with severe asthma / Chang PJ, Bhavsar PK, Michaeloudes C, Khorasani N, Chung KF // *J Allergy Clin Immunol*. – 2012, Oct; 130(4):877-85. e5. doi: 10.1016/j.jaci.2012.07.017. Epub 2012 Sep 1.
7. Global Initiative for Asthma (GINA), 2014. Available from: [www.ginasthma.org](http://www.ginasthma.org).
8. Global Guideline for Type 2 Diabetes, 2012. Available from: [www.idf.org](http://www.idf.org)
9. Hatori K. Fractalkine and fractalkine receptors in human neurons and glial cells / Hatori K, Nagai A, Heisel R, Ryu JK, Kim SU // *J Neurosci Res*. – 2002, Aug 1; 69(3):418-26.
10. Ito K. Expression and activity of histone deacetylases in human asthmatic airways / Ito K, Caramori G, Lim S, Oates T, Chung KF, Barnes PJ, Adcock IM. // *Am J Respir Crit Care Med*. 2002, Aug 1; 166(3):392-6.
11. Loxham M Allergenic proteases cleave the chemokine CX3CL1 directly from the surface of airway epithelium and augment the effect of rhinovirus / Loxham M, Smart DE, Bedke NJ, Smithers NP, Filippi I, Blume C, Swindle EJ, Tariq K, Howarth PH, Holgate ST, Davies DE // *Mucosal Immunol*. 2017, Jul 5. doi: 10.1038/mi.2017.63. [Epub ahead of print]
12. Matsubara, T. Fractalkine-CX3CR1 axis regulates tumor cell cycle and deteriorates prognosis after radical resection for hepatocellular carcinoma / T. Matsubara, T. Ono // *J Surg Oncol*. – 2007. – 95 (3). – P. 241-9.
13. Pachot A. Decreased expression of the fractalkine receptor CX3CR1 on circulating monocytes as new feature of sepsis-induced immunosuppression / Pachot A, Cazalis MA, Venet F, Turrel F, Faudot C, Voirin N, Diasparra J, Bourgoin N, Poitevin F, Mouglin B, Lepape A, Monneret G. // *J Immunol*. – 2008, May 1; 180(9):6421-9.
14. Po-Jui Chang. Corticosteroid insensitivity of chemokine expression in airway smooth muscle of patients with severe asthma / Po-Jui Chang, Pankaj K. Bhavsar, Charalambos Michaeloudes, Nadia Khorasani // *J Allergy Clin Immunol*. – 2012, Oct; 130(4):877-85
15. Ruster C. The role of chemokines and chemokine receptors in diabetic nephropathy / C Ruster , G Wolf // *Front Biosci*. – 2008, Jan 1; 13:944-55.
16. Ruster, C The role of chemokines and chemokine receptors in diabetic nephropathy / Ruster C, Wolf G // *Front Biosci*. – 2008. – 13. – P. 944-55.
17. Sans, M. Enhanced recruitment of CX3CR1+ T cells by mucosal endothelial cell-derived fractalkine in inflammatory bowel disease/ M. Sans, S. Danese // *Gastroenterology*. – 2007. – 132 (1). – P. 139-53.
18. Sawai, H. Fractalkine mediates T cell-dependent proliferation of synovial fibroblasts in rheumatoid arthritis / H. Sawai, Y.W. Park, X. He // *Arthritis Rheum*. – 2007. – 56 (10). – P. 3215-25.
19. Standards of medical care in diabetes – American Diabetes Association // *Diabetes Care*. – 2016. – Vol. 39 (Suppl. 1). – S.1–S.109.
20. Szukiewicz D. High Glucose Level Disturbs the Resveratrol-Evoked Curtailment of CX3CL1/CX3CR1 Signaling in Human Placental Circulation. / Szukiewicz D, Pyzlak M, Szewczyk G, Stangret A, Trojanowski S, Bachanek M, Braksator W, Wejman // *J. Mediators Inflamm*. – 2017; 2017:9853108. doi: 10.1155/2017/9853108. Epub 2017 Jun 1.
21. Umehara H, Bloom ET, Okazaki T, Nagano Y, Yoshie O, Imai T. Fractalkine in vascular biology: from basic research to clinical disease // *Arterioscler Thromb Vasc Biol*. – 2004. – No. 24. – P. 34-40.
22. Yoshimoto, S. Elevated levels of fractalkine expression and accumulation of CD 16+ monocytes in glomeruli of active lupus nephritis / S. Yoshimoto, K. Nakatani // *Am J Kidney Dis*. – 2007. – 50 (1). – P. 47-58.



## MEDICALIZATION OF THE MODERN UKRAINIAN SOCIETY: PRO ET CONTRA



**Dr MYKHAILO  
MYROSHNY-  
CHENKO**

Associate  
Professor,  
Department of  
Pathological  
Anatomy,  
Kharkiv National  
Medical University,  
Ukraine  
msmyroshnychen  
ko@ukr.net



**Dr OLHA  
OMELCHENKO**

Associate  
Professor,  
Department of  
Pathological  
Anatomy,  
Kharkiv National  
Medical University,  
Ukraine  
oomelcenko77@  
gmail.com



**Dr ELENA  
LYTVYENKO**

Associate  
Professor,  
Department of  
Pathological  
Physiology,  
Kharkiv National  
Medical University,  
Ukraine  
lytvynenko\_  
elena@mail.ru



**DMUTRO  
MOLODAN**

Assistant,  
Department of  
Fundamentals of  
Internal Medicine  
No. 1,  
Fundamentals  
of Bioethics and  
Biosafety,  
Kharkiv National  
Medical University,  
Ukraine  
molodanvi@gmail.  
com

### **Abstract**

*Medicine has a great and constantly increasing power over people, it continues to acquire new abilities to preserve and restore human health. An increasing influence of medicine on different spheres of the social life of the man brought forth the problem of medicalization, typical for different countries of the world. The authors of the article analyse the content of the concept of «medicalization», show positive and negative aspects of this process as well as characterize the main agents, which take a direct part in the spread of medicalization in the Ukrainian society. In their conclusion the authors emphasize that the modern man should make aware of the necessity of the healthy lifestyle and a correct use of the abilities of medicine, where the main task of doctors and society should consist in exclusion of the situation when the healthy man as Homo sapiens becomes a patient and turns into a new unique species, Homo medicus, who is completely dependent upon medicine.*

**Key words:** modern Ukrainian society, medicalization.

Scientific and technological progress, which touched upon all aspects of the society life, has produced its influence on medicine too [10]; as a result, medicine has achieved tremendous successes in cognition and decipherment of the superfine life activity processes in the human organism and correction of their disorders [3].

Medicine has a great and constantly increasing power over people, it continues to acquire new abilities to preserve and restore human health. Medicine has got a power to determine and term the phenomena, which are of the fundamental importance for the human existence [12]. The increasing influence of medicine on different spheres of the social life brought forth the problem of medicalization that is typical for different countries of the world [14, 15], including Ukraine.

The purpose of the present article consists in discussion of the problem of medicalization in the modern Ukrainian society.

By medicalization one means: firstly, a growing power of medical institutions in the society with their resultant fulfillment of the function of social control rather than functions of treatment and prevention only; secondly, adoption of concepts of professional health workers by the population and, as a result, some social problems begin to be interpreted at best as diseases or pathologies [9]. Taking into consideration a rapid development of medicalization, it is possible to expect appearance of a new definition of this term in future.

The term «medicalization» is not new; it appeared in the field of vision of scientists in 1960's-1970's. It is considered that the above term was registered at first in the work by the French philosopher and historian of human sciences Michel Foucault «The birth of the clinic» – a treatise about the development of medicine as an institution from the times of the early modern age [6].

Medicalization of the Ukrainian society has both positive and negative aspects with the resultant confrontation of opponents and advocates of this process demonstrated in the media discourse space [6].

In the majority of cases, medicalization is a benefit since it shows preoccupation with the problem and suggests rather effective means for its solution [5]. For example, people with bronchial asthma, hypertensive disease and diabetes mellitus live a more happy, productive and long-lasting life when they regularly take proper medicines.

More and more popular in the modern Ukrainian society becomes the opinion about the necessity to form the healthy lifestyle, the healthy and beautiful body and healthy nutrition, thereby making it possible to state the

fact of an increasing rating of health in the value system of the society. Numerous broadcasts on television channels, radio programmes, heads in magazines and newspapers become carriers of medical information for people. Leading positions among the above carriers is taken by Internet, which accumulates in itself all previous sources of information and ideas about diseases. The virtual space is known to have forums, specializing in information about diseases, and even on-line consultations. Using the newest means of communication, any person can get information about diseases and their treatment irrespective of his/her place of residence, and this is undoubtedly a positive aspect. Also a positive fact consists in the possible anonymity of a medical consultation, the opportunity to share with one's personal doubts or sensations [7].

But sometimes the perception of medicalization can cause its uncontrolled extension and negative consequences. For example, medicalization results in pathologization of the society and formation of the patient's self-actualization, because one begins to interpret the human life as a medical problem, the man begins to look at himself as an eternal patient, the human body and consciousness from birth to death becoming an object of acute medical control and regulation [12].

Modern people try to solve all their problems with help of different medical technologies or drug preparations. For example, if before the beauty was regarded as an external manifestation of the health of body and spirit, now the rush toward external attraction with help of diets, medicines and surgical interventions leads, in some cases, to loss of health [2]. It is believed that achievements of modern medicine make it possible to improve one's outward appearance, memory, attention, mental and physical abilities [4].

Scientists state that medicalization of the Ukrainian society through Internet has resulted in the appearance of the so-called «Internet patients» [7], who self-medicate despite absence of any medical education, i.e. prescribe different pharmaceutical products for themselves or their relatives and acquaintances, change dosages or cancel them on their own initiative, thereby causing of course a lot of concerns in medical workers. Here mass media, scientific journals and popular magazines, rather than Internet only, can serve as the source of medical information for self-medication. Within the framework of this situation an alarm is caused, for example, by uncontrolled taking of medicines by pregnant women for the purpose of self-medication. The conducted studies showed that pharmaceutical products were taken during pregnancy by approximately 100 % of women, more than 80 % of them not suffering from any diseases [8].

It should be noted that the appearance of the category of self-medicating people can be caused by their personal initiative to improve their own health, a low level of professional culture of some doctors, presence of queues in medical institutions, lack of time in part of doctors for individual consultations or talks [7].

The processes of medicalization result in spread of the medical language and medical methods of analysis to other spheres, which do not have any connection with medicine. For example, medical terms are used for describing an economic situation in the country (concepts «depression» and «shock therapy» in economics) [4].

A reckless access of the people, who do not have any special education, to different medical information can, as scientists believe, lead to the situation that the modern medicine will again get the features characteristic of ancient quackish practices [10].

An increase of the degree of medicalization spread in the society objectively entails dilation of the risk space and related unfavourable consequences. Here the appearing unfavourable and uncontrolled phenomena and events spread on the whole environment of the acting subject rather than on the above subject alone and lead to the state, which Ulrich Beck characterized in his book as the «risk society» [1, 2].

And who are the main agents in spreading medicalization in the modern Ukrainian society? The major part in medicalization is played by doctors. According to the meaning of their professional role, doctors cannot cause any purposeful harm to the patient. But the benefit, which they bring, can turn into evil, if the number of medical interventions rises [2].

Doctors become the only experts and their power over other groups increases. The combination of medicalization and financial structure of the society forms a specific style of the doctor's behaviour with respect to the patient. If their aim consists in getting money, doctors explain every symptom to the patient as a separate disease that requires compulsory treatment. But if the society orients to reduce expenditure the doctors may ignore rare cases or complex medical problems, which require long-term studies and checks [7].

The pharmaceutical industry is an important agent of medicalization; its economic interest in the intensification of this process is evident, because medicalization is by all means connected with medicamentation and often interpreted as taking of medicines. With the help of the same doctors the pharmaceutical industry solves problems of the patient's

health and diseases, i.e. determines his/her destiny [5, 12].

Advertizing in mass media, among medical workers, during conferences, seminars and master classes is one of the central elements in the strategy of the pharmaceutical business [2]. Advertizing activities in pharmacy result in a change of consumption of medicinal products by the population, so one can say about proper medical and social consequences of advertizing activities [12].

In more recent times, unfortunately, it is necessary to state a change in the professional role of the pharmacist. In virtue of the specificity of his professional duties and market environment the pharmacist uses excessively the ability of drug intervention into his patient's state, as he gives different recommendations for taking some or other pharmaceutical products [2]. For example, one can often observe a situation at the chemist's, when the pharmacist prescribes pharmaceutical preparations to a person without knowing anything about the state of his/her health and individual peculiarities of the organism.

Patients are agents of medicalization too. Intensification of the process of medicalization of life implies formation of specific relationships between the doctor and the patient [13]. Quite reasonable is the person's desire to secure oneself against a fatal ailment and, if the latter appears, to leave the situation with «minimal losses». Thereby within the framework of his/her social role the patient provokes extension of medical interventions, which in some cases are more harmful than useful [10].

As it is known there are three models of relationships in the «doctor-patient» coordinate system. The first model describes an active doctor and a passive patient. The second model is characterized by the fact that the doctor suggests his/her instructions to a cooperating but submissive patient. The third model is the model of mutual participation, when the doctor and the patient are equal. The first and second models have been found to accord with extension of medicalization [10].

Thus, having its both positive and negative aspects, medicalization is a significant problem for the modern Ukrainian society. Medical workers, pharmaceutical industry and patients act as agents of medicalization. The modern man should make aware of the necessity of the healthy lifestyle, a correct use of the abilities of medicine, where the main task of doctors and society should consist in exclusion of the situation when the healthy man as *Homo sapiens* becomes a patient and turns into a new unique species, *Homo medicus*, who is completely dependent upon medicine.

## References

1. Beck U. Risk society: towards a new modernity / Translation from German by V. Sedelnik, N. Fedorova. – M. : Progress-Tradition, 2000. – 383 p.
2. Dobrorodni D.G. Medicalization as a socio-cultural phenomenon and the object of interdisciplinary research / D.G. Dobrorodni, Y.G. Chernyak // *Philosophy and social sciences*. – 2012. – Issue 1-2. – P. 82-86.
3. Dyachenko V.G. Scientific and technological progress and safe medicine // V.G. Dyachenko, V.B. Prigornev // *Far Eastern Medical Journal*. – 2015. – No. 1. – P. 64-70.
4. Kovtyukh G.S. The Relationship between medicine and culture / G.S. Kovtyukh, M.A. Kozlova // *Likars'ka sprava*. – 2016. – No. 2. – P. 71-75.
5. Kulik P.Yu. Ethical risks of medicalization / P.Yu. Kulik // *Materials of the republican scientific-practical conference with international participation «Bioethics and modern problems of medical ethics and deontology» (Vitebsk, December 2, 2016)*. – Vitebsk : VSMU, 2016. – P. 269-271.
6. Makarova O.S. «Official medicine»: analysis of the term / O.S. Makarova // *Vestnik of Yaroslav the Wise Novgorod State University*. – 2014. – No. 83, Part 1. – P. 95-98.
7. Medvedeva L.M. Homo medicus as possible result of the medicalization // L.M. Medvedeva // *Historical and social-educational thought*. – 2012. – No. 1(11). – P. 210-214.
8. Medicalization of pregnancy / M.V. Andreeva, A.V. Myzgin, E.P. Shevtsova et al. // *Mother and Child in the Kuzbass*. – 2014. – No. 3 (58). – P. 12-15.
9. Michel D. Medicalization of society: theory, history, micro politics / D. Michel // *Journal of Social Policy Studies*. – 2009. – Vol. 7, No. 3. – P. 293-294.
10. Nenarokomov A.Yu. The medicalization as a problem in modern oncology / A.Yu. Nenarokomov // *National Association of Scientists*. – 2015. – No. II (7). – P. 59-61.
11. Implication of modern medical technologies in improvement of population reproductive health quality / L.M. Gorokhova, N.A. Martynova, L.V. Kochorova et al. // *Human ecology*. – 2008. – No. 8. – P. 7-11.
12. Shvydka L.I. The socialization of society as a social problem: essence, agents, consequences / L.I. Shvydka // *Bulletin of Dnipropetrovsk University (Sociology)*. – 2010 – Vol. 20, No. 9/2. – P. 80-86.
13. Shkomova E.M. Philosophical aspects of the medicalization of life (case study on modern transplantology) / E.M. Shkomova // *Prospects of Science*. – 2015. – No. 10 (73). – P. 216-218.
14. Gupta A. Medicalization: a growing menace / A. Gupta, S. Kohli // *Delhi Psychiatric Journal*. – 2012. – Vol. 15, No. 2. – P. 255-259.
15. José M. Ceriani Cernadas The growing medicalization of life: Are physicians aware of the damage it causes? / José M. Ceriani Cernadas // *Arch Argent Pediatr*. – 2012. – No. 110 (6). – P. 459-460.



**Dr AYESHA AHMAD**

PhD, lecturer in Global Health, St George's University of London,  
Honorary lecturer in Global Health, Institute for Global Health, University College London  
Guest lecturer in Transcultural Psychiatry, Queen Mary's University of London, UK  
a.ahmad@ucl.ac.uk



**MEDICAL ETHICS: AN OVERVIEW**

**Abstract**

*The signature of humanity is in the way we treat another human life. This is the realm of ethics. How is this signature carried over to the unborn life, the embryo? Such a question has been dominated by issues of abortion and termination, but how is the embryo configured in its scientific study, and does this raise ethical questions? In particular, how is the embryo represented in developmental biology within medicine and medical education? In the interface of our innovations in scientific and clinical medicine, our fascination and curiosity about the development of a new human life is embodied in the explicit images we can now gather, and the ways in which we can monitor, examine, and measure signs of life as a new form of governmentality.*

**Key words:** *medical ethics, humanity, human life, innovations.*

Clinical medicine is fetching the ‘unseen’ human embryo into our world and giving it a particular kind of visibility. The human embryo is appearing against all odds and is greatest where it is not – in our imagery, symbolism, and metaphors, and on our screens, in our laboratories, and at hospital bed-sides. While such appearances of the human embryo can be seen as the effect of multiple ontologies, it can be argued that such appearances are brought about through a single method of reductive science offering descriptions that present the human embryo as an object, which is unified, neutral, and value-free. Clearly, scientific reductionism can be a positive instrument, a tool for making sense of human life. However, what becomes of human life when our understanding of who we are is reduced as a form of impoverishment

**Situating the body in medicine — an ethical conceptualization.**

This article critically reviews definitions of the body located in the perspective of reductionism, contrasting these definitions with alternative views from sociological, phenomenological, and anthropological approaches. The aim of the article is to expose ‘neutral’ biological images of the body as deficient, and indeed

‘inhumane’ in the sense that the body reduced to physics necessarily ignores the metaphysical body that embraces ethical considerations. The physical body may offer a dehumanizing perspective as it excludes discussion of what it is to be ‘human’ and ‘humane’. The human embryo can be seen as a part of the wider ‘human condition’ and not merely the ‘sum of its parts’ in a biological sense. I contextualize the human embryo as a metaphorical symbol in society, in contrast to the scientific description of a de-contextualized object, where the body is taken as an ageless and timeless object.

**Beginning of the human (condition).**

We experience the human embryo as a dualism, namely, the human embryo in nature and the human embryo that is subject to social, political, historical, and cultural forces. From this polarization, various definitions of the body, including that of the human embryo, are drawn – broadly falling into the categories of the beginning of an individual human (embryo) and the beginning of our human condition, whereby the human embryo is a scientific object and the human condition is an inherently irreducible existence. Moral and ethical arguments about the status of the human embryo

therefore tend to default to a line of inquiry that investigates the ontological status of embryos – which, in turn, is pivoted between the embryo as a person, or potential person, or biological material (Eberl and Brown 2011: 43). In this section, I explore the problems involved in conceptualizing the beginning of the human (condition) - how can the human ('scientific') embryo be both physical (or material) and a metaphorical symbol for what Scott Gilbert et al (2005) describes as the origin of all human life? Consequently, the ontology of the 'scientific embryo' can be afforded two statuses of significance. On the one hand, scientific and technological innovations have created a pragmatic need to address the status of the embryo in light of new knowledge in modern embryology, which now offers a molecular biological account of development. Peter R. Braude and Martin H. Johnson (in Dunstan 1990: 8) corporeal, that which is the changing organization of knowledge about the 'scientific embryo's' structure.

In 'The Embryo in Contemporary Medical Science', the authors state that over the last century, embryology has transformed from being a 'largely descriptive subject' to become an 'exciting modern science concerned with cell interactions and subcellular biochemical mechanisms'. These 'interactions' and 'mechanisms' are detailed in embryology textbooks used in medical education reflecting current dominant biomedical paradigms, for example, and account for the processes and developments that occur during the initial eight-weeks' period of gestation to complete the formation of the human embryo. The 'scientific embryo', then, is presented through its totality; its entirety can be referenced and explained and the embryonic period's completion signifies the embryo as an object, a body that can be examined, monitored, and accessed in unprecedented ways. On the other hand, the embryo is situated in myth and religious traditions, where, embryos are the 'central actors in the origin stories that many modern, educated people tell themselves – ourselves – about who we are and how we came to be' (Morgan 2009: 4). However, simultaneously, the human embryo is also an 'ambiguous' entity, where it 'defies classification and slips seamlessly between moral and biological categories' (Devolder and Harris 2007: 153). Again, my claim is that the ontological status of the embryo is then multiple. The way we structure our concept of the body also has implications for clinical medicine, and these implications originate from even the most fundamental – conceptual and theoretical - of levels. For example, Edmund Pellegrino (2008: 309), points out that 'Man's most daring creations promise to annihilate him as a person unless he can decide who he is and what his existence is for and where it should lead.

Pellegrino argues that the current context of medicine – one whereby the boundaries between life and death are no longer fixed points (Lizza 2009: 1) – requires us to

re-examine our understanding of the body. Pellegrino is critical of medicine's conceptualization of the body, or at least the lens it is viewed through, fearing that the impact of a description about the body that is considered as neutral and value-free will forego a conscientious and responsible analysis of society. The implicit reference in Pellegrino's observations is that without a conscientious and evaluative analysis of the way that medicine uses the body for its action, both our bodies and our societies may suffer. Furthermore, it implies that how we treat the body reflects our society, a premise from which Foucault (1973) established his conception of ethics. The human condition is not merely experienced, it is enacted; a 'good' society, body, ethic, or medicine is not 'discoverable', but is 'practiced' (Foucault 1973), or, alternatively, our understanding of the human condition is formed through practice discourses. In contemporary practices, the body is considered as an inactive, timeless, ageless, object. Such a body, as an object, is enacted through medical practices (Mol 2002).

In contrast, it is through the embodied person that the effects of medicine are received and experienced - Pellegrino (2008) reminds us that the body has a relation to the human condition and its societal situation, and not just its counterpart, the individual person. How we conceptualize the body as a reflection on our own existence, then, has further implications on current debates on the statuses of different stages of the human body, especially attitudes concerning the human embryo, which represents the most fragmented conceptualization of the body pertinent to clinical medicine, but also to our society as a whole. The body of the from human embryo is a baseline for other stages of the human body. In other words, concepts can have as much effect as techniques. But what may we derive from such representations about the body? Is the body in medicine the 'same' body that is a part of our relation to the world in our human condition, or is the ill, failed, afflicted body a separate body, a 'medical body'?

Since the status of the unborn, developing body has inevitably been called into question (Tooley 1983; Engelhardt 1988; Singer 2002), what, therefore, is the conceptualization of the body, the developing body from the unborn to the born; To answer this question, I will now look at why the current distinction of the embryo as a neutral, scientific object is deficient, and critically review alternative views.

### **The 'scientific' embryo and reductionism.**

In light of rapid growth in scientific knowledge linked with technological innovation, morality in medicine is playing an increasingly important role. How are we to treat the 'scientific body', and, more specifically the 'scientific embryo'? We cannot ignore the role of morality in our biological understanding of the human

body in light of the unpredictable potential of technology. Leon Kass (1972: 18), in 'Making Babies – the New Biology and the Old Morality', writes: 'Thoughtful men have long known that the campaign for the technological conquest of nature, conducted under the banner of modern science, would someday train its literal guns against the commanding officer, man himself. That day is fast approaching, if not already here. New biomedical technologies are challenging the formulations which have served since ancient times to define the specifically human – to demarcate human beings from the beasts on the one hand, and from the gods on the other. Birth and death, the boundaries of an individual life, are already subject to considerable manipulation'. The concept of the 'body' has become increasingly significant in recent years, where who we are has been succeeded by the normative inquiry of who we should become. New biomedical technologies are resulting in a changing ontology of medical practice, where medicine is no longer confined to the 'ill', the 'unwell', the 'diseased', or the 'unhealthy'.

As Kass (1972: 18) states above, the 'boundaries' of our 'individual' lives are 'already subject to considerable manipulation', questioning the notion of a 'natural' body privileged through the practices of scientific medicine. Paradoxically, in light of artificially reproduced bodies, altered physiologies via surgeries, the abilities to detect and diagnose more abnormalities, and the trajectory towards the negation of disease and disability, there remains an 'unexamined assumption about the uniformity of human bodies' which continues to 'inform most biomedical practice' (Lock and Nguyen 2010:1). The era of 'personalized' medicine, preventative medicine, and the impact on the trajectory of human lives via fast technological change, including the advent of contemporary prenatal medicine, has created a complex, cultural and historical context in which bodies are situated. Charles E. Rosenberg (1999: 27) calls this scenario a 'crisis', which is resulting from the 'difficulty of creating an institutional and economic, as well as moral, context in which these new clinical, policy, and research options can be managed'. William B. Hurlbut's (2006) description of a 'conceptual revolution' is evident in our current dominant discourse of the body, such as how to define the body in light of 'advances in basic biology', which, in turn, is the 'source of our moral standing and the ways human life is morally different from other species' (Hurlbut 2006: 4).

Through ultrasound or diagnostic testing the embryo is 'brought to life' so to speak, where previously its emerging physicality would have been hidden. Not only is the internal living body able to be viewed and examined, but also we are privy to the developing embryo within this other individual body. Mapping out the anatomical structures of the human body and related

information about physical processes has led to a certain knowledge that generates power. As noted previously, Foucault (1973) refers to this as the 'medical gaze' (see also Armstrong 2006). He considered the result of such knowledge to provide medicine with power based upon descriptive 'in-sights'. Medicine gained its dominance because of its ability to control information about the body and then to define what is a normal and abnormal body, extending to the human embryo. Reflecting on Foucault's (1973) work on pathologies of the body, Mol (2002) observes that, prior to the categories of 'normal' and 'pathological', disease was not 'taken to be a condition of the body, contrasting with that other condition, health ... The crucial difference to attend to was not between one body (normal) and another (pathological) as is the contemporary conceptualization, but between one disease and another' (Mol 2002: 125). This trajectory towards the negation of disease and disability is based on an 'unexamined assumption about the uniformity of human bodies' which continues to 'inform most biomedical practice' (Lock and Nguyen 2010: 1).

With the advent and increasing focus of scientific medicine as the main discourse representing the human body, philosophical descriptions about the human body have been supplemented and overturned by machines and measuring outputs that establish whether levels such as hormones, blood components, or the size of organs, are as they 'ought' to be. Assuming too easily the content of scientific descriptions as purportedly metaphysics-free means that during theorizations about the body, there has been a serious neglect of the ontology of its physical structure(s). As the social body has become an object of medicine, the ontology of medicine as both a biological and moral enterprise, is, in a parallel movement, developing an increasingly reductionist approach.

### **Reductionist medicine**

The reductionist position holds that persons are nothing but a physical body, which in turn, can be explained with reference to physical properties. For example, the 'literal-ness' of emerging physicality of the human embryo is reducible to processes on the molecular biology level. All other activities, such as our sentience or personhood, are understood in terms of our physicality - the physical equals what is 'real' or indeed, 'truth'. In medicine, the real body is a physical object. In the process of scientific reductionism, there is a movement from embodiment to physical body, to particular parts, or objects, that make up who we are. In other words, our human condition is explainable through recourse to individual parts of our existence. Reductionism implies partism (rather than holism). Our behaviour, traits, values, morality, and also our physicality are understood in terms of what is

‘scientific’ in the sense of observable, manipulable, and traceable material and material processes. All else is illusory – it cannot be ‘real’ unless it is explained in the discourse that provides the reference necessary for describing the material of the world and its living things. There is, then, both an ontological and epistemological aspect to reductionism. The former is the nature of the experienced world, and the latter is the method that we use to inquire about the nature of the world. For example, reductionism in medicine corresponds to viewing the body as a neutral object through empirical investigation. This has implications for how the body is treated in medical practice. If the body is merely an object, then what utility do our cultural beliefs, moral values, and phenomenological experiences carry? Where metaphysics is reduced to physics, what value does medicine place upon the very language and symbol systems that allow doctors to appreciate and understand the sciences of the body?

Normal embryonic development is based upon descriptions of the embryo’s emerging physicality, which are directly related to legitimate and strong definitions of health and disease, translated to, and operating through, clinical literal practice. These definitions are taken as neutral and value-free, producing a naturalized and singular object. This is also partly due to the pressure to reach a level of standardization in contemporary clinical practice as a way of explaining our experiences of the body. Categorizing disease and illness makes these aspects of our human condition ‘real’ (Lock and Nguyen 2010: 33). Christopher Boorse (1977) claims that the main elements of health are ‘biological function and statistical normality’. For these premises to be sustained, reductionism has to develop a way of measuring the body - what is it to be normal or to be healthy? The technological medium of prenatal medicine depends on this reductionism and it can yield positive therapeutic advantages. Yet, reductionism (in medicine) is also problematic where it must bracket out certain elements that are part of our ‘being human’, such as morality and its metaphysical underpinnings. This includes addressing the questions: when does ‘personhood’ begin, what is potentiality a sufficient condition for a moral status?, and can the detection of abnormalities in the embryo justify termination? My ethical concern here is that the metaphysical underpinnings of the ‘scientific embryo’ situated in a biomedical frameworks, as an object in reductionist medicine, are also bracketed out - which will lead on to implications for the debate about the moral status of the embryo. However, the reductionist view is also problematic because objects, that are part of how we experience the world around us but not necessarily constitutive of the human body, are a ‘remainder’ - they are bracketed out from the definition of the body. This creates a disparity.

Whilst we rely on reductive descriptions about the body in order to practice medicine, we also recognize other essential characteristics about ourselves as humans, in that we are also persons with interests, rights, and value concepts such as dignity and autonomy. Medical ethics is an established aspect of the medicine curriculum, yet such ethics seem to be situated firmly within materialist discussions and assumptions. With the embryo’s emerging physicality comes a corresponding emerging metaphysicality, which raises issues such as definitions about the beginning of personhood, or the moral status of the embryo, to become points of concern in clinical medicine.

The reduction of the embryo to a mapping out of its anatomical structures has therefore allowed it to become a physical object with an unacknowledged metaphysics of naturalism. Reductionists make two claims here in the context of modern medicine: that the embryo is equal to the sum of its parts, and that its emerging physicality corresponds with models describing the interactions of the body’s smallest components. The reductionist, however, will fail to reflect on, or actively, work to remove or ignore, metaphysical content from explanations or concepts in the organization of scientific knowledge, and the problems for this in conceptualizing the emerging physicality of the embryo in frameworks of scientific medicine underpin this thesis.

In contrast to reductionist positions, the anti-reductionist views on the body permit the integration of phenomena other than physical forces. But in doing so, the antireductionist presupposes a structure within the world that can contain multiple ontologies, relations, and substances. This view forms the basis of complexity literalism and theory, where nested systems are studied at differing levels of complexity in order to frame an understanding of the world, influenced by Alfred N. Whitehead’s (1997) metaphysical thinking and process philosophy in the early twentieth century. However, even within complexity theory, there remains a reliance on preconceived view of a structure in order to examine the nature of organization of the parts within it.

Systems are considered holistic in the sense that the whole is a unit, rather than identifying the whole in relation to its parts. Complexity has an ally in pluralism, refuting a final or singular object in favor of a pluralism of approaches. Nevertheless, both reductive and anti-reductionist views conform to a shared aim: to understand our reality or a particular aspect within it, and most significantly, to impact on the conceptualization of the human body. In standard texts on development of the human body, a second discourse notably joins reductionism – that of developmentalism, characterizing human development as ‘growth’ through ‘developmental stages’. In summary, critical analyses of the materialist approach to the body and its processes

are lacking in medicine and medical education. Anti-reductionist discourses act in opposition and resistance to reductionism and, consequently, do not examine the body, which is made objective, through reductive biomedicine. Rather, they emphasize the domains of time and space that extend the body beyond the boundaries of scientific knowledge, to include metaphysics and ethics (and, also poetry and symbol). Treating both the 'scientific embryo' and the embryo that is part of the human condition (and then a socio-historical-political being) as separated in a dualistic fashion will only ever yield either a surplus of metaphysics or a requirement to be supplemented by another physical structure.

### **Conclusion**

The conceptualization and framing of the human body is subject to analysis and examination from dominant biomedical paradigms. These then, in turn, affect the modes of ethics that are reflected in the conceptualization of various states of the human body such as the human embryo. The human embryo continues to be a source of moral inquiry into the ways we treat humanity at a stage where life is unseen, unknown, and unheard. We must bear in mind that the ways in which we engage in ethical debates and discussions about the body in medicine is an ethical encounter. Our ethics originate in our concepts, just like life originates in the embryo.

## About authors



### VALERY KAPUSTNYK

**Professor, First Vice-Rector for Research and Education,  
Kharkiv National Medical University,  
Ukraine**

[prorector1@knmu.kharkov.ua](mailto:prorector1@knmu.kharkov.ua)

Valery KAPUSTNYK is a Professor and the First Vice-Rector for Research and Education in the Kharkiv National Medical University, Ukraine.

**Scientific interests:** problems of medical education, management, occupational diseases.

---



### DU HONGWEI

**Doctor of Philosophy, Cultural Scholar,  
China**

[duhongwei1717@163.com](mailto:duhongwei1717@163.com)

Du HONGWEI is a Doctor of Philosophy, China. He has graduated Chinese and Ukrainian universities and continues working as a Professor of philosophy, Chinese language, business development. He works on development of the experts' network between China, France and Ukraine on cultural and economic exchanges.

**Scientific interests:** cultural exchanges, business communications, economic development, international cooperation, linguistic philosophy.

---



### VITALIY TSYMBALIUK

**Professor, Academician, President of National Academy of Medical Sciences of Ukraine,  
State Institution "Romodanov Neurosurgery Institute National of Academy of Medical Sciences of  
Ukraine",  
Ukraine**

[tsymbaliuk@neuro.kiev.ua](mailto:tsymbaliuk@neuro.kiev.ua)

Vitaly TSYMBALIUK is a Professor, Academician, President of National Academy of Medical Sciences of Ukraine, State Institution "Romodanov Neurosurgery Institute National of Academy of Medical Sciences of Ukraine".

**Scientific interests:** neurolinguistics, phenomenology of nervous diseases, autologous stem cells, history of medicine, ethical-philosophical area of medicine, art, European ethnography.

---



### INNA TORIANYK

**PhD, Associate Professor, Laboratory of a New and Little-Studied Infectious,  
State Institution "Mechnikov Institute of Microbiology and Immunology of National Academy of  
Medical Sciences of Ukraine",  
Ukraine**

[kamvsh\\_in@ukr.net](mailto:kamvsh_in@ukr.net)

Inna TORIANYK as a PhD. She works as an Associate Professor in the Laboratory of a New and Little-Studied Infectious, State Institution "Mechnikov Institute of Microbiology and Immunology of National Academy of Medical Sciences of Ukraine".

**Scientific interests:** morphological design of infectious disease, scan electronic microscopy, mortal contour plastics, embalming, thanatology, nontraditional medicine.

---



### **IRYNA SOROKINA**

**Professor, Head of the Department of Pathological Anatomy,  
Kharkiv National Medical University,  
Ukraine**  
[soririna@gmail.com](mailto:soririna@gmail.com)

Iryna SOROKINA is a Professor. She works as a Head of the Department of Pathological Anatomy in Kharkiv National Medical University, Ukraine.

**Scientific interests:** bioethical aspects in medicine, higher education, pathology the system of «mother-placenta-fetus», medicine and art.

---



### **ALEKSANDR SHISHKIN**

**Professor, Department of Physiology,  
Izhevsk State Agricultural Academy,  
Russia**  
[shishkinlab@yandex.ru](mailto:shishkinlab@yandex.ru)

Aleksandr SHISHKIN is a Professor at the Department of Physiology in Izhevsk State Agricultural Academy, Russia.

**Scientific interests:** immunodiagnostics, development of diagnostic systems, development of the medical and laboratory equipment.

---



### **NIKOLAY KIRYANOV**

**Professor, Head of the Department of Pathology,  
Izhevsk State Medical Academy,  
Russia**  
[kirnik@list.ru](mailto:kirnik@list.ru)

Nikolay KIRYANOV is a Professor. He works as a Head of the Department of Pathology in Izhevsk State Agricultural Academy, Russia.

**Scientific interests:** pathology of bone marrow and lymphatic tumors.

---



### **NATALIA OVCHININA**

**Associate Professor, Department of Pathological Physiology,  
Izhevsk State Medical Academy,  
Russia**  
[shishkinlab@yandex.ru](mailto:shishkinlab@yandex.ru)

Natalia OVCHININA is an Associate Professor at the Department of Pathological Physiology in Izhevsk State Agricultural Academy, Russia.

**Scientific interests:** immunology, immunodiagnostics, development of diagnostic systems.

---



### **TETYANA OSPANOVA**

**MD, PhD, Professor, Head of the Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**

[tat\\_os@yahoo.com](mailto:tat_os@yahoo.com), [t.ospanova1@gmail.com](mailto:t.ospanova1@gmail.com)

Tetyana OSPANOVA has a MD, PhD. She is a Professor and works as a Head of the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** pulmonology, nephrology, medicine and art, bioethics.

---



### **ZHANNA SEMYDOTSKA**

**MD, PhD, Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**

[vade\\_mecum2001@yahoo.com](mailto:vade_mecum2001@yahoo.com)

Zhanna SEMYDOTSKA has a MD, PhD. She is a Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** medicine, art, bioethical aspects in medicine.

---



### **INGEBORG CHERNYAKOVA**

**PhD, Associate Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**

[irinakaramazina805@gmail.com](mailto:irinakaramazina805@gmail.com)

Ingeborg CHERNYAKOVA has a PhD. She works as an Associate Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** medicine, ethical and legal aspects in medicine.

---



### **OLENA PIONOVA**

**PhD, Assistant Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**

[olena\\_pion@meta.ua](mailto:olena_pion@meta.ua)

Olena PIONOVA has a PhD. She works as an Assistant Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** medicine, historical aspects in medicine.

---



### **NATALIIA TRYFONOVA**

**PhD, Assistant Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**  
[energyna1@ukr.net](mailto:energyna1@ukr.net)

Nataliia TRYFONOVA has a PhD. She works as an Assistant Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** pulmonology, cardiology, nephrology, bioethical aspects in medicine.

---



### **MYKHAILO MYROSHNYCHENKO**

**PhD, Associate Professor, Department of Pathological Anatomy, Kharkiv National Medical University, Ukraine**  
[msmyroshnychenko@ukr.net](mailto:msmyroshnychenko@ukr.net)

Mykhailo MYROSHNYCHENKO has a PhD. He works as an Associate Professor at the Department of Pathological Anatomy in Kharkiv National Medical University, Ukraine.

**Scientific interests:** medical education, health care system, bioethical aspects in medicine, pathology the system of «mother-placenta-fetus».

---



### **NATALIIA KAPUSTNYK**

**PhD, Associate Professor, Department of Obstetrics and Gynaecology No. 1, Kharkiv National Medical University; Head of Gynaecological Department No. 2, Kharkiv Regional Clinical Perinatal Center, Ukraine**  
[naukapathomorphology@ukr.net](mailto:naukapathomorphology@ukr.net)

Nataliia KAPUSTNYK has a PhD. She works as an Associate Professor at the Department of Obstetrics and Gynaecology No. 1 in Kharkiv National Medical University. Dr Kapustnyk is also a Head of Gynaecological Department No. 2 in Kharkiv Regional Clinical Perinatal Center, Ukraine.

**Scientific interests:** reproductive health, health care system, bioethical aspects in medicine.

---



### **ALEKSANDR SOLOV'EV**

**Associate Professor, Department of Histology, Izhevsk State Medical Academy, Russia**  
[histolog@igma.udm.ru](mailto:histolog@igma.udm.ru)

Aleksandr SOLOV'EV is an Associate Professor at the Department of Histology in Izhevsk State Medical Academy, Russia.

**Scientific interests:** development of diagnostic systems, development of the medical and laboratory equipment.

---



### **GALYNA YERYOMENKO**

**PhD, Associate Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**  
[galyna0512@ukr.net](mailto:galyna0512@ukr.net)

Galyna YERYOMENKO has a PhD. She works as an Associate Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine. She is also a Member of European Academy of Allergy and Clinical Immunology.

**Scientific interests:** pulmonology, endocrinology, ethical aspects in medicine.

---



### **TETYANA BEZDITKO**

**Doctor of Medical Sciences, Professor, Department of Propaedeutics of Internal Medicine No. 2 and Nursing, Kharkiv National Medical University, Ukraine**  
[tvbezdetko@gmail.com](mailto:tvbezdetko@gmail.com)

Tetyana BEZDITKO is a Doctor of Medical Sciences. She works as a Professor at the Department of Propaedeutics of Internal Medicine No. 2 and Nursing in Kharkiv National Medical University, Ukraine.

**Scientific interests:** pulmonology, endocrinology.

---



### **OLENA VYSOTSKA**

**Doctor of Technical Sciences, Associate Professor, Professor, Biomedical Engineering Department, Kharkiv National University of Radio Electronics, Ukraine**  
[olena.vysotska@nure.ua](mailto:olena.vysotska@nure.ua)

Olena VYSOTSKA is Doctor of Technical Sciences. She works as an Associate Professor and Professor at the Biomedical Engineering Department in Kharkiv National University of Radio Electronics, Ukraine.

**Scientific interests:** statistical analysis, art.

---



### **ANNA PECHERSKA**

**PhD, Senior Research Associate, Biomedical Engineering Department, Kharkiv National University of Radio Electronics, Ukraine**  
[anna.pecherska@nure.ua](mailto:anna.pecherska@nure.ua)

Anna PECHERSKA has a PhD. She works as a Senior Research Associate at the Biomedical Engineering Department in Kharkiv National University of Radio Electronics, Ukraine.

**Scientific interests:** statistical analysis, art.

---



### **OLHA OMELCHENKO**

**PhD, Associate Professor, Department of Pathological Anatomy,  
Kharkiv National Medical University,  
Ukraine**  
[oomelcenko77@gmail.com](mailto:oomelcenko77@gmail.com)

Olha OMELCHENKO has a PhD. She works as an Associate Professor at the Department of Pathological Anatomy in Kharkiv National Medical University, Ukraine.

**Scientific interests:** reproductive health, pathology the system of «mother-placenta-fetus», music and art.

---



### **ELENA LYTVYENKO**

**PhD, Associate Professor, Department of Pathological Physiology,  
Kharkiv National Medical University,  
Ukraine**  
[lytvynenko\\_elena@mail.ru](mailto:lytvynenko_elena@mail.ru)

Elena LYTVYENKO has a PhD. She works as an Associate Professor at the Department of Pathological Physiology in Kharkiv National Medical University, Ukraine.

**Scientific interests:** medical education, management in health care, pathological physiology.

---



### **DMUTRO MOLODAN**

**Assistant, Department of Fundamentals of Internal Medicine No. 1,  
Fundamentals of Bioethics and Biosafety, Kharkiv National Medical University,  
Ukraine**  
[molodanvi@gmail.com](mailto:molodanvi@gmail.com)

Dmuro MOLODAN works as an Assistant at the Department of Fundamentals of Internal Medicine No. 1, Fundamentals of Bioethics and Biosafety in Kharkiv National Medical University, Ukraine.

**Scientific interests:** bioethical aspects in medicine, therapy, history and medicine.

---



### **AYESHA AHMAD**

**PhD, lecturer in Global Health, St George's University of London,  
Honorary lecturer in Global Health, Institute for Global Health, University College London,  
Guest lecturer in Transcultural Psychiatry, Queen Mary's University of London,  
UK**  
[a.ahmad@ucl.ac.uk](mailto:a.ahmad@ucl.ac.uk)

Ayesha AHMAD has a PhD in philosophy of medicine/ medical ethics. She works as a Lecturer in Global Health at St Georges University of London, and Honorary Lecturer in Global Health at the Institute for Global Health, University College London, UK. Ms. Ahmad is also a guest lecturer in Transcultural Psychiatry at Queen Mary's University of London. She sits on the Clinical Ethics Committee at Great Ormond Street Hospital for children in London. Ms. Ahmad specialises in gender-based violence during conflict and mental health, particularly exploring cultural and religious narratives in cross-cultural mental health. She was on the Managing Committee for a 4 year COST Action grant on Disaster Bioethics.

**Scientific interests:** medical ethics, cross-cultural mental health, gender-based violence, bioethics, trauma therapeutic interventions.

---

## Requirements for papers

- Papers are accepted in English and French. Good English and French spelling and punctuation are preferred. Papers should be written in a third person, impersonal style and any use of 'I/we' should be avoided.
- Papers should not normally exceed 10,000 words. All papers are refereed by acknowledged experts in the subject.
- Abstracts of approximately 300 words are required for all papers (abstract in English and French is required for articles written in French).
- Paper should include no more than 7 keywords.
- Papers should be compiled in the following order: title page; abstract; keywords; main text; acknowledgments; appendixes; references.
- The introduction should clearly define the nature of the problem being considered. The new contribution the paper makes should be identified and situated in relation to the relevant scientific literature and, wherever possible, the practical relevance of its results should be indicated. The "Regional Innovations" journal will publish papers that evaluate important topics relevant to new areas of emerging research and policy.
- All the authors of a paper should include their full names, affiliations, postal addresses, telephone numbers and email addresses on the cover page of the article. One author should be identified as the corresponding author. We wish for Review Articles to be written by experts who are personally committed to writing the manuscript, and therefore limit authorship to a maximum of 3 authors.
- For all papers non-discriminatory language is mandatory.
- The use of tables and color figures to summarize critical points is encouraged. Tables should be prepared on separate sheets; they should not be embedded within the text. Each table should have an appropriate caption.
- All photographs, maps, charts and diagrams should be referred to as "Figures", and should be numbered consecutively in the order in which they are referred to in the text. They should be prepared on separate sheets.
- Endnotes should be marked clearly in the text at a point of punctuation, and listed consecutively at the end of the paper. They should not be listed at the bottom of each relevant page.
- The full references should be listed at the end of the paper. They must include the names and initials of all the authors, the year of publication in parentheses, the full title of the paper (or book), the full name of the journal, the volume number and pages and, for books, the publisher's name and city of publication. The references in the text should be done in square brackets (for example, [2; 4; 15]).

### Reproduction of copyright material

As an author, you are required to secure permission to reproduce any proprietary text, illustration, table, or other material, and any supplemental material you propose to submit. This applies to direct reproduction as well as "derivative reproduction" (where you have created a new figure or table which derives substantially from a copyrighted source).

## Call for Research Articles

**International journal “Regional Innovations”**, the international, peer-reviewed, independent and Internet-based journal published in English and French, announces an **international Call for Research Articles in Medical Science and other innovative allied research areas for 2018**.

Currently, we are seeking research articles, case studies, critical reviews, surveys, opinions, commentaries and essays. Types of manuscripts suitable for this thematic issue include medical research, clinical research, health care innovations, reviews, medical teaching, medical law, ethics and policy environmental medicine, integrative general practice.

The journal welcomes the submission of manuscripts that meet the general criteria of significance and scientific excellence, as well as high standards for clarity, validity, and generalizability. All submitted papers will undergo evaluation by independent peer reviewers.

Authors should consult the instructions for authors for the Regional Innovations Journal for advice on manuscript preparation and submission. Guide to authors and other details are available on our website: <http://irn.center/category/our-journals>

Please submit your manuscript(s) for publication **before 04 June 2018** at [info@irn.center](mailto:info@irn.center)

Our committed team of editors and reviewers will let you know the acceptance status of your manuscript at the earliest.

The price of publication is 50 euros.

### **Aims of the thematic medicine issue:**

1. To stimulate discussion and debate in the field of integrative medicine;
2. To encourage international and inter-disciplinary collaboration and networking between organisations, associations, institutions and practice based communities;
3. To spread the best practices;
4. To focus on rigorous clinical research, including both qualitative and quantitative, systematic and narrative reviews, case studies and surveys and other clinically relevant articles.

The Regional Innovations Journal is a truly integrative international journal, with an international editorial board and associate editors possessing a broad range of expertise in both the academic and practical fields, including Integrative Medicine.



Contacts: [info@irn.center](mailto:info@irn.center)

E-mail:

Address: 16, rue de la Roche,  
Crégy-lès-Meaux, 77124, France  
Tel. : +33 648 188 695

[www.irn.center](http://www.irn.center)