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Everyone who is concerned by the health of future Ukrainian citizens understands the need to cope with increasingly complex tasks, protect not only the right to life, but also ensure the most complete quality of life. This requires qualitative training of medical, pedagogical and social professionals, continuous healthcare staff upgrading, development of scientific potential and introduction of modern innovative technologies.

Development of palliative care for children is a priority in many countries around the world. Joint efforts of communities, researchers, doctors, psychologists, social workers, and clergy in this regard are one of the key steps taken to enhance the proficiency of Ukrainian specialists by studying international experience and disseminating Ukrainian one.

Close attention to palliative care for children, the need to introduce national and regional programs on this issue are conditioned not only by the necessity to improve the social status of the child population, but also moral and ethical issues.

Implementing the medical reform, we understand that it is necessary to raise the standards of care for children, including palliative care. The mission of academics and researchers is to become the standard of introduction of scientific achievements and best practices of the leading countries in order to take the next level in health care and improve the quality of life of our young patients.

I wish you success in achieving this ambitious goal!

Rector of Kharkiv National
Medical University,
Doctor of Medical Sciences,
Professor **Volodymyr Lisovyi**

HISTORICAL INFORMATION ON KHARKIV REGIONAL SPECIALIZED INFANT ORPHANAGE: ONE HUNDRED YEARS

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The article presents historical data, which are currently known, on the organization and transformation with the time of the public health institution "Kharkov Regional Specialized Child Home No.1". Modern approaches to accompanying children not only of orphans, but also children with special needs are presented: rehabilitation, early intervention services, pediatric palliative care. As the clinical base of the Kharkiv National Medical University, the institution carries out an educational program for the training of students, interns, clinical residents, educational work, scientific work, which is represented by a large number of participation in national and international conferences and congresses, publications, thesis, internship.

KeyWords: Kharkiv Regional Specialized Child's Home, Kharkov National Medical University, children of early age.

Kharkiv Regional Specialized Infant Orphanage No. 1 (Infant Orphanage) is a health care institution, which provides medical, social, and palliative care for young children who have been left without parental authority, as well as children who are brought up in families [1].

Specialists of different fields work in the infant orphanage. There are doctors, nurses, special educators, speech therapists, psychologists.

The Infant Orphanage is one of the oldest in Ukraine and was founded approximately in 1918 by the decree of Nadezhda Krupskaya and it was situated in 3 Revolution street; it started functioning as the Infant Orphanage No.7 of the City Health Department.

During the Second World War and occupation, all children were brought up under the supervision of the remaining employees, who preserved the records of the children's movement, books of orders (according to the senior worker of the Infant Orphanage N.E. Sitnikova).

Upon liberation of Kharkiv from German-Fascist invaders on 23 August, 1943, the Infant Orphanage was moved to 47 Artema street and was named "Regional Specialized Infant Orphanage No 1" of the Regional Health Department, where the children of soldiers who died in the war were brought up.

In 1945 a similar institution at the Infant Orphanage was created in a suburb of Kharkiv, in the village of Zeleniy Gai.

The Board of Trustees, which was established on 7 September, 1945 functioned at the Infant Orphanage from 1945 to 1955, and it conducted its work according to the Statute of the Board of Trustees, approved by the USSR Ministry of Health on 15 August, 1945.

In January 1956, the prefix "specialized" in the documents was omitted and the name Kharkiv Infant Orphanage of the Regional Health Department appeared

In 1972 the Infant Orphanage moved to a new premise in 9 Rybalko street Kharkiv, where it has been situated until now.

By the order of the Directorate of Health of Kharkiv Regional State Administration as of 26.06.2001, the Infant Orphanage was given a specialized status, and it was renamed as "Kharkiv Regional Specialized Infant Orphanage No 1" [3].

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Groups of medical and social rehabilitation for children with special needs and Early Intervention Service have been functioning in the Infant Orphanage since 2010 (*Fig. 1, Fig. 2*).

Fig. 1. Individual rehabilitation of a disabled child

Fig. 2. Group rehabilitation of disabled children with parents

On 29 January, 2018 the department of palliative care for children was founded, the five new separate chambers for children and their relatives were opened. The World Health Organization defines the pediatric palliative care as follows: "Active integrated care for body, mind and spirit of child and his family" [4–7].

Palliative care starts when the child is diagnosed with an incurable disease, continues regardless of whether the child's illness is directly treated and it requires a versatile, multidisciplinary approach. The first in Ukraine palliative mobile teams start working at patient's home [8] (*Fig. 3*).

Fig. 3. Pediatric palliative mobile team

Principles of palliative care consist of : 1) improving the quality of the child's life and his family; 2) involving the child and his family to identify needs; 3) provide all necessary medical, psychological, cognitive, educational, entertaining and educational resources; 4) provide round-the-clock care with the help of qualified specialists of the healthcare system, complementing each other's functions [6–11].

The Infant Orphanage No 1 has become the first home for seven thousand orphans for nearly century-long history.

Doctors and educators of the Infant Orphanage are convinced and sincerely support the idea that the family is the only place where a child can be really happy and healthy. The most important thing that all the infants who live in the Infant Orphanage need is a huge amount of human care and attention.

Since 2008, the Infant Orphanage has been a teaching clinic of the Department of Pediatrics No. 1 and Neonatology. It trains Ukrainian and English-medium six-year students, interns, clinical residents etc.

It also develops educational work with students as volunteers.

Physicians of Infant Orphanage have completed 3 Ph.D. theses and one is being written:

- R. V. Marabyan Optimization of malnourishment diagnostic tools in early age children with paralytic disorders (2015);
- A.Yu. Pen'kov Improving of prevention of health status in children with paternal deprivation by determining the effect of stress hormones on development. – Manuscript (2015);
- I.V. Gordienko Diagnosis and prediction of physical disorders, neuro-mental development of young preterm children. (2017);
- N.M. Konovalova Diagnosis of developmental disorders and optimization of rehabilitation of young children from mothers with alcohol exposure.

There are more than 90 publications (articles and abstracts), 7 educational and tutorial recommendations, 1 monograph, as a result of teamwork.

There were four participations in Salzburg CHOP Seminar of Open Medical Institute (American Austrian Foundation) in 2009, 2013, 2017.

The results of cooperative work were introduced on 36 congresses, conferences, forums in Ukraine and include the following:

- Congress of the European Academy of Pediatrics (Lyon, France, 2013);
- De-institualisation Project of IC Lumos (London, Great Britain, 2013);

- 5th Congress of the European Academy of Pediatrics (Barcelona, Spain, 2014);
- International Neonatal Associations Conference (Valencia, Spain, 2014);
- 2rd International Congress on Pediatrics Palliative Care (Rome, Italy, 2014);
- St. Sophia Hospital training (Rotterdam, Netherlands, 2014);
- 4th International Conference on Pediatrics Chronic Disease, Disability and Human Development (Jerusalem, Israel, 2015);
- Congress of the European Academy of Pediatrics (Oslo, Norway, 2015);
- 1st Congress of joint European Neonatal Societies (Budapest, Hungary, 2015);
- 1st International Developmental Pediatrics Congress (Istanbul, Turkey, 2015);
- 3rd Congress on Pediatrics Palliative Care (Rome, Italy, 2016);
- 6th Congress of the European Academy of Pediatrics Societies (Geneva, Switzerland, 2016);
- British children's hospice training (London, Great Britain, 2016);
- EPEC-Pediatrics Conference (Montreal, Canada, 2017);
- 15th World Congress of the European Asso-ciation for Palliative Care (Madrid, Spain, 2017);
- 15th International Rare Diseases Conference "Rare Diseases – Open Your Heart and Mind" (Bialobrzegi, Poland, 2017) [10–18].

Now the Infants Orphanage and Kharkiv National Medical University are working on the palliative care, de-institualisation and rehabilitation under the guidance of European Union, IF Renaissance, UNICEF and GIZ (Germany) authorities.

References

1. Kharkiv regional specialised infants' home ¹ . 1/ http://hippocrat.org.ua/

2. Historical reference of the infant's home ¹ 1 (1975) Archive of KhRSIH, No.1; 6 p.

3. Benini, F., Drigo, P., Gangemi, M., Sellaroli, V., Lazzarin, P., Jankovic, M., Vecchi, R. (2013). Charter of the rights of the dying child – the trieste charter. Retrieved from: http://www.fondazionemaruzza.org/en/charter-of-the-rights-of-the-dying-child-the-trieste-charter/

4. Riga, O.O., Marabyan, R.V., Penkov, A. Yu., Osichnyuk, L. M., Drokina, V. M., Konovalova, N. M., Gordienko, ². V. (2015). Problems and development prospects of children's palliative care in Ukraine. Family Medicine, 6 (62), 138–140.

5. Penkov, A. Yu., Marabyan, R.V., Riga, O.O. (2015). Respect the right to health individuals of vulnerable groups. Recommendations for the development of children's palliative care Retrieved from: http://khpg.org/index.php?id=1432464675,

http://med-expert.com.ua/media/PM_02_2015/PM_02_2015/assets/basic-html/page11.html.

6. World Health Organization. (?2010)?. WHO model formulary for children 2010. Geneva: World Health Organization. Retrieved from: http://www.who.int/iris/handle/10665/44309

7. Goddard, J. M. (2014). Chronic pain in Children and Young People. Pediatrics and Child Health, 24: 2, 89–91.

8. Riga, O., Marston, J., Penkov, A. (2016). The first experience of mobile pediatric palliative team in Ukraine. Zaporoxhian Medical Journal, 6(99), 62–66.

9. Weaver, M.S., Heinze, K.E., Bell, C.J., Wiener, L. (2016). Establishing psychosocial palliative care standards for children and adolescents with cancer and their families: An integrative review. Palliat Med, 30 (3), 212–223.

10. Riga, O., Gonchar, M., Konovalova, N., Marabyan R. (2016). Outcomes And Need Of Palliative Care For Children With Paralitics Syndrome. 6th Congress of the European Academy of Paediatric Societies, Geneve, 409.

11. Penkov, A., Riga, O., Gonchar, M., Marabyan, R., Shapoval-Deinega, K., Konovalova, N. (2016). "Access To Palliative Care For Children In Ukraine – Challenges And Views". 3rd Congress on Pediatrics Palliative Care, Rome, 112.

12. Makieieva, N., Penkov, A., Marabyan, R., Polyakov, V. (2013). Health and Physical Development: Comparison of Orphanages and Children Living with Birth Parents. Congress EAP, Lyon, 192.

13. Riga, Î ., Gordienko, I., Konovalova, N., Khotsenko, G. (2013). Follow-up of Very Low Birth Weight Infants and Infants with Fetal Alcohol. Abstracy book of Ñongress EAP, Lyon.

14. Riga, Î ., Znamenska, T., Senatorova, G., Kurilina, T., Kondratova, I., Gordienko, I., Kukuruza, G. (2014). Follow-up of Preterm and Term Infants up to Two Years in Kharkiv Regional Perinatal Center. INAC, Valenc³a, 122.

15. Riga, O., Znamenska, T., Kurilina, T., Kondratova, I., Penkov, A., Gordienko, Kukuruza, G. (2014). Improving Quality Of Care and Rehabilitation of Children with High Perinatal Risk. EAPS, Barselona, 99: Suppl 2 A387 doi: 10.1136 / archdischild – 2014 – 307384. 1075.

16. Riga, O., Znamenska, T., Kurilina, T., Senatorova, G., Penkov, A., Gordienko, I., Kovalova, O. (2015). Follow-up of high risk neonate and Ukrainian National Project "Newlife: New quality of maternity and childhood protection". 4th International Conference on Pediatrics Chronic Disease, Disability and Human Development, Jerusalem, 89.

17. Riga, O., Znamenska, T., Kurilina, T., Senatorova, G., Mavropulo, T., Gordiienko, I., Penkov, A. (2015). Follow Up of High Risk Group Neonates in Different Regions of Ukraine. EAP Congress and Master Course, Oslo, 238.

18. Riga, O., Marabyan, R., Konovalova, N., Iermolaieva, M., Matvieieva, G. (2017). Rare Diseases in Young Children and Pediatrics Palliative Care in Kharkiv region of Ukraine. 15th International Conference on Rare Diseases "Rare Diseases-Open Your Heart and Mind", Bialobrzegi, .37.

ENSURING ACCESS TO PAIN RELIEF AS HUMAN RIGHTS

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Abstract. The article presents the results of a selective study on the access to anesthesia. It has been determined that in most cases the goal of chronic pain management has not been achieved for a long time, the expected level of successful anesthesia has not been achieved in 80-90% of those in need, anesthesia is prescribed formally ("any prescription is a good prescription"), without taking into account clinical recommendations and clinical guidelines, that is doctors do not adhere to the principles of the WHO regarding the prescription of analgesics, approved by the Order of the Ministry of Health No. 311 as of 15 April 2012 "On the approval and implementation of medical and technological documents for standardization of palliative care in chronic pain syndrome". The authors believe that professional training of doctors requires changes regarding the quality of palliative care in accordance with WHO standards, wide implementation of modern scientific concepts of anesthesia in all areas of medical staff training.

Key words: palliative care, anesthesia, human rights.

"An acquaintance of mine, who is at the fourth stage of cancer, is not able to receive a prescription for anesthesia, morphine pellets, from the district doctor. According to international rules, a refusal to provide patients with anesthesia is equated with torture. How long will this last? Our lectures, trainings, and orders are all in vain. It is happening in Kharkiv region. Where to complain, where to write?"
(posted on Facebook, September 2017)

In 2010, representatives of the international organization Human Rights Watch (HRW) [1], who at that time conducted research on access to anesthesia and palliative care from the point of view of human rights in different countries of the world, drew the attention of the human rights community of Ukraine to a flagrant violation of human rights in the healthcare sector. The state of Ukraine tortures its sick citizens through numerous bureaucratic barriers and the lack of effective medicines in the pharmaceutical market that the whole world has recognized as the "gold standard" for the treatment of critically-ill patients with severe pain [1, 2].

Thus, during 2010, the first Ukrainian study on access to pain relief for patients with chronic pain was conducted. The findings of this study were published in two separate reports: the Human Rights Watch report "Uncontrolled pain. Obligations of Ukraine in the field of providing palliative care under the standards of evidence-based medicine" and a report by Ukrainian human rights organizations "We have the right to live without pain and suffering: a report by human rights organizations on the observance of the rights of palliative patients in Ukraine" [3, 4].

The 2010 studies allowed a number of important conclusions and recommendations that should be taken into account by the state of Ukraine in improving the state of human rights in the provision of palliative care. The researchers found that the rights of patients living at home, in the countryside and away from district centers and hospitals were largely not respected.

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The studies showed violation of the following fundamental human rights:

– The right not to be subjected to torture or cruel, inhuman or degrading treatment or punishment;

– The right of every person to the highest achievable level of physical and mental health [5].

In order to prevent the violation of the rights of people in need of palliative care and patients suffering from pain, in 2011, within the framework of the report of the Government of Ukraine, recommendations were made for improving the situation, most of which were fulfilled [6].

In 2016, seven human rights organizations, together with Human Rights Watch and with the support of the International Foundation "Renaissance", conducted a repeated study.

The purpose of the study was to determine the state of observance of the rights of patients in need of palliative care and access to anesthesia in Ukraine.

Materials and methods of the study. Separate observations, interviews and analysis of current legislation were carried out till September 2017. Respondents lived in large cities and rural areas or were treated at inpatient facilities that provide palliative care (hospitals, hospices). Interviews were conducted at patients' homes or in institutions with the assurance of the right to privacy, and with the informed consent of the respondents. Family physicians, therapists, and oncologists were interviewed for the purpose of examining the opinion of medical workers who directly provide medical care. A separate survey was conducted among government officials in the health care system of the city and regional levels. In total, the study involved assessment of 94 patient histories from 10 regions of Ukraine, as well as interviews with 50 health professionals and 11 public health officials.

Conflict of interest. Part of the study was funded by the International Foundation "Renaissance".

Results. The study in Ukraine was conducted on the basis of evidence-based medicine on the provision of palliative care and anesthesia (*Table 1*).

Table 1

"Uncontrolled pain" Obligations of Ukraine to provide palliative care according to the principles of evidence-based medicine 2011–2016

HRW recommendations, 2011. The Government of Ukraine shall immediately:	The status of implementation of the recommendations, 2016
Ensure the availability of oral morphine The government should actively involve the company "Health of the people" and other pharmaceutical companies in the development and manufacturing of oral morphine. The public health system must ensure that morphine is availableat all levels of medical care	**Recommendation was implemented in 2013.** There are two national producers of oral morphine of immediate release in Ukraine. On January 1, 2013 INTERKHIM Additional Liability Company, Odesa city, became the first producer of morphine sulfate tablets (5 mg and 10 mg). “Zdorovia Narody” Kharkiv Pharmaceutical Company Ldt, Kharkiv city became the second producer and received a license for production of tablet Morphine-ZN (morphine hydro chloride, tablets 5 mg and 10 mg) on December 27, 2013
Cancel requirement that injectable morphine and other strong pain relief medications should be administered to patients at home by medical personnel. In collaboration with doctors from WHO and other relevant experts to foresee new standards for medications that patients take home to ensure a constant supply of pain relief medications. For example, in areas where service that delivers medicine to health care facilities is functioning, patients should be allowed to receive the medication for 7 days to ensure continuous availability of pain relief medications while in rural areas where access to health facilities that are licensed to work with narcotic medications is difficult– allow patients to store needed medications for at least 14 days.	**Recommendation was partially implemented in 2013, fully implemented in 2015.** On May 13, 2013 the Cabinet of Ministers of Ukraine adopted Resolution №333 “On approval of the procedure of acquisition, transportation, storage, dispensing, use and elimination of narcotic drugs, psychotropic substances and precursors in health care institution”, which changed the procedure for prescription, sale and introduction of opioid analgesics. But until September 22, 2015 the provisions of the CMU Resolution №333 contradicted with MoH Order №11 as of 21.01.2010 “On approval of the Procedure on circulation of narcotic drugs, psychotropic substances and precursors in health care institutions in Ukraine”, even though according to the CMU Resolution №333, three months were given to harmonize the legislation. MoH Order №11 was declared void by the MoH Order №494 as of 07.08.2015 “On certain questions on acquisition, transportation, storage, dispensing, use and elimination of narcotic drugs, psychotropic substances and precursors in health care institution” http://zakon5.rada.gov.ua/laws/show/z1028-15

	MCU Resolution №333 changed the procedure of prescription and introduction of narcotic pain relief medications: *Paragraph 27. Patients being treated on an outpatient basis, including at home, shall be provided with narcotic drugs, psychotropic substances and precursors by health care institution or according to prescription by pharmaceuticals institutions in amounts that does not exceed ten-day needs and during palliative and hospice care - **fifteen-day needs**.* *Paragraph 28. To receive narcotic drugs, psychotropic substances and precursors for use at home patient himself or a person who provides care for him (family member, guardian or trustee) shall submit a request addressed to head of health care institution in the form set in Annex 3. Head of institution shall make a note of approval, after which the request is added to the outpatient's medical record.* CMU Resolution №333 as of May 13, 2013 does not require the introduction of injectable analgesics only by medical workers. Moreover, MoH Order №494 approved Information sheet for the patient or care-giver (family member, guardian or care-giver). The Information sheet includes information about the introduction of injections and rules for handling narcotic drugs. On March 15, 2013 Ministry of Health approved the Order №203 "On amending MoH Order № 360 as of July 19, 2005", which allowed patients not only to receive narcotic pain relief medications at the expense of the health care facilities, but to get them in pharmaceutical facilities upon prescription. *Paragraph 1.18 "During the provision of palliative care to patients, including those who are entitled to a free-of-charge or subsidized provision of medications, it is allowed to prescribe the medications for fifteen-day **need** on one prescription form. When writing out such prescription, a doctor shall indicate "For chronically ill person".* ***Note:*** *MCU Resolution does not distinguish residents of urban and rural areas with regard to access to pain relief medications. Pain relief medications may be prescribed to palliative patients in the amount for 10-15 day need regardless of the place of residence of the patient (CMU Resolution №333 as of May 13, 0213, MoH Order №41 as of January 21, 2013).* MoH Order №311 "On the approval and implementation of medical and technological documents on standardization of palliative care for patient with chronic pain syndrome" as of April 24, 2013 approved standards and principles of the WHO for the treatment of chronic pain, including pain scale, three step ladder pain management, principles of pain relief "by the clock" and others. Instruction on the introduction of tablet morphine of Ukrainian production is based on the WHO recommendations: "Initial dose of the medication depend of the severity of pain and peculiarities of previous introduction of analgesics. Medication shall be administered every 4 hours. In case of increased severity of pain or tolerance to morphine, the dosage may be increased, and 5 mg and 10 mg dosage shall be used". At the same time, the instruction for administration of morphine of Ukrainian production still does not meet the WHO recommendations; in particular regarding addiction. The instruction says: "... Morphine triggers strong euphoria.

	Repeated use of morphine lead to rapid development of psychic and physical dependence (after 2-14 days of treatment). Withdrawal symptoms may occur several hours after cessation of prolonged treatment and reach a maximum after 36-72 hours"- even though the treatment of chronic pain within the appropriate therapeutic dose cannot be accompanied by euphoria and repeat (multiple) usage cannot cause physical dependence (WHO recommendations). Also maximum single and daily dose specified in the instruction do not meet WHO recommendations: "The maximum dose for subcutaneous administration for adults is 2 ml (20 mg morphine) single dose and 5 ml (50 mg morphine) daily" - although according to the WHO recommendations dose should be selected individually for each patient and his/her needs, single and daily doses may significantly exceed the instructions without impacting patient's health
Change the licensing requirements for health facilities in rural areas Requirements for licenses to work with narcotic drug should be such so that all rural clinics could obtain such a license, including medical and obstetrical stations. In particular, the Government shall consider whether there is a necessary requirement for a separate room for the storage of drugs in rural facilities, and whether it's an appropriate measure to protect against unauthorized use, and whether similar results may by achieved if safe is used in those facilities. The Government should introduce a procedure where health care facilities can get a license if they have simple sound and light signal system, rather than a system connected to the police station. If the Government makes a decision to keep the current requirements that require expensive solutions, then the state should provide appropriate state funding for health care facilities.	**Recommendation is partially implemented:** Order of the Ministry of Internal Affairs of Ukraine № 216 "On approval of requirements for facilities and premises for activities with narcotic drugs, psychotropic substances, precursors and storage of seized drugs and such substances" as of 15.05.2009 in paragraph 2.1.4. sets the requirements for premises for storage of controlled medications: *«…separate room in a capital building shall have safes or metal cabinets, secured to floor(walls); doors shall be well adjusted to the box, metal or wooden solid blocks with thickness not less than 40 mm, and shall have at least two locks which cannot be closed independently; window aperture shall be equipped with metal bars on the inside or between the frames. Use of shutters which are not weaker than metal bars may be used".* **Paragraph 3.1.4** of the MIA Order №216 states that: "*…must be equipped with autonomous alarm system that protect the internal space and area, safes (metal cabinets) used for storage, with connection of alert signal to the remote district surveillance* ***or local sound and light signal***.
Distribute WHO guidelines on pain relief among all health care facilities. The Ministry of Health should encourage all physicians to implement the recommendations of the Guidelines on pain assessment and treatment based on accurate pharmacological principles.	**Partially implemented.** On April 14, 2016, MoH approved Guidelines "Development of local protocols on palliative care for management of chronic pain syndrome" Ministry of Health of Ukraine does not conduct inspections of health care facilities regarding their implementation of local protocols. Such monitoring, as well as training on skills for development of local protocols are carried out by NGOs.
Provide in-service training on the use of protocols on pain relief for doctors throughout the health care system.	**Partially implemented.** Training for doctors about changes in legislation on handling controlled substances in health care facilities and usage of protocol on pain relief is conducted by NGO supported by donor organizations, including the International Renaissance Foundation.
Legislation and regulations	
Develop a system of palliative care provision at home. Review the structure of the staff of health care facilities in order to enable hospices and other institutions to provide palliative care to patients at home; provide funds to hospices to develop such services; to reform the current system of delivery of strong medications (nurses visiting patients at home) and transform it into a system of palliative care provision.	**Partially implemented.** In 2012 Law of Ukraine "On amendment to the basic law of Ukraine on health care regarding improvement of health care provision" was adopted. The Law defined the palliative care as one of the types of medical care: *"Article 35.4. Palliative care* *In the course of the last stages of incurable diseases patients are provided with palliative care, which includes measures aimed at alleviating physical and emotional suffering of patients and providing psychosocial and moral support to their families.* *Palliative care is provided free of charge upon referral of health institution where the patient was provided with secondary (specialized) or tertiary (highly specialized) medical care, which has an agreement on health services provision for the population. The procedure on palliative care and a list of medical indications for its provision are defined by central executive body in health care."*

	But these changes came into effect only on January 1, 2015. Acting MoH Order №41 as of January 21, 2013 contains no specific staff regulations for hospice or on-site services. Therefore, services based their activities on the Annex №50 to the MoH Order №33 as of February 23, 2000 until its cancellation on September 2, 2016. Currently (as of December 2016) there are no regulations on the staffing, organizational structure of institutions providing palliative care. The cancellation of MOH Order №33 allows health care facilities to independently decide on the structure of the staff. Approval MOH Order №41 preceded the entry into force of the Law of Ukraine. In 2016 amendments to the MOH Order №41 are being developed by a working group of activists and practitioners. Among other important things, these changes shall define the peculiarities of pediatric palliative care. The system of delivery of pain relief medications was changed by CMU Resolution №333 as of May 13, 2013. But in some areas there are still "narcotic treatment teams" which are carrying out the injections of morphine to patients. At the request of human rights organizations in particular in Kropyvnytskyi city, Kirovograd region, regarding the necessity of such type of service, the Department of Health during the “Forum on palliative care" held on September 23, 2016 reported that such service is necessary for the attendance of single patients or patients who do require such services. Since 2014 Institute for Legal Research and Strategies NGO, together with the National Preventive Mechanisms under Ombudsman, investigates the situation of all health care facilities and social protection institutions, which could be considered as those that provide palliative care. Preliminary monitoring results indicate that 2/3 of facilities designed to provide palliative care, do not meet the minimum standards of WHO and international organizations regarding palliative care
Develop protocols on palliative care and pain management. The Ministry of Health, medical universities, organizations providing palliative care and respective NGOs should develop protocols on palliative care and pain management based on information from international best practices. This clinical protocol should be widely distributed to all medical workers, and it will form the basis for training of medical professionals in palliative care and pain management.	**Partially implemented.** Order of the Ministry of Health of Ukraine №311 " On the approval and implementation of medical and technological documents on standardization of palliative care for patient with chronic pain syndrome” as of April 24, 2012 " established standards and principles of WHO for the treatment of chronic pain syndrome. In 2016 medical and technical documents on standardization of palliative medical care for adults with chronic pain syndrome are being reviewed by a working group of Ministry of Health of Ukraine. In 2016 working group selected WHO protocol as a priority document to work on the development of medical and technical documentation for pharmacological treatment of chronic pain for children. In 2016 working group is finalizing medical and technical documents on standardization of palliative care for patients with HIV/AIDS. The initial protocol was approved by the MoH Order №368 as of July 3, 2007. According to the provisions of MoH Order №41 "On organization of palliative care" as of January 21, 2013 patients with HIV/AIDs cannot stay in general hospices or palliative care departments. The main reasons for refusal to take such patients is the inability to provide sanitary conditions for HIV-infected patients in these institutions. According to human rights advocates, this provision is discriminatory and shall be removed from the Order.
Ensure the integration of palliative care into strategies for disease prevention. The national programs on HIV/AIDS and cancer, as well as respective strategies for prevention of other diseases shall include a powerful palliative component have a list of steps to be taken to integrate palliative care into these strategies, and provide targeted and appropriate funding for the development of palliative care.	**Partially implemented.** The issue of palliative care is included into program for prevention of cancer by 2016. But, unfortunately, there is no funding foreseen http://zakon2.rada.gov.ua/laws/show/1794-17/page2

Education	
Introduce palliative care courses as a part of educational programs for doctors and nursing staff. Set a clear standard of education in the field of palliative care and pain management for medical workers to receive at least basic knowledge in this discipline.	**Partially implemented.** With financial and organizational support of the International Renaissance Foundation in Ukraine two modules - EPEC-O and ELNEC - were translated, adapted and successfully introduced in Ivano-Frankivsk National Medical University, Kharkiv Medical College №1 and Cherkassy Medical College. There is no clear standard of education in the sphere of palliative care and pain management.
Introduce questions on palliative care into state exams to receive the diploma in medical sphere	**Not implemented.** Experts note the extremely low level of knowledge among medical personnel on palliative care and pain management principles.
Introduce internships in palliative care. The Ministry of Health should establish internship in departments of palliative care for students of some postgraduate training programs including oncology, geriatrics, infectious diseases to ensure that they receive clinical practice of palliative care**.**	**Not implemented.** Student from only few medical schools undertake internship in palliative care. Ministry of Health of Ukraine has not introduced specific legal and regulatory standards for internship in palliative care.
Develop expert training centers. The Ministry of Health should develop geographically dispersed training centers for palliative care, possibly on the basis of existing hospices.	**Partially implemented.** Two training centers in palliative care, one based in Ivano-Frankivsk Regional Palliative Care Center in Ivano-Frankivsk (Western Ukraine) and one at Kharkiv Regional Palliative Care Center in Kharkiv (eastern Ukraine) were opened and successfully operate in Ukraine. The training centers provide training according to international programs EPEC-O and ELNEC for medical workers, social workers, volunteers, clergy, psychologists, NGO activists. Learning is supported by the International Renaissance Foundation and conducted in cooperation with state educational institutions.
Develop training modules. The Ministry of Health should translate key documents on palliative care into Ukrainian and develop training modules for doctors, nurses, social workers, counselors and volunteers in collaboration with hospices, civil society and international experts in palliative care.	**Partially implemented.** With financial and organizational support of the International Renaissance Foundation in Ukraine two modules - EPEC-O and ELNEC - were translated, adapted and successfully introduced in Ivano-Frankivsk National Medical University, National Pharma University (Kharkiv), Kharkiv Medical College №1 and Cherkassy Medical College.
Introduce the postgraduate medical education. Palliative care and pain management should be part of the mandatory programs of postgraduate education for all general practitioners, oncologists, infectious disease specialists, anesthesiologists, gerontologists and others. The issue of palliative care and pain management should be included in the list of exams that doctors and nurses have to pass at the end of these programs.	**Partially implemented.** A Department of Palliative Care at the P.L. Shupyk National Medical Academy of Postgraduate Education was established. Currently the process of creating departments at other medical universities is extremely difficult. Questions on adequate pain relief and palliative care are not included in the list of exams.
Availability of narcotic medications	
Ukraine needs to conduct comprehensive review of procedures for circulation of narcotic drugs and make any amendments in such a way that they ensure adequate availability of strong opioid analgesics, while minimizing the risks of abuse	CMU Resolution №735-р "On approval of strategy of state drug policy for the period till 2020" as of August 28, 2013. Strategy provides, inter alia: ***"Ensuring availability of narcotic drugs*** *To ensure the availability of narcotic drugs it is necessary to:* • *Evaluate the need for narcotic drugs, following international methodologies in this area with the establishment of appropriate quotas;* • *Develop and implement standard schemes for application of narcotic drugs for treatment based on international experience;* • *Introduce access to narcotic drugs through primary link of health care, general practitioners - family doctors;* • *Reorganize and expand network of pharmacies with the right to store and issuance of narcotic drugs.* ***Promoting development of palliative care*** *An important step to humanization of narcotic policy shall be:* • *Conduction of national assessment of need in palliative care, in medications, primarily for pain relief;* • *Development and adoption standards and clinical protocols of palliative care in accordance with the principles of the WHO;*

	• *Promoting domestic production of tablet morphine;* • *Establishing a system of state support for drug producers and pharmacies that have license for circulation of narcotic medications in order to expand their range and availability;* • *Providing health care facilities and pharmacy network with tablet forms of prolonged opioid analgesics;* • *Creating the necessary conditions for the safe use of narcotic drugs in the "in patient facility at home";* • *Prescribing narcotic medications to patients with chronic pain of cancer and non-cancer nature by doctor without further approval and revision by medical board;* • *Including compulsory course on palliative care into undergraduate and postgraduate training programs for doctors, paramedics, nurses, counselors and social workers. “*
Licensing requirements. These requirements should be the less burdensome, while providing protection from possible misuse and theft. The Government should consider the possibility of using safes for storage of small amounts of opioid medications, which are likely to be stored in rural hospitals.	**Partially implemented.** The government did not consider the use of safe, which can quite reliable protect small amounts of opioid medication in rural hospitals. Licensing requirements were simplified and system of filling in documents for obtaining a license was improved under the CMU Resolution №282 “Some issues of licensing the cultivation of plants included into Table I of the List of narcotic drugs, psychotropic substances and precursors, approved by the Cabinet of Ministers of Ukraine, development, production, manufacture, storage, transportation, purchase, sale (delivery), import into Ukraine, export from Ukraine, use, destruction of narcotic drugs, psychotropic substances and precursors included in this list" as of April 6, 2016. In particular, the list of required documents to obtain a license was simplified to 8 items. Also paragraph 28 of the Resolution states: “In case two health care facilities share the space for storage, narcotic drugs, psychotropic substances and precursors shall be stored in individual safes (cabinets). Sharing space is confirmed by the relevant agreements”, which reduces the cost of preparing the facilities for the storage of controlled medications.
Medicines for use at home. In many countries in the world it is a standard practice to give patients morphine supply for use at home for a period from two weeks to one month.	**Implemented.** Pain relief medications may be prescribed to palliative patients for a period of 10-15 days regardless of the place of residence of the patient - CMU Resolution №333 of May 13, 2013; MoH Order №360 as of July 19, 2005. ***Note:*** *Medical staff having all legal grounds to prescribe adequate pain relief medications, often do not ensure the sufficient amount of medications for palliative patients. This primarily happens due to limited finances to purchase pain relief medications, lack of understanding of managers of health care facilities of need to clearly identify the need and lay the funds for the purchase of pain relief medications, lack of regular mechanisms for calculating needs.* There have been cases recorded when managers of health care facilities, referring to the CMU Resolution №240 as of February 7, 2014 “Issue of declaration of change of wholesale selling prices for medicines and medical products" emphasized that it is very hard to set procurement prices for the pain relief medications: "1) Since August 1, 2014 changes in wholesale prices shall be declared excluding taxes and fees for: medicines included in the list of medicines of domestic and foreign production, which can be purchased by health care facilities and institutions, that re fully or partially financed from state and local budgets approved by the CMU Resolution №1071 as of September 5, 1996 “Order of procurement of medications by health care facilities and institutions at the expense of the budget "(Article 480 of the Law of Ukraine №17, 1996), **except narcotic and psychotropic drugs**, precursors, drug substances (substances), medical gases and dosage forms produced in pharmacies from the substances and excipients permitted according to prescription and as requested by health care facilities."
Recording procedures should be simplified to minimize waste of imited resources	**Implemented** CMU Resolution №333 as of May 13, 2013. MoH Order №360 as of July 19, 2005. MoH Order №494 as of August 7, 2015

Number of signatures for a prescription shall be reduced. Doctors in most countries can make their own decisions about prescription of opioid analgesics.	**Implemented** CMU Resolution №333 as of May 13, 2013. MoH Order №360 as of July 19, 2005. MoH Order №494 as of August 7, 2015. Decisions about prescription of opioid analgesics are taken by the attending physician and recorded to the patient history\card. CMU Resolution №333 as of May 13, 2013: *“Paragraph 26. Prescription of narcotics drugs, psychotropic substances and precursors to patients for more than ten days shall be done by the attending doctor with obligatory reasoning of further use of such drugs, which is recorded in the medical record of the patient. Prescription sheet shall be stored in the patient's medical record.”* MOH Order №360 as of July 19, 2005: *"1.4. Prescriptions shall be stamped with square stamp of the health care facilities and certified by signature and personal seal of a doctor, and in the cases stipulated by this order (para. 1.14 (appointment of narcotic (psychotropic) drugs on the prescription form F-3)) additionally by a round seal of the entity, which carries out activities related to medical practice.* *1.13. Prescription form F-3 shall be additionally signed by the head of health care facility or deputy head on clinical work (and in their absence - the signature of the head of the department, who is responsible for the appointment of narcotic (psychotropic) drugs) and certified by the seal of the entity, which carries out activities related to medical practice.* *1.12. All specific instructions, notes of the medical worker ("Chronically ill", "For special purpose") are additionally certified by signature and seal of the doctor.* *1.18. If necessary (business trip, vacation etc.), patients, including those who are entitled to free or subsidized provision of medication, is allowed to receive prescription for medications in amount for three-month need, taking into account the rules of supply of medicines.* *When providing palliative care to patient, including those who are entitled to free or subsidized provision of medications, is allowed to receive prescription for medications in amount for fifteen-day need. When writing out prescription, an indication “Chronically ill” shall be made".*

Conclusions:

1. A sampling study showed that in most cases, the goal of treatment for chronic pain, namely the elimination of pain or its significant reduction for a long time, was not achieved.

2. The expected level of successful anesthesia has not been achieved in 80–90% of those in need; conditionally successful anesthesia has been achieved in 5–14% of patients.

3. Anesthesia is prescribed formally ("any prescription is a good prescription"), without taking into account clinical recommendations and clinical guidelines, that is, physicians do not adhere to the principles of the WHO regarding the prescription of analgesics, approved by the Order of the Ministry of Health No.311 as of 25 April 2012 "On the approval and implementation of medical and technological documents for standardization of palliative care in chronic pain syndrome".

4. According to interview materials, the formal prescription of anesthetic regimens and the lack of doctors' desire to achieve success in pain management can only be explained by the reluctance of medical professionals to perform their professional duties – to treat chronic pain syndrome. Separate explanations from physicians concern the fears of causing drug dependence, or fears of provoking respiratory depression in patients, or ignorance of the orders of the Ministry of Health – all these excuses cover the Soviet tradition of medical education: not to prescribe opioids for pain relief in any case.

5. Professional training of doctors requires changes regarding the quality of palliative care in accordance with WHO standards, wide implementation of modern scientific concepts of anesthesia in all areas of medical staff training [8–18].

References

1. Human Rights Watch, 350 Fifth Avenue, 34th floor, New York, NY 10118-3299 USA, Tel: +1 212 290 4700, Fax: +12127361300, hrwnyc@hrw.org

2. Human Rights Watch (2009). Please, do not make us suffer any more. Access to Pain Treatment as a Human Right. Ruth Fremson/The New York Times/Redux, ð. 45. Available at: https://www.hrw.org/sites/default/files/reports/health0309ruwebwcover.pdf

3. Human Rights Watch (2011). Uncontrolled Pain. Ukraine's Obligation to Ensure. Evidence-Based Palliative Care. Scott Anger & Bob Sacha/Open Society Foundations, ð. 94. Available at: https://www.hrw.org/sites/default/files/reports/ukraine0511rusWebVersion.pdf

4. Rohanskij A., Kotenko A., Lazarevich Ju. i drugie (2012). My imeem pravo zhit' bez boli i stradanij otchet pravozashhitnyh organizacij o sobljudenii prav palliativnyh pacientov Ukrainy. [We have the right to live without pain and suffering the report of human rights organizations on the observance of the rights of palliative patients in Ukraine]. Kiev: Izdatel'skij dom "Kalita", p. 112.

5. Senjuti ².Ja. (2015). Prava ljudini v galuz³ ohoroni zdorov'ja 2007-2016. [Human rights in the health galusies 2007–2016]. 5-te vid., dop. - L'v³v: Vidavnictvo LOBF "Medicina ³ pravo", p. 989.

6. Theunissen, J.M., et al. (2007). Symptoms in the palliative phase of children with cancer. Pediatr Blood Cancer, 49(2), pð. 160–165.

7. Riga O.O., Marabyan R.V., Penkov A. Yu. et al (2015). Problems and development prospects of children's palliative care in Ukraine. Family Medicine, 6 (62), ðð. 138–140.

8. Joan MarstonrI GA, Riga O., Marston J, Penkov A. (2016) The first experience of mobile pediatric palliative team in Ukraine. Zaporoxhian Medical Journal, 6(99), ðð. 62–66.

9. Riga O., Gonchar M., Konovalova N., Marabyan R. (2016). Outcomes And Need Of Palliative Care For Children With Paralitics Syndrome". 6th Congress of the European Academy of Paediatric Societies, ð.409.

10. Penkov A., Riga O., Gonchar M., Marabyan R. et al (2016). "Access To Palliative Care For Children In Ukraine - Challenges And Views". 3rd Congress on Pediatrics Palliative Care), Abstract book, ð.112.

11. R³ga O.O., Gonchar' M.O. Marabjan R.V., Pen'kov A.Ju. i drugie (2016). Problemi ta perspektivi rozvitku ped³atrichno¿ pal³ativno¿ dopomogi. [Problems and prospects of pediatric palliative care development]. Reab³l³tac³ja ta pal³ativna medicina ¹ 2(4), pp. 73–76.

12. R³ga O.O., Osichnjuk L.M., Marabjan R.V. (2016). Oc³nka bol'ovogo sindromu u d³tej ³z nevrolog³chnoju patolog³º ju H³rurg³ja Donbasu. [Evaluation of pain syndrome in children with neurological pathology of the Donbass Surgery]. Tom 5, ¹ 3, pp. 59–64.

13. R³ga O.O., Marston Joan, Gonchar' M.O., Pen'kov A.Ju. (2016). Ped³atrichna pal³ativna dopomoga v praktic³ ditjachogo endokrinologa. [Pediatric palliative care in the practice of children's endocrinologist]. Mater³ali naukovo-praktichno¿konferenc³³ z m³zhnarodnoju uchastju "Endokrinna patolog³ja u v³kovomu aspekt³", ðð. 74–75.

14. R³ga O.O. Marabjan R.V., Gavrish T., Pen'kov A. i drugie (2015). Chi º lokal'n³ protokoli pal³ativno¿ dopomogi dlja d³tej v ustanovah. [Are there any local palliative care protocols for children in institutions]. Mater³ali naukovo-praktichno¿ konferenc³¿: pal³ativna dopomoga v Ukra¿n³: skladov³ ta shljahi rozvitku. Reab³l³tac³ja ta pal³ativna medicina, ¹ 1(1), pp. 88–89.

15. Gonchar' M.O., R³ga O.O., Pen'kov A.Ju. (2015). Principi nadannja pal³ativno¿ dopomogi d³tjam: pershij dosv³d vi¿znih pal³ativnih brigad v Hark³vs'kij oblast³ Navchal'nij pos³bnik. [Principles of the provision of palliative care for children: the first experience of visiting palliative brigades in the Kharkiv region]. Vidavnictvo RA ART-MAK, Hark³v, p. 112.

16. R³ga O.O., Koval'ova O.M., Korobka O.V., Gonchar' M.O. i drugie (2015). Pal³ativna dopomoga u novonarodzhenih: mediko-etichn³ ta f³nansovo-ekonom³chn³ aspekti. [Palliative care for newborns: medical and ethical and financial and economic aspects]. Ekonom³ka ³ pravo ohoroni zdorov'ja, ¹ 1, pp. 31–35.

17. R³ga O.O. (2015). Kroki dlja sprijannja vprovadzhennja neonatal'no¿pal³ativno¿dopomogi v Ukra¿n³. [Steps to Promote the Implementation of Neonatal Palliative Care in Ukraine]. Neonatolog³ja, h³rurg³ja ta perinatal'na medicina T V ¹ 2 (16), pp. 5–10.

18. Rohans'kij A. O. (2016). Prava ljudini v galuz³ ohoroni zdorov'ja 2015–2016 (persha polovina): dopov³d' pravozahisnih organ³zac³j. [Human rights in the field of healthcare 2015–2016 (first half): report of human rights organizations]. ²n-t prav. dosl³dzh. ³ strateg³j. Hark³v: Prava ljudini, p. 107.

OPEN QUESTIONS ABOUT THE USE AND DEFINITION OF THE STATUS OF A PALLIATIVE PATIENT

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The article discusses the issue of determining the status of a palliative patient in the context of institutionalization of the national system of palliative care in Ukraine and the statistical obscurity of palliative patients. The definition of "palliative status of a patient" is studied using the materials of scientific Ukrainian and foreign sources. Semantics of the concepts of "status", "patient" and "palliative" are featured. The criteria for determining the patient's palliative status and its differential diagnosis are discussed using modern approaches to its categorization. Recommendations for determining the patient's palliative status, including that of a child, were developed.

Conclusion. The question of the status of a palliative patient still remains unanswered in practice, especially when palliative care is not finally institutionalized as an integral part of both clinical practice and collective consciousness of Ukrainian society.

Key words: palliative care, status of a palliative patient, discrimination.

As it has been emphasized by the World Health Organization (WHO), the global need in palliative care (PC) will continue to increase as a result of the growing burden of non-communicable diseases and the continuing aging of the population [1]. The WHO also recognizes that of the 40 million people on the planet who require PC annually, only 14% receive it (data of 2011), which is the evidence of a low level of PD and pain relief accessibility and is a sign of the global humanitarian crisis [2]. Unfortunately, most patients requiring PC do not receive it [3, 4, 6]. This situation, in our opinion, has a predictor of a methodological, cultural and bioethical kind that requires some theoretical and practical elaboration. Moreover, the complexity and inconsistency of the definition and differential diagnosis of palliative patient status (PPS), the question of its diagnostic limits and classification complicates the introduction of PC, which is accompanied by a certain degree of misunderstanding among the medical community, patients and their families.

In the United Kingdom and the United States, where PC system is institutionalized, the project of the National Consensus on PC Quality Improvement emphasizes its "importance ... as a viable option for patients of any age with a life-threatening, debilitating chronic illness or injury" (cit. in [3; 7]). Such phenomenological descriptions, lack of specificity, normalized unambiguous determinants and practical recommendations in a language unified to specialists of a certain national health and social protection system that would enable the patient identification as a palliative and provide him with the necessary PC services. The necessity of terminological unification and standardization for the greater accessibility of PC, was emphasized by the WHO in 2009 [1; 278]. It should also be noted that such terminological interference, according to the WHO, is also observed with the methodology used for the global assessment of disability, which is still not up to date and is being improved [8].

The aim of this work was to raise the problem of determining the clinical and legal boundaries

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of the concept "patient's palliative status" in Ukraine, which increases the PC accessibility and prevents statistical obscurity of palliative patients.

The object of the study was the definition and differential diagnosis of the status of a seriously ill (incurable) patient.

The method of research was content analysis of scientific literature on the semantics, legal and clinical content of the concept of "patient's palliative status".

Conflict of Interest. The authors state that there is no conflict of interest.

Results and discussion. In Ukraine, there is a clinical protocol that addresses the issue of PC, but at the same time there is insufficient implementation (about 25% were fulfilled fully) of Human Rights Watch's recommendations on PC standards in Ukraine. Human rights activists point out that, despite the changes in the normative framework, the legislation on PC (pain relief) is ignored by the doctors and not implemented [9]. Obviously, Ukraine "needs an immediate restructuring of the health system based on humanism, human rights, 'patient-centeredness' in the provision of medical services" [10; 1]. It is also clear that by introducing a palliative approach in Ukraine, professionals and decision makers in the health sector who are responsible for ensuring that PC is accessible to the population are faced with the problem of ***determining the palliative status*** per se, since it is extremely difficult to explain such situation using only economic reasons. We also assume that this is precisely the methodological "stumbling block", which nevertheless has the foundation of the collective consciousness of a nation that allows such a state of affairs.

Historically, PC programs focus primarily on the needs of cancer patients with a very heavy burden of aggravating symptoms [7]. Therefore, the status of a palliative patient has been discussed especially actively in cases that go beyond the traditional focus of oncology [1], or neglected because of the so-called phenomenon of "medicalization" [11; 4]. Specialists deciding on the initiation of PC, also discuss the moment at the time of the terminal stage of the disease, when PC should necessarily be proposed to the patient, because of the difficulties associated with the development of precise predictive criteria, in particular, for non-malignant diseases [4; 12]. The socio-psychological aspect of PPS is also actively debated by Ukrainian professionals and experts because of fears of a ***certain stigmatization on the basis of the presence of an incurable disease/condition***, even despite the legal possibility for the patient with a similar status to freely use pain relievers [12].

In Ukraine, since 2013, it has been legally determined that "a palliative patient is a patient of all age groups whose illness does not respond to the treatment aimed at recovery, and is accompanied by chronic pain syndrome and significant limitation of vital activity in its absence"; the legal status of "palliative" is determined by "a physician since the diagnosis of an incurable progressive disease with a predicted life expectancy "[13]. A similar definition, despite the criteria for exclusion from these medical indications: acute and chronic (infectious, mental) diseases in the stage of exacerbation, acute surgical states and conditions after surgical interventions, is obviously rather multiple and not sufficiently deterministic. The situation of statistical obscurity, obviously, originates from normative (legal) plurality and incorrectness.

In the first approximation, the meaning of PPS is disclosed clinically and can be systematized by ICD-10, DSM-IV and ICF headings [14]. The features of classification of the phenomenological diversity of the palliative human state have not received the appropriate nomenclature yet, which, as a consequence, has an unambiguous diagnostic conclusion of the doctor and is the legal basis for the further route of the patient in the medical and social plane of his life. It should also be noted that the differential diagnosis of a palliative condition/disease is still not defined, and even the experts of the countries leading in the field of PC (Great Britain, Australia) in spite of the high level of achievement of their national PC systems, still discuss the questions of the clinical aspects of PPS [7, 11].

The most relevant answer to the dilemma being discussed seems to have been found by the experts from Australia and Germany in the methodology for calculating the population's needs in the PC services.

Palliative status and its derived assessment of the needs for PC are complex and controversial issues, and the corresponding methodology is improved by the gradual specification of the inclusion-exclusion criteria adjusted by regional peculiarities of the population of palliative patients, resources of regional experts. The latter, in turn, are regulated by national professional (ethical) standards, which directly reflect the level of culture and humanity of society.

It should be noted that palliative child patients occupy a special place in solving the discussed dilemma. To determine PPS in a child patient, there is "List of Lifestyle Restrictions" containing about 400 ICD-10 codes associated with illnesses that can restrict the child's life. The classification of the state as one that "restricts life" means: its dynamics can be accurately described by at least one of the archetypes set forth in the standards of the Royal College of Pediatrics and Child Health in 1997, along with the Association for child PC [15]. This catalog was obtained in 2011 by grouping diagnostic data from children's hospices and specialized groups on PC provision from all over the UK and combining these data with death certificate data [16]. As the authors point out, the catalog is not exhaustive. There are certain conditions that also limit life, but they were not included in the catalog because of the fact that they were encountered extremely rarely.

The catalog is not decisive. This is a list of conditions that can restrict life, not a list of children, who should be sent to a specialist for PC. Not every child with a condition from this list will need a specialized PC at any time, and it will probably never be necessary for some, as some conditions may be of varying degrees of severity, such as cerebral palsy; even those children who will need PC at some stage may not yet need it; not all PC needs to be provided by specialists.

The catalog is not final. What is considered "life-restricting" requires a certain subjective judgment, which is influenced by modern concepts, the availability of technologies that can change over the time. The emergence of gene therapy can make the states of the directory list curable and they will not need to be included in the list. An acute trauma, such as a road accident, on the other hand, is not considered to be a "life-restricting" state at this stage, but there are reasons to consider it as such in the future.

Consequently, such multiplicity, polysemy and etiologic diversity constitute the obligatory context of the palliative status process, which must be taken into account by the clinician. The variety of nosologies, clinical forms and pathological health conditions that according to their transfinitum have a subjective significance of destruction of autonomy and self-service abilities of the patient and, above all, a limited life expectancy and an over-threshold risk of death for the patient, in our opinion, constitute the fundamental content of the palliative status per se.

From the standpoint of multidimensionality the above clinical manifestations consider that in an individual with a palliative status, it is possible to detect a wide variety of damage at almost all levels of life: chronic life-threatening and persistent dysfunction of organs and systems of the body, including due to pain syndrome, psychophysiological exhaustion, a sense of loss of dignity and the right quality of life. Multidimensionality, criterion uncertainty, correlation with regional peculiarities of the problem of PPS determination is confirmed, in particular, by the definition of the European Palliative Care Association (EPCA) in the White Book, "... PC is required by a much larger number of patients suffering from both cancer and non-cancer illnesses. The number of these patients also depends on the incidence of different nosological forms in different countries. The duration of PC can also be different - from several days to several years, because due to the possibilities of modern medicine, PC will be needed for some patients for a longer time, and not only during the last year of life "[4; 5].

A generally accepted European definition is crucial: "PC is indicated to all patients since the diagnosis of a life-threatening or debilitating disease is made", which emphasizes the life-threatening and debilitating illness of the palliative patients"... who are constantly or periodically in a state which negatively affects their everyday life" [4; 12].

Semantically, PPS is defined using the generic concepts of "status", "patient" and "palliative". The latter two, as opposed to the first one (legal), are purely clinical. Their intersection area is denoted by the legal fact that the doctor identifies a certain illness/condition as requiring PC, thus legitimizing all subsequent clinical and social routes of a particular palliative patient. Let us consider the notion of PPS both from the legal perspective, and from its clinical presentation.

The notion of "status" (Latin status - state, position) has a social and legal connotation, and denotes a stable position of an individual within the social system, associated with certain expectations, rights and obligations [17], which is determined by a number of features (economic, professional, ethnic, etc.) [18]. The term "status" relates to the state of a seriously ill patient within the social stratification system of society, reflecting the gradual destruction of his social roles and situation with the course of the disease. For our analysis, the semantic load, the explicit (declarations and legal norms of society concerning the seriously ill patients) and the latent (the real attitude of the society to the incurably sick person), which accumulates and reflects the social system of values and morals, is decisive. Given the specific lifestyle that unites the totality of individuals in a similar status situation (incurable illness), we can talk about the corresponding status group.

Due to a limited life expectancy, the human condition a priori has a downward trend in line with the level of actual social and psychophysiological damage. It should be noted that the notion of status has one more facet, a legal one, which implies the direct effectiveness of the constitutional rights and freedoms of any citizen, including the rights of a seriously ill person, and is ensured by the protection by justice (the content of normative legal acts, direction of the activity of all branches of government, etc.). Consequently, the concept of "status" of a person determines the social and legal status situations between the person and society: rights, duties, normative communication, which stigmatize and/or discriminate the patients. For example, in Ukraine there is a special legal status of an individual for persons with disabilities and victims of Chornobyl accident, which are defined by the rules of a special legislation [19]. Actually, the existence of a legal status defines a person as a subject of law, thus legally establishing a range of possible and appropriate actions in his relations with the society. It should be noted that only the legal determination of the corresponding status (as a collective decision of the state medical and social expert commission, on the recommendation of the doctor, who establishes the preliminary diagnosis) allows a certain level of provision of this category of the population resources: financial, social, etc.

With regard to the concept of "patient", the national legal framework provides the following definition: "a patient is an individual who has applied for medical care and/or is provided with such care" [20, 21], which, according to some experts, is concise and incomplete, because it contains "one-sided characteristics of the patient as a consumer of medical services" (cited by [22]). In the context of palliative issues, this meaningful interference does not cause conceptual remarks of the specialists, but is an important component of the existing semantic field of the concept of PPS, which complicates the question of its definition.

In our opinion, the main complexity and contradictory of PPS definition are the practical problems of establishing its diagnostic boundaries through polynosology that is immanent. Based on the definition of the WHO, which focuses on the complexity of the physical, psychosocial and spiritual problems, "associated with life-threatening illnesses" and suffering [23], we tend to distinguish the main problem not only in its medical components, but, first of all, of the main psychophysiological performance indicators.

In general, the status of a palliative patient makes debut a little later after setting the "patient status", namely with the onset of a palliative stage of the disease, when clinical manifestations of the disease already contain indications of incurability and/or the loss of self-care (autonomy) of the patient. PPS should legally confirm the already existing "patient status", emphasizing the deterioration of the clinical presentation and limitation of the patient's life expectancy. The clinical aspect of PPS is poorly explored due to phenomenological manifestations of the corresponding condition/disease, which, in turn, are indicated by the codes of the known international classifiers.

It is obvious that certain diagnostic collisions are concentrated in the dynamic peculiarities of the palliative status and its possible changes: the diagnosis, the start/stop of the palliative period of the disease/condition, possible exacerbation/ remission of the disease, the death of the palliative patient, which, according to pp 2.4 of the order of the Ministry of Health No. 41, "monitoring the state ... when changing the patient's status" [24]. Consequently, the notion of "palliative" obviously attributes the state of health of a person who is on the verge of abnormal functioning and/or life-death, when the basic psychophysiological indices indicate the presence of a threatening pathology, which makes impossible a decent quality of life. The impossibility of normative functioning to some extent can be offset by medical, psychosocial measures, but no means (technology) can provide dignity of a person's life/death, as they reflect the plane of the attitude towards the sick person, his/her needs and values from the environment (micro, meso- and macrosocium).

It seems that the very concept of "palliative" concentrates methodological dilemma, which leads to existing collisions of hypo- and hyperdiagnosis of PPS. In fact, the determinant definition of "palliative" in the order of the Ministry of Health No. 41 is semantically disclosed through the diagnostic procedure and clinical signs: "acute" "chronic" and "exacerbation", together with a negative particle "no". This method of determining PPS, as it seems to us, requires urgent correction to a level that will make statistical obscurity of palliative patients and their discriminator impossible [26; 56].

There is also a need to distinguish between the palliative status and the diagnosis, which was pointed out by the WHO and WPCA that call for caution when using ICD-10 diagnostic headings for such an assessment, since not all patients with a definite diagnosis require PC [25]. To clarify the PPS, they distinguish three groups of patients who definitely need PC: (1) those who have a palliative period of a progressive disease; (2) with a stable/unstable course of the disease, with a relatively small number of symptoms, whose condition may deteriorate even to sudden death; (3) and those suffering from chronic illnesses, when the disease does not progress, with periods of progression and remission, and who benefit from the use of PC. The WHO and WPCA emphasize the uncertainty of the proportions of these three groups of patients and indicate the specific symptoms of PPS: pain, end of life period. Relative diagnosis is also indicated by the European standard of PC, the White Paper: "PC is not limited to providing care to the patients with some definite diagnosis, it should be accessible to all patients with life threatening illnesses" [4; 21].

Conclusion. Our brief critical review of the state of PPS diagnosis can be summarized as follows: PPS definition is the result of interaction of conventional (legal, social), expert (professional) and ethical (traditional, social) markers. These include, in particular, mortality data of the region (country), the resources of the regional health system, and, above all, the ethical standards of society, which imply the meaning of the semantic field "palliative". It is this content that reproduces humanistic national standards that broadcast to the professional environment the relevant thresholds of sensitivity to the level of psychophysiological exhaustion, which enables the physician to include/exclude a patient who is seriously ill to a palliative status, and initiates PC.

Obviously, multiplicity of PPS etiology, which we reviewed, involves the appropriate fluctuation of the focus of gravity in the process of setting up and defining the diagnosis/condition, which involves the indispensable start of PC. In the legal field of the state, PPS determination is a guarantee of the normative functioning of social mechanisms for providing vital functions to vulnerable groups of the population. In the context of incurable, severe illness (state), it refers to the quality of life, survival of the patient and, in general, the conformity of the humanistic standards of Ukrainian society to civilization standards.

Palliative patient status definition remains without an adequate response, especially when PC is not finally institutionalized as an integral part of both clinical practice and the collective consciousness of Ukrainian society and requires further professional discussion.

References:

1. VOZ (2015). Palliativnaja medicinskaja pomoshh'. Informacionnyj bjulleten' ¹ 402. [Palliative care. Newsletter No. 402]. Available at: https://goo.gl/8VprDq

2. Gerasimenko N. (2017). Organizacija palliativnoj pomoshhi v stranah SNG. [Organization of palliative care in the CIS countries]. Available at: https://goo.gl/55Vraa

3. Cancer control: knowledge into action : WHO guide for effective programmes ; module 5. WHO Library Cataloguing-in-Publication Data. Available at: http://goo.gl/9DzSIJ

4. Radbruch L. & Payne S. (2009). White paper on standards and norms for hospice and palliative care in Europe part 1. In : European Journal of Palliative Care. 16, 6, p. 278–289.

5. Nakaz MOZ ¹ 368 (2007). Pro zatverdzhennja Kl³n³chnogo protokolu nadannja pal³ativno¿ dopomogi, simptomatichno¿ ta patogenetichno¿ terap³¿ hvorim na V²L-³nfekc³ju/SN²D. [On Approving the Clinical Protocol for the Provision of Palliative Care, Symptomatic and Pathogenetic Therapy for HIV / AIDS Patients]. Elektronnij dokument / Rezhim dostupu: https://goo.gl/Tqt5ik

6. Human Rights Watch (2011). Uncontrolled Pain Ukraine's Obligation to Ensure Evidence-Based Palliative Care. Available at: https://goo.gl/TmuRMA

7. Nakaz MOZ Ukra¿ni ¹ 420 (2011). Pro zatverdzhennja Metodichnih rekomendac³j shhodo rozrahunku potrebi naselennja u medichn³j dopomoz³. [On Approval of Methodological Recommendations on Calculation of the Population's Need for Medical Aid]. Elektronnij resurs / Rezhim dostupu: http://goo.gl/PI63yB

8. WHO (2017). Programmes. Disabilities and rehabilitation. Available at:http://www.wpro.who.int/rehabilitation/en/

9. Pres-sluzhba "Shhotizhnevika APTEKA" (2016). Nedostupn³st' adekvatnogo znebolennja: l³kar³ ³gnorujut' nov³ vimogi zakonodavstva. [Inaccessibility of adequate anesthesia: doctors ignore the new requirements of the law]. Elektronnij dokument / Rezhim dostupu: https://www.apteka.ua/article/396502

10. The Association for the Prevention of Torture (APT) (2016). Putting prevention into practice. 10 years on: the Optional Protocol to the UN Convention against Torture. Available at:https://goo.gl/9tcSQL

11. Scholten N. et al. (2016). The size of the population potentially in need of palliative care in Germany – an estimation based on death registration data. BMC Palliative Care, ð. 15–29. Available at:https://goo.gl/NRHtgf

12. Guz³j O.V. (2017). Pac³ºntor³ºntovana statistika ta pal³ativna dopomoga v Ukra¿n³. [Patient-oriented statistics and palliative care in Ukraine]. Redakc³ja zhurnalu "Ukra¿ns'kij medichnij chasopis", 4 (120), pp. 6–7.

13. Nakaz MOZ ¹ 41 (2013). Pro organ³zac³ju pal³ativno¿dopomogi v Ukra¿n³. [About the organization of palliative care in Ukraine]. Elektronij resurs / Rezhim dostupu: http://zakon3.rada. gov.ua/laws/show/z0229–13

14. Stinson J, Nasser B. (2003). Pain management in children with sickle cell disease. Pediatric Drugs, 5, pp. 229–241.

15. Hofman M. et al. (2007). Posttraumatic stress disorder in children affected by sickle-cell disease and their parents. American Journal of Hematology, 82, pp. 171–172.

16. Hain et al. (2013). Paediatric palliative care: development and pilot study of a 'Directory' of life-limiting conditions. BMC Palliative Care, 12, p. 43.

17. Kelly Nicole Michelson and David M. Steinhorn (2007). Pediatric End-of-Life Issues and Palliative Care. Clin Pediatr Emerg Med, 8(3), pp. 212–219.

18. Il'ichjov L. F., Fedoseev P. N., Kovaljov S. M., Panov V. G. (1983). Filosofskij jenciklopedicheskij slovar'. [Philosophical Encyclopedic Dictionary]. M.: Sovetskaja jenciklopedija. Elektronnij dokument / Rezhim dostupu: https://goo.gl/YffG6n

19. Shemshuchenka Ju. S. (2007). Velikij enciklopedichnij juridichnij slovnik: slovar'. [Great encyclopedic legal dictionary: dictionary]. K.: Jurid. dumka, 992 s. Elektronnij dokument / Rezhim dostupu: https://goo.gl/NTbXKh

20. O'Malley P. (2006). American Academy of Pediatrics Committee on Pediatric Emergency Medicine. Patient- and family-centered care and the role of the emergency physician providing care to a child in the cmergency department. Pediatrics,118 (5), pp. 2242–2246.

21. Weaver M.S., Heinze K.E., Bell C.J., Wiener L. (2016). Establishing psychosocial palliative care standards for children and adolescents with cancer and their families: An integrative review. Palliat Med., 30(3), pp. 212–223.

22. On³shhenko O.V., Soroka G.M. (2012). Kol³z³¿ reguljuvannja okremih prav pac³ºnta pri nadann³ medichno¿ dopomogi. [The collisions of regulation of individual rights of the patient in the provision of medical care]. Juridichnij v³snik 2 (23), pp. 90–93.

23. WHO Definition of Palliative Care. Available at: http://www.who.int/cancer/palliative/definition/en/

24. Nakaz MOZ ¹ 41 (2013). Pro organ³zac³ju pal³ativno¿dopomogi v Ukra¿n³. [About the organization of palliative care in Ukraine]. Elektronij resurs / Rezhim dostupu: http://zakon3.rada. gov.ua/laws/show/z0229–13

25. Connor S. and Bermedo M. (2014). Global Atlas of Palliative Care at the End of Life. Worldwide Palliative Care Alliance Edited. Available at: https://goo.gl/rxID0t

26. Zhogno Ju. P., B³rjukov V. S. (2017). Oc³nka potreb naselennja Odes'ko¿ oblast³ v pal³ativn³j dopomoz³. [Assessment of the needs of the population of the Odessa region in palliative care]. Anal³tichna dov³dka za rezul'tatami dosl³dzhennja. Odesa: TOV "²NVAC", 112 s. Elektronnij resurs / Rezhim dostupu: https://goo.gl/Q5A4au

AN ASSOCIATION BETWEEN PALLIATIVE MEDICINE AND EDUCATIONAL PROCESS IN KHARKIV

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The article presents the experience of the Kharkov Regional Medical College for the training of nurses and social workers in the field of basic concepts of palliative care. Aspects of motivation to acquire knowledge and skills of dealing with incurable patients are presented. The issues of cooperation of the Kharkov regional medical college with the German delegation of the European project on pediatric palliative care considered. It's shown qualitative palliative care dependency on the level of professional competence. The problems of psychological support of the staff, which provides the palliative care, are revealed.

Key words: incurable patient, psychological help, training of social workers.

> *"Do not leave me!*
> *Listen to me!*
> *Help me!"*
> *Cecily Saunders*

In one of the most important documents of the modern medical ethic, namely "Lisbon's declaration of patient's rights" of The International Medical Association, the "the patient's right to death with honor" is formulated quite clear and has a very deep international sense [4].

The process of population aging in Ukraine and Europe leads to changes in the structure of morbidity and death rate. The number of people dying from different types of somatic diseases becomes greater and this is accompanied by different physical and mental diseases [2, 6].

Besides, a very limited access to effective anesthetizing and lack of necessary medical sources and the low accessibility of palliative institutions in the combination with lack of qualified experts and practical impossibility to attract non-state organizations to the situation – all these factors result in the absence of adequate timely medical assistance. This stipulated the expedience of studying the development of palliative and hospice help in Ukraine and the role of the medical staff in caring for hospice patients [1].

The term "palliative therapy" comes from the Latin word "pallium" which means "the woolen coat" and implies a possibility to eliminate the suffering of the patient at the final stage of the illness. It also means to supply the patient with the necessary help. Palliative help prevents from the absence of help to the person who suffers but does not complain or to a person on the stage of incurable disease without a chance to recover. Palliative treatment has the idea not to relieve pain in one particular area but to give the patient the opportunity to feel that he is not alone in this world and surround him with help and understanding until the last moments of his life. The goal of palliative medicine is not to prolong or shorten life, it serves to the natural process of the existence and the end of the individual's life [3, 5, 7].

The doctors and nurses of Kharkiv and Kharkiv region had a unique opportunity to take part in the project, and also share the achievements and problems, meet some friends among German colleges, exchange the experience of transportation of seriously ill patients (being at different stages of illness and in different condition).

There were several master-classes, where the chief methods of biomechanics were demonstrated. We received valuable knowledge,

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learnt how to look after critically ill people, people with trophic ulcers, and how to work with such complication as hypostatic pneumonia. The scientific-practical conference was held at Kharkiv City Multispecialty Hospital No.17 to exchange knowledge on providing palliative care to seriously ill patients.

The doctors and nurses of Hospital No.17 and teachers and students of Kharkiv Medical College No.2 attended the conference.

The students of the medical college had special practical training for mastering different methods of caring after seriously ill patients.

The students were shown the methods, how to transport such patients according to the rules of biomechanics: moving the patient from chair to chair, or moving the sitting patient from the couch to the moving armchair.

The conference was held just in time in order not only to exchange and extend knowledge between the staff of hospices and clinics, but also to help medical educational establishments of the first and second accreditation level.

In March with support from the Coordination Committee for Palliative and Hospice Medicine in our city, Kharkiv Medical College started to train social workers from the territory centers of the residential service.

The working program of education includes 88 hours for three months course. The program incorporates chapters of practical classes from human anatomy, and care about patients as well as medical procedures involving safe transportation of seriously ill people, assistance in observing personal hygiene, prophylaxis of trophic ulcers, patient`s feeding, assistance in dysfunction of physiological needs, etc. We consider that the classes incorporating communication with such type of ill people would be very helpful.

Kharkiv Medical College pays particular attention to the work with incurable patients while training groups of people and working with such patients.

Hereafter the programs will imply teaching social workers to understand correctly all the needs of the patient and will be enable them to make their urgent decision, if necessary. In addition, it will help to work with the patient's relatives.

The quality of palliative treatment greatly depends on the level of qualification of the social workers as they perform both physically and psychologically difficult work. Not all the medical staff members are able to cope with this work. Nurses have a specific role in hospice and palliative treatment. That is why it is equally important not only to train the staff members professionally, but also to prepare them psychologically [4, 8].

References:

1. The state and perspectives of the palliative help development. To oncological patients-G.N. Novikov, V.I. Ishizov, B.M. Prokhorov and others 'Palliative medicine and rehabilitation' 2005 ¹ 2 p. 6–8

2. Voronenko Yu. U. The palliative help us integral. The part of the medical care reform .The urgent questions to give palliative help in Ukraine. Law-medical and pharmacological aspects. The materials of the All-Ukrainian Conferense 20-21. 11. 2013 (edit by Voronenko, Gruleskiy, Talkom p. 49–62.

3. Goyda N.G. Family medicine the fundamental in the health case reform in Ukraine. The Art of treatment. The journal of the modern doctor. 2013 ¹ 7.p. 16

4. Gubsky, Yu.I. Optimization of medical and social assistance to the elderly in Ukraine through the development of the service palliative and hospice care [Text] / Yu. I. Gubsky, AV Tsarenko, V. V. Tchaikovsky, O. M. Kollyakova // Problems aging and longevity. – 2010. – Vol. 10, No. 3. – P. 310.

5. Prague Charter "Obtaining Palliative Care – Human Right" [Text]. – EAPD, 2013.

6. About the organization of palliative care in Ukraine [Text]. – Ministry of Health of Ukraine, 2013. – ¹ 41. – Mode of access: http: //moz.gov.ua/ua/portal/dn_20130121_0041.html

7. 19-th Model List of Essential Medicines [Electronic resource]. – WHO, 2015. – Available at: http://www.who.int/ medicines/publications/essentialmedicines/EML2015_8-May-15.pdf

8. Strengthening of palliative care as a component of integrated treatment with in the continuum of care [Electronic resource]. – The Resolution of the 67-th World Health Assembly. WHO. World Health Assembly, 2014. – Available at: http://apps.who.int/gb/ebwha/pdf_files/EB134/B134_R7-en.pdf

NUTRITIONAL SUPPORT OF PALLIATIVE CHILDREN WITH SERIOUS NUTRITION DEFICIT

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Children with severe injury of nervous system compose high risk group on nutrition deficit. The purpose of the study is to assess the degree of nutrition deficit, calculate its actual requirement in enteric substrate and organization of adequate feeding. Indices of Broke 2, Pine, Z-score were used for determination of nutrition insufficiency degree. Physiological and actual requirements were defined by Schofield (WÍ) equation. Broke 2 index accounted for 40 %, BWI – 9.18, Z-score for BW on age – "-"6, for height on age – "-"12, for BW on height – "-3.5", which attested about extreme degree of nutritive insufficient (cachexia) and significant delay in physical development. High requirements in energy and low tolerance for necessary volume of feeding determine the administration of specialized isocaloric clinical product. **Conclusion.** Employment of simple standardized indices allows to determine the degree of nutrition deficit in palliative children. The definition of actual, instead physiological, requirements and administration of special clinical products permits to provide adequate nutrition in spite of low tolerance for high volume of feeding.

Keywords: children, palliative care, nutrition's deficit, clinical feeding, polymeric enteral products.

Introduction. The development of medical technologies and an increase in survival rate of children with critical anomalies or illnesses during recent years have led to an increase in the proportion of children who are in need of a complete palliative care system, including a range of nutritional support. It is this category of children where a high incidence of nutritional deficiency is observed, whereas malnutrition of alimentary origin among other children's population, changes its structure and decreases its frequency [1].

Due to the presence of severe chronic diseases that contribute to the inappropriate delivery of substratum substances, and cause an increase in the needs of certain constituents of the enteric substrate depending on the type of pathological condition in the child, significant quantitative and qualitative deficiencies of nutrients in such children can be expected. Insufficiency of feeding and its imbalance in children of the palliative group leads to changes in body composition, which is determined by the total content of fat and lean mass (muscle, visceral structures, bone tissue) [2, 3]. Determination of the body composition component is a complex and expensive method for assessing nutrition that requires certain equipment and staff and is not usually performed in clinical practice.

Close attention to the insufficiency of feeding and nutritional deficiency is due to the development of stress in each functional system of the organism, triggering an increase in cortisol production and augmentation in the correlation of cortisol/insulin [4]. The intensification of catabolism under these conditions is deepened by a decrease in synthesis of growth factors and hormones of the thyroid gland. The main priority of the body is the provision of a substrate (glucose) into the brain tissue which causes starvation of other tissues, impaired insulin-dependent tissue growth, weight loss and deceleration of linear growth, deep disorders of the function of organs and systems, immunity. Severe malnutrition leads to a decrease in the rate of physical development, physiometric disorders, thus much more

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complicating the intake of the disease and affecting functional systems of the body [2, 4, 5].

A separate problem is the provision of necessary nutrients to orphans at child welfare institutions. Lack of nutritionists, adequate financing of the costs on the corresponding food substrates, insufficiency of staff of the facilities of orphanages causes a high frequency of severe forms of nutritional deficiency in children not only of the palliative group, but also of those with uncritical chronic somatic morbidity.

Particular group is assembled of children with pathology, which leads to severe damage of nervous system. Disturbances in nutrition in mentioned above children are combined, both due to the nutritional factor, and as a result of violation of the assimilation of macro- and micronutrients and the increased need for them [6, 7]. The term malnutrition is used to characterize the nutritional status of such children, which is wider than protein-energy deficiency.

The assessment of the child's nutrition and calculation of his needs, taking into account the lack of growth, is the key to the organization of nutrition for palliative children [8, 9]. Most common methods of diet calculation or a simple "empirical" approach (will eat or not, will tolerate or not) cannot be the basis for the organization of catering for children with diseases of the nervous system, although, unfortunately, is the reality of most orphanages.

The aim of the study is the evaluation of the degree of nutritive deficiency in palliative group children, calculation of necessary enteric substrates and organization of catering.

The study was approved by the human research ethics committees of the participating hospitals, and informed consent was obtained for infants. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Materials and methods. The study involved the employment of anthropometric method of diagnosing the degree of protein-energy insufficiency with the definition of the percentage of body weight deficiency, indices of physical development in children with severe congenital pathology.

Several indices recommended by the WHO for physical growth were used to determine the degree of nutritional deficiency [3, 4]. Brock 2 index is the determination of the degree of hypotrophy or obesity as a percentage relative to the average values in the population according to the formula 100 x MT (kg) / M (kg), where MT is the child's body weight, M is the average body weight of children of the corresponding sex and age. The Piney Index is an index of proportionality between the indices, which is determined by the formula P – (O + M), where P is height, M is the body weight, O is the circumference of the chest, the fluctuations around 20 are normal values. The assessment of the physical development indices for the Z-score, which is accepted as the most accurate by using the median of the reference population, and is calculated by the following formula: individual value – median value / value of the average reference population, is the most commonly used. Recent years working groups of the WHO nutrition experts recommended using the body mass index (BMI) or Kettle index, which is determined by the formula: body weight (kg) / height (m) in the square. The standard value of the BMI is 19.5 – 22.9 kg/m2).

Apart from calculation of indices of physical development we evaluated clinical signs of nutritional deficiency.

The second phase of the child's examination was to determine the actual energy and protein consumption, and calculate the energy requirements of the WHO, Schofield (W) and Schofield (WN) equations [4,10]. We also calculated the child's physiological needs and actual needs according to additional correction coefficients: factor of activity, thermal factor, body weight deficit, factor of damage. The calculation of basal metabolism was adjusted according to the introduced coefficients [5].

The next step was to identify food and to develop a plan for administering the enteric substrate to monitor food tolerance, clinical signs and anthropometric indices, as well as working out recommendations for the child after discharge from the hospital.

Results and its discussion.

A boy I., at the age of 1 year 2 months weighs 4 kg, height 66 cm, entered the hospital from an orphanage due to acute lower respiratory tract disease secondary to chronic aspiration syndrome. A child was born preterm at 36 weeks, with body weight of 1920 g, height of 46 cm, with asymmetric form of the 3rd degree intrauterine growth retardation syndrome with multiple congenital malformations of the bone and muscular system. At present, the main diagnosis of the child is microcephaly, spastic tetraparesis, Larsen syndrome, neurotrophic syndrome. At the age of 4.5 months he entered the orphanage. From the 5th month of life up to the present condition he had six cases of acute respiratory infection (ARI) with complicated intake. He is fed every two hours through a catheter, a semi-customized milk formula with conventional feed additives appropriate for his age. He tolerates small capacity of food, up to 60–80 ml. Between feedings the child is not calm, periodically cries. The sleep is not deep, with the changed formula, difficulty in falling asleep. An increase in body weight over the last six months is 250 g.

Establishment of the degree of body weight and height deficiency. The assessment of the child's physical development was difficult due to the extremely small body weight (more than 4 δ) and large deformations of the joints and bones that influenced the accuracy of the measurement of growth and required segment measurement, taking into account combined muscle contractions and spasticity [11].

Brock 2 index was 40 %, BMI 9.18. The Z-score for body weight for the age representing acute nutritional deficiency was "-" 6, a Z-score for the growth for the age that indicated long-term growth retardation secondary to chronic nutritional deficiency, was "-" 12. The Z-score for body weight on body length, evaluating the harmony of the child's development, and proving acute fasting, was "-3.5". The obtained data confirmed extreme degree of nutritional insufficiency (cachexia) and a significant retardation in physical development.

Despite the apparent nutritional deficiency, the Piney index was 19, thus indicating proportionality between the growth rates, the body weight and the circumference of his chest. That is, with a symmetric delay in all indices of physical development, the assessment may be normotrophy, while the child has a severe form of malnutrition.

That is why the child had criteria for the diagnosis of severe chronic protein-energy deficiency (ICD-10 – E43) in the form of extreme expression of the main syndromes: trophic disorders, edema disorders, dysfunction of the nervous system and a decrease in immunological reactivity.

Calculation of real energy and protein intake. The child received 60 ml every two hours with a break at night during the day10 times a day, which is 600 ml per day. Composition of the enteral substrate: 20 ml of anti-reflux formula and 40 ml of the usual milk formula, during the illness the addition of vegetables and cereals was not provided due to a marked decrease in tolerance. The actual intake of energy at a dose of 600 ml/day was 100.5 kcal/kg, protein – 2.2 g/kg/day.

Calculation of physiological and actual needs of the child in energy and protein according to the degree of nutritional deficiency 4,12 . It should be noted that calculation of physiological needs should be based on the weight loss and certain states that increase energy costs and it is necessary to apply basic coefficients of the amendments.

The basic energy requirement in all age groups increases because of inflammation, fever, chronic cardio-pulmonary disease 4,5 . For children with severe nutritional deficiencies, the calculation of the initial needs is based on the ideal body weight and height that corresponds to 50 ‰ per child's actual age [2, 3, 8, 12]. This approach is recommended by leading nutrition committees to achieve catch-up growth.

Different equations are used to determine basic needs in energy of infants, such as the WHO, Schofield (W) and Schofield (WN) equations. Calculation of the physiological energy requirement according to the WHO recommendations for the examined child is 189.6 kcal/day, Schofield (W) – 207.59 kcal/day, Schofield (WN) – 384.55 kcal/day. This difference is due to different approaches to data computation, taking into account the presence of additional factors that increase the outgoes of energy and protein. That is why it is considered that the Schofield (WN) equation is most appropriate in determining the energy needs of infants with the presence of pathological conditions.

The evaluation of energy expenditure of this patient revealed that the actual needs, taking into account all coefficients, were 460.92 kcal/day (115.23 kcal/kg/day), and were based on the actual body weight, and not on the ideal one. Calculating energy needs for an ideal body weight gives much higher index – up to 140-150 kcal/kg. However, considering the impossibility of a sharp load and an increase in feed volume, the energy demand was estimated at 115 kcal/kg during the adaptation period.

According to ESPHGAN recommendations, protein needs for children with neurological pathology are similar to healthy children [2] . Exclusions are children with bedsores. The additional administration of protein due to high protein metabolism in enteric nutrition can be reviewed in case of reduced level of albumin in serum and urea, combined with high levels of cognitive impairment.

High protein intake in children with severe nutritional deficiencies can have a negative effect on the function of kidneys and organs of the digestive tract. As a result, the needs in protein for children are set at 1.2–1.5 g/kg per day. The actual intake of high quantity of protein is due to the extremely low body weight of the baby and does not require additional correction. For the examined patient, the protein requirement is 6 g per day, in recount on the real body weight and 12–15 g per day for the ideal body weight.

After determining the real energy loss, the main issue for children with severe diseases of the nervous system, especially in combination with another congenital somatic pathology, is to determine the way to increase the energy supply capacity. Most of these children have major problems with the feeding process itself (decreased capacity of the gastrointestinal tract, intolerance to large volumes of food, lack of oromotoric skills, etc.). For one-year-old children the only solution is the enrichment of breast milk or the use of special formulas. In the world's practice it is common to administer one-year-old patients special products of clinical nutrition with a low risk of overloading fluid, electrolytes, having the ability to accurately calculate caloric intake and dosage 13 .

Since ESPGHAN recommendations for high nutritional deficit and reduced tolerance to high levels of food recommended the introduction of a high-calorie polymer substrate (1,0 kcal/ml) [2], it was decided to add the product of clinical nutrition Infatrini (composition on 100 ml: proteins – 2.6 g, fats – 5.4 g, carbohydrates – 10.3 g), which corresponded to these requirements.

The calculation of needs in relation to the real child's weight is carried out at the beginning of the adjustment of feeding during a certain period of adaptation 4,14 . When the positive effect and evaluation of the product's tolerance are received, the recount of needs is performed according to the ideal body weight. Abrupt initial hyperalimentation may worsen the state of a child 14 .

Regular assessment of the needs of the child depending on the time course of the body weight and the correction of the enteric substrate composition depending on the period of the outlet from the state of nutritional deficiency (adaptation, reparation, enhanced nutrition) is an extremely important stage in the organization of nutrition. Except taking into account the results of the assessment and calculation of data on the physical development of a child, clinical examination should be conducted in children with implementation of nutritional adequacy and specific signs of insufficiency of the individual components of food.

Children with a severe degree of protein-energy deficiency have the greatest risk during the first week since the start of the adaptation period in feeding. Initial enteric feeding for infants with severe nutritional deficiencies (BMI less than 16 kg/m^2, body weight loss more than 15%) begin with 75% of the needs in the nutrients 4,14 . In case of good tolerance the initial adaptation period can be reduced to 5–7 days. Small volumes of enteric isocaloric nutrition help avoiding fluid loading.

During five days of life, the gradual replacement of the enteric substrate with a product of clinical nutrition was provided. At the end of the week, the child assimilated 70 ml of food, of which: 20 ml of anti-reflux formula, 50 ml Infatrini. The reception mode was left as the previous one, namely 10 times a day. Thus, 480 kcal/day (120 kcal/kg/day), 16.2 g per day protein was hold in the volume of the enteric substrate, which the child tolerated well. Checking the residual stomach contents in the child indicated lack of residual volume. The child less vomited which suggested the possibility of a progressive increase in volumes of bolus nutrition.

During 10 days of specialized nutrition administration the child increased body weight by 100 g. After 5 days of receiving an adjusted nutrition, the child became calmer, for a long time he could observe the staff or toys, showed interest in environment, sleep duration increased after feeding. The child was discharged from the hospital and returned to the orphanage with further recommendations in accordance with the rates of increase in volume and changes in the composition of the enteric nutrition.

Recommendations for the organization of further nutritional support included the maintenance of a high level of energy supply during the reparation period (120 kcal/kg/day) with the progressive transfer of energy needs for the ideal body weight. In future, the child will have to undergo a long period of intense feeding with a possible increase in energy intake to 130-145 kcal/kg/day, introduction of other food products (vegetables, cereals and fruits), an increase in the single volume of food.

The way and methods of administration of the enteric substrate are also crucial aspect of the organization of feeding for the examined child. Dangerous swallowing with constant aspiration pneumonia requires adjustment of gastrostoma, administration of proton pump inhibitors and active speech therapy with sensomotor therapy for the improvement of the function of the orofacial zone.

Conclusions. Children of the palliative group have a high risk of nutritional deficiency, both of alimentary nature and due to insufficient digestive problems. Deep protein-energy insufficiency in children with combined neurosomatic pathology can be corrected by carefully calculating the actual energy and protein needs and the appointment of specialized clinical nutrition (1 kcal/ml). Infants of the palliative group, deprived of parental care and who are in orphanage, have the greatest risk of developing nutritional deficits.

Lack of a standardized approach to feeding such children, lack of qualified staff and insufficient financial support have extremely negative effects on the course of the disease, leading to even greater delay in the development and progression of pathology.

Employment of standardized indices of physical development to determine the degree of protein-energy deficiency and formulas for establishing energy needs in the practice of nutritional support for children of the palliative group can contribute to adequate nutrition.

Specialized products for clinical nutrition (isocaloric or high-caloric) can maintain nutritional needs of the child and help overcome such problem as reduced tolerance to the required amounts of food.

References

1. Prieto, M.B., Cid, J.L.H. (2011). Malnutrition in the Critically Ill Child: The Importance of Enteral Nutrition. Int. J. Environ. Res. Public Health, 8, 4353-4366; doi:10.3390/ijerph8114353
2. Romano, C., van Wynckel, M., Hulst, J., Broekaert, I., Bronsky, J., Dall'Oglio, L., … Gottrand, F. Mis, N.F.,… Gottrand, F. (2017). ESPGHÀN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Neurological Impairment. JPGN, 65, 242–264. doi: 10.1097/MPG.0000000000001646.
3. WHO child growth standards and the identification of severe acute malnutrition in infants and children. World Health Organization, United Nations Children's Fund, 2009.-11ð. www.who.int/childgrowth/standards/en/
4. Nazarenko, O.N., Yurchik, K.V., Dmitrachkov, V.V. (2015). Diagnostika i korrektsiya belkovo-energeticheskoy nedostatochnosti i narusheniy trofologicheskogo statusa u detey: Uchebno-metod. Posobie [Diagnosis and correction of protein-energy deficiency and violations of trophic status in children: Educational method. Allowance]. Minsk:BGMU, 2015. 54 s. (in Russian)
5. Botrán, M., López-Herce, J., Mencía, S., Urbano, J., Solana, M.J., García, A., Carrillo, A. (2011). Relationship between energy expenditure, nutritional status and clinical severity before starting enteral nutrition in critically ill children. Br J Nutr,105(5), 731–737. doi: 10.1017/S0007114510004162
6. Andrew, M.J., Parr, J.R., Sullivan, P.B. (2012). Feeding difficulties in children with cerebral palsy. Arch Dis Child Educ Pract Ed,97, 222–229 doi: 10.1136/archdischild-2011-300914.
7. Kuperminc, M.N., Gottrand, F., Samson-Fang, L., Arvedson, J., Bell, K., Craig, G.M., Sullivan, PB. (2013). Nutritional management of children with cerebral palsy: a practical guide. Eur J Clin Nutr,67(2), 21–23. doi: 10.1038/ejcn.2013.227.
8. Bell, K.L., Samson-Fang, L. (2013). Nutritional management of children with cerebral palsy.Eur J Clin Nutr,67(2), 13–16. doi:10.1038/ejcn.2013.227.
9. Samson-Fang, L., Bell, K.L. (2013). Assessment of growth and nutrition in children with cerebral palsy. Eur J Clin Nutr,67(2), 5–8. doi: 10.1038/ejcn.2013.223.
10. Kolacek, S. (2013). Enteral nutrition. World Rev. Nutr. Diet.,108,86–90. doi: 10.1159/000351490
11. Haapala, H., Peterson, M.D., Daunter, A., Hurvitz, E.A. (2015). Agreement between actual height and estimated height using segmental limb lengths for individuals with cerebral palsy. Am J Phys Med Rehabil,94,539–546. doi: 10.1097/PHM.0000000000000205.
12. Braegger, C., Decsi, T., Dias, J.A., Hartman, C., Kolacek, S., Koletzko, B., … van Goudoever J. (2010). Practical Approach to Paediatric Enteral Nutrition: A Comment by the ESPGHAN Committee on Nutrition. JPGN,51(1),110–122. doi:10.1097/MPG.0b013e3181d336d2
13. Cederholm T., R. Barazzoni, P. Austin, P. Ballmer, G. Biolo, S.C. Bischoff, C. Compher, … P. Singer (2017). ESPEN guidelines on definitions and terminology of clinical nutrition. Clinical Nutrition,36,49–64. doi.org/10.1016/j.clnu.2016.09.004
14. Hamilton, S., Mcaleer, D.M., Ariagno, K., Barrett, M., Stenquist, N., Duggan, C.P., ... Mehta, N.M.(2014). A stepwise enteral nutrition algorithm for`1 critically ill children helps achieve nutrient delivery goals. Pediatr. crit. care Med,15(7),583–589. doi:10.1097/PCC. 0000000000000179.

CYSTIC FIBROSIS RELATED DIABETES: CLINICAL CASES IN TERMS OF PRINCIPLES OF PEDIATRIC PALLIATIVE CARE

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Cystic fibrosis related diabetes (CFRD) – is the most common comorbidity in people with cystic fibrosis , occurring in 20% of adolescents and 40–50% of adults. According to the Guidetothe Development of Children's Palliative Care Services life-limiting conditions may be delineated at four broad groups. Cystic fibrosis is a problem from group 2 – conditions where there may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal childhood activities, but premature death is still possible.

Basic aspects of CFRD were discussed, such as cause of the disease, genetic defects, differential diagnosis and principles of treatment. Two clinical cases of pediatric CFRD patients resented to highlight problems of management in terms of potential palliative care. According to our observations, patients with the CFRD, unfortunately, are perceived as patients with cystic fibrosis with no clear attention to diabetes. Both of them were presented with pure diabetes control due to unclear understanding CFRD with concomitant diet incompliance, irregular records, missed insulin injections, exercising limitations.

We concluded that CFRD patients must be assessed by members of multidisciplinary team at CF centers, working by the principle of palliative care. There is necessary since the moment of CF diagnosing to involve endocrinologist and dietician due to of endocrine problems. Psychologist, social worker and well-trained educators are necessary to increase awareness of the CF comorbidities problem.

Key words: Cystic fibrosis, cystic fibrosis related diabetes, pediatric palliative care, multidisciplinary team.

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual (WHO, 1998) [1].

Palliative care for children and young adults, defined as the "active, total care" of a young person's body, mind, spirit, and family, from life-limiting diagnosis until death, is an internationally recognized priority [2].

There is a limited access to the pediatric palliative care in low- and middle-income countries [3]. It's clear as the growing demand for palliative care, coupled with financial constraints, demands a sustainable public health approach. That's why WHO emphasis that palliative care is a component of integrated treatment throughout the life course and demand a hierarchical approach to structure of relevant healthcare service with multidisciplinary management [4]. In this way, the first book in pediatric palliative care for doctors and other trainees published in Ukraine looks as a serious progress in the field [5].

Life-limiting conditions may be delineated at four broad groups [6]:

- Group 1. Life-threatening conditions for which curative treatment may be feasible but can fail. Palliative care may be necessary during periods of prognostic uncertainty and when treatment fails. Children in long-term remission

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or following successful curative treatment are not included. Examples include cancer, irreversible organ failure of heart, liver, or kidney.

- Group 2. Conditions where there may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal childhood activities, but premature death is still possible. Examples include cystic fibrosis and muscular dystrophy.
- Group 3. Progressive conditions without curative treatment options, for which treatment is exclusively palliative and commonly may extend over many years. Examples include Batten's disease and the mucopolysaccharidoses.
- Group 4. Conditions with severe neurological disability, which may cause weakness and susceptibility to health complications, and may deteriorate unpredictably, but are not usually considered progressive. Examples include severe multiple disabilities such as those that can follow brain or spinal cord injuries (including some children with severe cerebral palsy).

Cystic Fibrosis (CF) ICD-10: E84.0, E84.1, E84.8, E84.9; ORPHA: 586; OMIM: 219700 – is the most common genetic disorder among Caucasian children. The incidence varies between populations: the condition is considerably less common in Asian and African populations than in the white populations of Europe and North America, with variation within each country. The exact prevalence in Europe is unknown, but estimates range between 1/8,000 and 1/10,000 individuals.

CF is characterized by alterations in the CFTR protein, which plays a role in the regulation of transmembrane hydro electrolytic flux. Alterations in the protein lead to changes in the characteristics of exocrine excretions. An absence of functional CFTR in the epithelial cell membrane leads to the production of sweat with a high salt content (associated with a risk of hyponatremic dehydration) and mucus secretions with an abnormal viscosity (leading to stasis, obstruction and bronchial infection). Cystic fibrosis is a monogenic autosomal recessive disease caused by mutations in the CFTR gene (chromosome 7). More than 1250 mutations have been reported. Nearly 70% of all cases are caused by the delta F508 allele, with 30 other mutations accounting for a further 20% of cases. There is no clear correlation between genotype and phenotype. In addition to the allelic heterogeneity and the occurrence of multiple mutations in the same gene, a wide range of other factors may influence the phenotype, including the environment and disease modifying genes [7].

Certain CFTR genotypes that cause complete lack of protein function, such as delF508 (also referred to as F508del, p.Phe508del, or c.1521_1523delCTT), carry a much higher risk of pancreatic problems than do genotypes that partially spare protein function [8, 9].

Cystic fibrosis related diabetes (CFRD) – is the most common comorbidity in people with cystic fibrosis (CF), occurring in ~20% of adolescents and 40–50% of adults [10].

The primary cause is a relative insulin deficiency related to destruction of pancreatic islets. Insulin resistance also may play a role, especially in association with acute exacerbations or chronic progression of pulmonary disease [11].

Defective CFTR function reduces the volume of pancreatic secretions, predisposing to plugging of small ducts, and increases acidity, promoting premature activation of digestive enzymes [12].

Abnormal glucose tolerance is notably prevalent among young children with cystic fibrosis. Children with cystic fibrosis lack the normal increase in insulin secretion that occurs in early childhood despite increased glucose. Thus, glycemic abnormalities begin very early in cystic fibrosis, possibly because of insufficient insulin secretion. [13].

Cystic fibrosis-related diabetes is a distinct form of diabetes mellitus that is an important complication of cystic fibrosis. It is different from either type 1 or type 2 diabetes mellitus, but shares features of both [14].

There are common features between CFRD and both type 1 and type 2 diabetes (*table 1*).

Since the cause of diabetes associated with CF is insulinopenia due to damage to the pancreatic tissue, the main method of treatment is replacement insulin therapy. The long-term use of beta-cell-stimulating drugs is still limited. Patients with CFRD are susceptible to early onset of chronic complications of diabetes, and therefore require appropriate regular follow-up [16]. On the other hand, better glycemic control is associated with better respiratory function and less common infections [17].

On the one hand, CFRD is a violation of carbohydrate metabolism, which requires compliance with diet, exercise and insulin replacement therapy. Dietary recommendations for CFRD include individualized based reginens [18]. On the other hand, CFRD is one of the symptoms of cystic fibrosis with a high risk of premature death due to the rapid progression of pulmonary dysfunction, which requires intensive long-term therapy. Thus, Patients need to comply

Table 1

Differential diagnosis of CFRD [15]

Characteristics	Type 1. Diabetes	Type 2. Diabetes	CFRD
Age of onset	Young	Predominantly in adults	Young
Onset	Acute	Gradual	Gradual
Islet antibodies	Present	Absent	Usually absent
Genetics	Multiple susceptibility alleles including HLA class II	Polygenic association with more than 20 gene variants	Most common in patients with homozygous Phe508del mutation of CFTR. Possible association with TNF, HSP60 and chaplain 10.
Insulin secretion	Eventually absent	Diminished	Gradual deterioration
Insulin sensitivity	Variably decreased	Severely diminished	Diminished (severely during acute exacerbations)
Propensity to ketoacidosis	No	Yes	No

with the diet, constant respiratory therapy and insulin injections.

Obviously, children with CFRD and their families need permanent social and psychological support. It's a reason for the creation of volunteer, parental and patients' organizations. Recent studies show that palliative care and intensive care do not exclude each other in CF patients.

We analyzed the medical records of two pediatric patientswith CFRD to highlight problems of management in terms of potential palliative care.

Clinical case # 1

The girl V., at the age of 3 weeks was diagnosed an acute pneumonia followed by several exacerbations for next months. After the examination, at the age of 8 months she was diagnosed with cystic fibrosis, pulmonary-intestinal form, severe course (genotype delF508).

The exacerbations occurred once a month, except for the summer months. At the age of 9 years, the child developed polydipsia, polyphagia, polyuria and CFRD was diagnosed. Basis-bolus regiment of Insulin treatment (Novo Rapid and Levemir) used to compensate hyperglycemia with an average dosage 1.07 U/kg/24h. Diabetes control was not satisfactory.

At the age 15 y.o. against the background of diabetes, number of CF exacerbations increased up to 8–10 times per year. Inflammatory process was more protracted with no response at massive antibacterial and enzymatic therapy. There was accelerated lung function deterioration – FEV1 decreased from 51 % to 30 % on spirometry [19], which is prognostically unfavorable for CF patients according to the literature as FEV1is a well-established predictor of survival in CF [20, 21].

Her physical development was disharmonious: weight – 38 kg, height – 146 cm (-2.3 SD), BMI – 17.82 kg/m^2 (15 percentile). Puberty – Tanner stage 1. Thus, girl presented with the short stature, underweight and delayed puberty. Fluctuations in blood glucose from 3.0 mmol/l to 20.0 mmol/l, HbA1 level – 8.6 %.

Clinical case # 2

The boy A was diagnosed with CF at the age 4 years. At the age 14 y.o. he was hospitalized to the ICU due to vomiting, thirst and polyuria, where CFRD was established when hyperglycemia with random blood glucose 17.9 mmol/l revealed.

After 6-month CFRD was diagnosed, he admitted clinic due to pneumonia with atelectasis. Portal hepatic fibrosis revealed as well. Diabetes control was not satisfactory due to problems with self-control. There were difficulties with diet and diary records. Fluctuations in blood glucose from 4.1 mmol/l to 21.1 mmol/l, HbA1 level – 8.9 %. Basis-bolus regiment of Insulin treatment (Actrapid and Protaphane) used to compensate hyperglycemia with an average dosage 0.92 U /kg/24h.

At the moment of admission his physical development was disharmonious: weight – 32.5 kg, height – 151 cm (-2.5 SD), BMI – 14.25 kg/m^2 (< 5 percentile). Puberty – Tanner stage 1. Asthenic body composition and clubbing fingers attracted attention during inspection (*fig. 1, 2*).

Patients had different course of CF and CFRD – patient #2 had later onset of CF and CFRD as well. In both cases, patients had delayed physical development (both short stature and underweight) and puberty. Both of them were presented with pure diabetes control due to common problems listed below:

- diet incompliance (wrong or absent calculation of bread units for carbs intake control; irregular records);
- insulin injections (which were missed time to time);
- exercising limitations due to impaired respiratory function;
- unclear understanding that DM is a serious complication of CF, which is an independently potentially life-threatening problem.

Figure 1. General appearance of 14 y.o. male patient with CFRD

Figure 2. Clubbing of fingers of 14 y.o. male patient with CFRD

Specific approach to management is recommended for CF and DM separately. So combination of respiratory therapy, insulin and diet are indicated for the patient with CFRD. Regardless of DM type, it is prognostically unfavorable for the complications. Thus, in patients with CFRD acute diabetic complications are associated with bad glucagon response to hypoglycemia [22]. They also have a brisk catecholamine response and normal hypoglycemia awareness. Meanwhile, severe hypoglycemia is less common in CF than in Type 1 diabetes [23]. Diabetic microvascular complications occur in CFRD, although the prevalence of retinopathy and nephropathy appears to be less than that found in other forms of diabetes [24].

According to our observations, patients with the CFRD, unfortunately, are perceived as patients with cystic fibrosis. There is a lack of a unified system of care for such children, which leads to difficulties in attracting the patient's family to work in the school of diabetes. As a consequence, these children do not adhere to the recommended diet, glycemic control, which affects the level of glycemic control and is especially aggravated by such factors as the restriction of physical activity.

Our data matches results of other researchers, who emphases on problems with patient and parent perceptions of the diagnosis and management of CFRD. Accessibility of the health care team is imperative for most patients. Patients valued that their health care team not only recognized how important it was for the CFRD regimen to fit into their lives, but also helped them come up with strategies to integrate it. It is important to find physicians who were knowledgeable about both CF and diabetes. According to the data, improvement in lung function associated with better diabetes control was motivating for patients [25].

There is no specific correction of nutritional status, growth and puberty for the CFRD. Meanwhile, endocrinologist and dietician are necessary members of multidisciplinary team as might early manage the named problems. Dietitians/nutritionists of the CF center are responsible for the recommendations and education of patients and their caregivers on the basic principles of diet in CF and CFRD. Some of them are: determining nutritional requirements and meeting these requirements at different stages of the disease, pancreatic enzyme replacement therapy, vitamin and mineral supplementation etc. Age-specific recommendations, plans for nutritional intervention and nutritional care, appropriate to the nutritional and clinical status, should be developed. Process of patients' education is a continuous and evolving process [26].

The same nutritionist should provide patient counseling both at the inpatient and outpatient stages of treatment to ensure continuity of care [27].

Conclusions

Complex of endocrine disorders aggravates the patient's quality of life, worsens the prognosis of the disease, leads to disability and is the basis for an additional increase in the number and duration of hospitalization.So endocrinologist, dietician must be a full members of CF management team since the moment of CF diagnosing. It is necessary because of risk of delaying physical development and puberty, as well as due to potential CRFD onset.

On the other hand, there are lot of psychological problems and social issues related to CFRD such as pure problem awareness of patients parents and, unfortunately, healthcare specialists. There is necessary to involve psychologist, social worker and well-trained educators into the team.

Thus, CFRD patients must be assessed by members of multidisciplinary team at CF centers, working by the principle of palliative care. Besides CFRD patients requires additional attention in the structure of palliative care of subjects with chronic diseases. Algorithm of specific multidisciplinary surveillance is a promising area of palliative service development in low- and middle income countries.

References

1. World Health Organization. WHO Definition of Palliative Care. Retrieved from: http://www.who.int/cancer/palliative/definition/en/

2. World Health Organization: WHO definition of palliative care. (2012). Retrieved from: www.who.int/cancer/palliative/definition/en/

3. Caruso Brown, A. E., Howard, S. C., Baker, J. N., Ribeiro, R. C., & Lam, C. G. (2014). Reported Availability and Gaps of Pediatric Palliative Care in Low- and Middle-Income Countries: A Systematic Review of Published Data. Journal of Palliative Medicine, 17(12), 1369–1383. Retrieved from: http://doi.org/10.1089/jpm.2014.0095

4. World Health Organization: Strengthening palliative care as a component of integrated treatment within the continuum of care. (2014). Retrieved from: http://apps.who.int/gb/ebwha/pdf_files/EB134/B134_R7-en.pdf (Last accessed February1, 2014)

5. Gonchar', M.O., Ryga, O. O., Pen'kov, A. Ju. (2016). Pryncypy nadannja paliatyvnoi' dopomogy ditjam . [Principles of Palliative Care for Children]. Harkiv: HNMU, 112, 18.

6. A Guide to the Development of Children's Palliative Care Services. Report of a Joint Working Party of the Association for Children with Life-threatening or Terminal Conditiona and their Families and the Royal College of Paediatrics and Child Health. (1997). Bristol-London.

7. Retrieved from: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=586

8. Kapranov, N.I., Kashirskaja, N. Ju., Petrova, N.V. (2004). Medicinskaja genetika""Mukoviscidoz. Dostizhenija i problemy na sovremennom jetape" [Medical genetics "" Mucoviscidosis: achievements of the problem at the present stage "Children]. Moskva: GUMGNCRAMN, ¹ 9., 398–412.

9. Marshall, B. C., Butler, S.M., Stoddard, M., Moran, A.M., Liou, T.G., Morgan, W.J., Pediatr, J. (2005). Epidemiology of cystic fibrosis-related diabetes. 146(5):681, 7.

10. Moran, A., Dunitz, J., Nathan, B., Saeed, A., Holme, B., Thomas, W. (2009). Cystic fibrosis-related diabetes: current trends in prevalence, incidence, and mortality. Diabetes Care, 32(9):1626, 31.

11. Moran, A., Brunzell, C., Cohen, R. C., et al. (2010). Clinical Care Guidelines for Cystic Fibrosis-Related Diabetes: A position statement of the American Diabetes Association and a clinical practice guideline of the Cystic Fibrosis Foundation, endorsed by the Pediatric Endocrine Society. Diabetes Care, 33(12):2697–2708. doi:10.2337/dc10-1768.

12. Ooi, C. Y., Durie, P.R. J. (2012). Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations in pancreatitis. Cyst Fibros, 11(5):355–62.

13. Yi,Y., Norris, A.W., Wang, K., et al. (2016). Abnormal Glucose Tolerance in Infants and Young Children with Cystic Fibrosis. American Journal of Respiratory and Critical Care Medicine, 194(8):974–980. doi:10.1164/rccm.201512-2518OC.

14. Classification and Diagnosis of Diabetes. American Diabetes Association.Diabetes Care. (2017).40(Suppl 1):S11–S24.

15. Rana, M., Munns, C.F., Selvadurai, H., Donaghue, K. C., Craig, M. E. (2010). Cystic fibrosis-related diabetes in children-gaps in the evidence? Nature Reviews Endocrinology , V.6, 371–378. doi:10.1038/nrendo.2010.85

16. Kerem, E., Conway, S., Elborn, S., Heijerman, H. (2005). Standarty terapii bol'nyh mukoviscidozom: Evropejskij consensus. [Standards of care for patients with cystic fibrosis: a European consensus]. For the Consensus Committee Department of Pediatrics and CF center, Mount Scopus, Jerusalem 91240, Israel Journal of ñystic fibrosis, 4 7–26

17. Belle-van, Meerkerk, G., de Valk, H. W., Stam-Slob, M.C., et al. (2016). Cystic Fibrosis-Related Diabetes with strict glycaemic control is not associated with frequent intravenous antibiotics use for pulmonary infections. Diabetes Res ClinPract, 116:230.

18. Moran, A., Brunzell, C., Cohen, R.C., Katz, M., Marshall, B. C., Onady, G., Slovis, B. (2010). Clinical Care Guidelines for Cystic Fibrosis-Related Diabetes. the CFRD Guidelines Committee. Diabetes Care, 33 (12) 2697–2708; DOI: 10.2337/dc10–1768.

19. Senatorova, G.S., Tel'nova, L.G., Chernenko, L.M., Dolgareva, S.B. (2017). [On the issue of the combined course of cystic fibrosis and diabetes in children]. Materiali naukovo-praktichnoji konferenciji "Aktual'ni pitannja fiziologiji, patologiji ta organizaciji medichnogo zabezpechennja ditej shkil'nogo viku ta pidlitkiv. Problemns pitannja komorbidnih staniv u ditej ta pidlitkiv". Harkiv.

20. Liou, T.G., Adler, F.R., Fitzsimmons, S.C., Cahill, B.C., Hibbs, J.R., Marshall, B.C. (2001). Predictive 5-year survivorship model of cystic fibrosis. Am J Epidemiol. 153: 345–352

21. Mayer-Hamblett, N., Rosenfeld, M., Emerson, J., Goss, C.H., Aitken, M.,L. (2002). Developing cystic fibrosis lung transplant referral criteria using predictors of 2-year mortality. Am J RespirCrit Care Med. 166: 1550–1555.

22. Moran, A., Diem, P., Klein, D.J., Levitt, M.D., Robertson, R.P. (1991). Pancreatic endocrine function in cystic fibrosis. J Pediatr, 118:715–723.

23. Moran, A., Brunzell, C.,Cohen, R. C., Katz, M., Marshall, B.C., Onady, G., Slovis, B. (2010). Clinical Care Guidelines for Cystic Fibrosis-Related Diabetes. the CFRD Guidelines Committee. Diabetes Care, 33 (12) 2697–2708; DOI: 10.2337/dc10–1768.

24. Schwarzenberg, S.J., Thomas, W., Olsen, T. W., Grover, T., Walk, D., Moran, A. (2007). Microvascular Complications in Cystic Fibrosis-Related Diabetes. Diabetes Care, 30 (5) 1056–1061; DOI: 10.2337/dc06–1576.

25. Millington, K., Miller, V., Rubenstein, R. C., & Kelly, A. (2014). Patient and parent perceptions of the diagnosis and management of cystic fibrosis-related diabetes. Journal of Clinical & Translational Endocrinology, 1(3), 100–107. Retrieved from: http://doi.org/10.1016/j.jcte.2014.07.003

26. Moran, A., Pillay, K., Becker, D.J., Acerini, C.L. (2014). ISPAD Clinical Practice Consensus Guidelines 2014. Management of cystic fibrosis-related diabetes in children and adolescents Management of cystic fibrosis-related diabetes in children and adolescents. Pediatric Diabetes, (Suppl. 20): 65–76.

27. Kerem, E., Conway, S., Elborn, S., Heijerman, H. (2005). Consensus Committee Department of Pediatrics and CF center. Israel Journal of Cystic Fibrosis, 4, 7–26.

TREATMENT OF CHRONIC PAIN IN CHILDREN WITH ONCOLOGICAL DISEASES
(CASE REPORT)

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Abstract. Acute myeloid leukemia accounts for about 4.2% of all forms of cancer in children and adolescents. Significant progress has been made in the treatment of oncohematological pathology in recent years, especially in the treatment of lymphoblastic leukemia (survival rate is up to 80%). However, unsolved problems remain in many diseases, in particular in myeloid leukemia, in which the survival rate is 38–41%. In this regard, the most critical issue is the provision of care for children with an unfavorable prognosis with malignant neoplasms. The death of a child is always incredibly difficult to accept, but understanding the feelings that causes death can help find the right approach to proper organization and provision of care for critically ill patients at the end of life.

Key words: chronic pain, children, palliative care, oncological blood diseases.

> *"Heal sometimes,*
> *heal often, comfort always"*
> *Ambroise Paré 1510–1590*

Relevance. Acute myeloid leukemia accounts for about 4.2% of all forms of cancer in children and adolescents. Significant progress has been made in the treatment of oncohematological pathology in recent years, especially in the treatment of lymphoblastic leukemia (survival rate is up to 80%). However, unsolved problems remain in many diseases, in particular in myeloid leukemia, in which the survival rate is 38–41%. In this regard, the most critical issue is the provision of care for children with an unfavorable prognosis with malignant neoplasms. The death of a child is always incredibly difficult to accept, but understanding the feelings that causes death can help find the right approach to proper organization and provision of care for critically ill patients at the end of life.

Clinical case

A 12-year-old child M. was brought to the hematological department with diagnosis: acute leukemia, myeloid variant M0, undifferentiated, second bone marrow relapse.

According to his medical history the child received polychemotherapy for acute myeloid leukemia for 6 months as part of the OML-95 program (chemotherapy protocol for the treatment of myeloid leukemia). After the main therapy, the child's condition improved, clinico-hematologic remission was achieved and the child was discharged home.

After 3 months the child's condition deteriorated sharply: he developed intoxication and hemorrhagic syndrome, in connection with which the child re-entered the hospital and was diagnosed with bone marrow relapse. As a result, palliative chemotherapy was started, in view of the non-curability of this case. I chemotherapy block was effective and the child was diagnosed with II clinical-hematologic remission (absence of blast cells in the periphery and less than 5% in the bone marrow). After 28 days, the condition deteriorated sharply (due to toxic-septic state, DIC syndrome) secondary to the second bone

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marrow relapse in connection with which palliative chemotherapy was continued.

Psychological aspects of the clinical case: the child was with the parents when the child was admitted and diagnosed, the diagnosis was made on the third day of the patient's stay in the hospital, which was communicated to the parents and the patient in the presence of the attending physician and the head of the department. It was also reported that the child entered a high risk group with a 38–41% survival rate. Parents of the patient took this information negatively, because they had an opportunity to observe patients in the department who received chemotherapy, and the results of the therapy were evident in these patients in the form of "Cushing's", alopecia and more serious complications. However, through a deep conversation with the mother of the child, the medical staff of the department managed to convince the expediency of protocol therapy. On the 15th day of chemotherapy, bone marrow remission was obtained, and the parents reacted positively to the continuation of therapy.

At the same time, parents had confidence in the medical staff. While the child was undergoing chemotherapy, the department was visited as part of the delegation of the "GLOBAL 2000" sponsorship fund, specialists in oncohematology from GermanyHe said: "Your child has no chances. Keep up your spirit!" After that the mother of the child refused to care for him and the child was transferred to the intensive care unit, where he spent the last days of his life, without relatives.

In recent decades, great advances have been made in the treatment of children with oncohematological diseases [4, 5]. Despite the use of intensive modern chemotherapy programs, complex treatment, a certain part of children with oncology is recognized as incurable at a certain stage, and therapeutic measures are directed not at attempts to completely cure the patient, but to alleviate his condition. It is extremely important to develop a strategy for care at the end of a child's life that will help provide effective palliative care, as well as support for all people involved in caring for it [6].

The problem of providing palliative care to children is extremely relevant and attracts the attention of many specialists in various countries of the world. There is lack of qualifies staff to care for children with potentially lethal diseases [7].

Psychological aspects (feelings of guilt, fear, personal suffering experienced by parents and health professionals) are a complex problem. Parents in some cases do not recognize the plight and incurability of the child and grieve, can lose vital signs and change their behavior [8, 9].

Understanding what is ahead, and the opportunity to alleviate suffering at the end of life, positively affects people who are suffering a loss. Pediatric palliative care is an active, comprehensive help to the body, mind and spirit of the child and family. It requires a broad interdisciplinary approach that mitigates the physical, psychological and social distress of the child, includes family members and uses available resources of society [10, 11].

The issue of training staff and specialists relevant to the provision of palliative care for children is extremely important. The well-coordinated work of the team of qualified specialists of children's palliative care can help organize round-the-clock assistance with patient's family and friends, as well as professional medical, psychosocial and spiritual support. Controlling the symptoms of the disease and alleviating the patient's condition are of paramount importance at the end of patient's life [12–15].

Conclusions. Thus, palliative care is created to alleviate the state of health, as the child himself, who suffers and experiences pain from the progression of the incurable disease, and his parents and other relatives, including healthy brothers and sisters who experience not only stress, but also psychological trauma both during illness and after separation.

References

1. WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses (2012). Publications of the World Health Î rganization, ð. 166. Àvailable at: http://apps.who.int/iris/bitstream/10665/44540/1/9789241548120_Guidelines.pdf

2. Lulu Mathews (2011). Pain in Children: Neglected, Unaddressed and Mismanaged. Indian J Palliat Care, 17, ðð. 70–73.

a. doi: 10.4103/0973-1075.76247

3. Hofman, M. et al (2007). Posttraumatic stress disorder in children affected by sickle-cell disease and their parents. American Journal of Hematology, 82, ðð. 171–172.

4. McGrath, P.A. (1996). Development of the World Health Organization Guidelines on Cancer Pain Relief and Palliative Care in Children. J Pain Symptom Manage, 12, ð. 87.

5. John Martin Goddard (2014). Chronic pain in Children and Young People. Pediatrics and Child Health, 24(2), ðð. 89–91.

doi: http://dx.doi.org/10.1016/j.paed.2013.08.005

6. Stefan J Friedrichsdorf and Andrea Postier (2014). Management of breakthrough pain in children with cancer. J Pain Res. ðð. 117–123.

doi: 10.2147/JPR.S58862

7. Theunissen, J.M., et al. (2007). Symptoms in the palliative phase of children with cancer. Pediatr Blood Cancer, 49(2), pð. 160–165.

8. Walsh, D., Donnelly, S. and Rybicki, L. (2000). The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer, 8(3), pð. 175–179.

9. Wolfe, J., et al. (2000). Symptoms and suffering at the end of life in children with cancer. N Engl J Med, 342(5), pð. 326–333.

10. Cartoni, C., et al. (2009). Hemorrhagic complications in patients with advanced hematological malignancies followed at home: an Italian experience. Leuk Lymphoma, 50(3), pð. 387–391.

11. Hongo, T., et al. (2003). Analysis of the circumstances at the end of life in children with cancer: symptoms, suffering andacceptance. Pediatr Int, 45(1), pð. 60–4.

12. Selwood, K. (2006). Constipation in paediatric oncology. Eur J Oncol Nurs, 10(1), pð. 68–70.

13. Weschules, D.J., et al. (2006). Toward evidence-based prescribing at end of life: a comparative analysis of sustainedrelease morphine, oxycodone, and transdermal fentanyl, with pain, constipation, and caregiver interaction outcomes in hospice patients. Pain Med, 7(4), pð. 320–329.

14. Woolery, M., et al. (2006). A constipation assessment scale for use in pediatric oncology. J Pediatr Oncol Nurs, 23(2), pð. 65–74.

15. Loeser, J.D., Treede, R.D. (2008). The Kyoto protocol of IASP Basic Pain Terminology. Pain, 137, pð.473–477.

CATAMNESTIC OBSERVATION OF CARDIOVASCULAR STATUS IN PRETERM INFANTS

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To identify peculiarities of the diastolic function development of the heart ventricles in preterm infants following clinical and instrumental examination in the neonatal period and in the process of catamnestic observation the study involved examination of 244 preterm infants at gestation age from 26^{0-7} to 37^{6-7} weeks. Control group comprised 100 healthy full-term infants. The study showed that peculiarities of the development of diastolic function of the heart ventricles in prematurely born children included diastolic dysfunction by the type of delayed relaxation, which is typical for the fetus, until the child reaches the postconceptual age of 39–41 weeks. Normalization of the diastolic function of the heart ventricles occured in 46/61 (75.41 ± 5.51%, $p = 0.1 \cdot 10^{-6}$) prematurely born children to 5–6 months of actual age, in 15/61 (24.59 ± 5.51%) children to 6–8 months of actual age. Spontaneous closure of open oval window up to the age of 1 year occurred in 22/32 (68.75 ± 8.19%, p = 0.009) full-term newborns and in 21/61 (34.43 ± 6.08%) preterm infants. Hemodynamically significant patent arterial duct in 58.82 ± 11.94% of children spontaneously closes during the first three months of life. The incidence of myocardial dysfunction in newborns from mothers with extragenital pathology increased to 89.39 ± 3.79% versus 76.67 ± 5.46%, p = 0.046 children born from healthy women. The presence of extragenital pathology in mothers, including cardiovascular disorders, is a risk factor for the development of cardiovascular diseases in preterm children.

Key words: preterm infants, myocardial dysfunction, catamnesis.

The transition from fetal to extrauterine life is the most complex physiological process of adaptation of the newborn. The beginning of independent breathing results in radical changes not only in the respiratory tract, but also in the cardiovascular system [1], which is associated with changes in pressure in heart chambers, the direction of blood flow on the level of fetal communication, as well as in remodeling of heart chambers and great vessels due to changes in hemodynamic load. Preterm labor causes difficulties in adaptation of premature infants [1], triggering a delay in neonatal remodeling of intracardiac and systemic hemodynamics. An instance of blood circulation adaptation impairment after birth is persistent pulmonary hypertension [2]. Issues of the development of diastolic function of heart ventricles and interpretation of the rate and time parameters according to echocardiography data remain urgent not only in the neonatal period [3, 4, 5, 6], but during the first year of life.

Proper assessment of hemodynamic state and detection of myocardial dysfunction in newborns enables promptly diagnose the first signs of cardiovascular involvement, even as early as at preclinical stage. Polymorphism and nonspecific clinical manifestations of cardiovascular maladaptation create certain diagnostic challenges that can only be solved with time, in the process of catamnestic observation.

The purpose of the study: to identify peculiarities of the diastolic function development of the heart ventricles in preterm infants following clinical and instrumental examination in the neonatal period and in the process of catamnestic observation.

Object and methods of the study: The study involved examination of 244 preterm infants at gestation age from 26^{0-7} to 37^{6-7} weeks. The

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newborns were divided into the following groups: Group 1 (<28 weeks – extreme degree of prematurity) – 25/244 (10.25 ± 1.94%), Group 2 (28^{0-7}– 31^{6-7} weeks – very early preterm infants) – 40/244 (16.39 ± 2.37%), Group 3 (32^{0-7}– 33^{6-7} weeks – early preterm infants) – 61/244 (25.0 ± 2.77%), Group 4 (34^{0-7}– 36^{6-7} weeks – "late preterm infants") – 118/244 (48.36 ± 3.2%) children. "Late preterm infants" was the most numerous group, which was associated with general statistical data [7]. Given that "late preterm infants" have a higher level of short-term morbidity compared to full-term children [8], this group was analyzed separately.

Control group included 100 healthy full-term newborns, with uneventful early neonatal period.

The study implied assessment of medical histories, clinical and laboratory-instrumental examination of children in the neonatal period and at the age of 3, 6, and 12 months of the actual age.

Doppler echocardiography (DECG) was performed using ultrasound scanner "MyLab25Gold" manufactured by "Esaote" (Italy) with determination of indices characterizing the systolic and diastolic function of the ventricles in accordance with the recommendations for neonatologist performed echocardiography in Europe: Consensus Statement endorsed by European Society for Pediatric Research (ESPR) and the European Society for Neonatology (ESN) [9].

Statistical processing of the data was carried out using SPSS Statistics 17.0 and STATISTICA-10 software. Comparison of the studied groups by quantitative features was carried out using the Mann-Whitney and Student criteria. For qualitative signs, statistical significance of the differences was checked by nonparametric criteria: χ^2, the exact Fisher criterion with calculation of the ð value. The value of $p < 0.05$ was taken for the threshold of statistical significance.

Results of the study and their discussion. Assessment of obstetric history showed pathological course of pregnancy (threatened abortion, placental dysfunction, antenatal distress of the fetus, premature rupture of membranes) in 68/105 (64.76 ± 4.66%, p = 0.00001) women. Multiple pregnancy occurred in 19/105 (18.1 ± 3.76) women. Two triplets and 17 twins were born.

Extragenital pathology was found in 54/105 (51.43 ± 4.88%, p = 0.38) of women. Exacerbation of chronic pyelonephritis was observed most frequently (16/105 (15.24 ± 3.51%). Allergic diseases and bronchial asthma, which complicated the course of pregnancy, were diagnosed in 3/105 (2.86 ± 1.63) mothers. Gastrointestinal diseases (chronic gastritis, duodenal ulcer, chronic cholecystitis) were found in 6/105 (5.71% ± 2.26%) women, endocrine pathology (primary hypothyroidism, medication compensated, obesity) in 3/105 (2.86 ± 1.63%) of women. The course of pregnancy secondary to anemia of mild and moderate severity was reported in 16/105 (15.24 ± 3.51) mothers. The study showed that extragenital pathologies complicated the course of pregnancy in 40/55 (72.73 ± 6.01%, p = 0.036) women. Every fourth woman, 22/105 (20.95 ± 3.97%), had compromised heredity for cardiovascular disease, and almost every fourth one 18/105 (17.14 ± 3.68) had cardiovascular pathology. More often, cardiovascular pathology was registered in mothers of newborns with extremely low birth weight (11/30 (36.67 ± 8.8%)) and mothers of newborns with very low birth weight (9/28 (32.14 ± 8.83%, $\chi^2 = 14.672$, p = 0.001)) compared to mothers of low birth weight children (5/68 (7.35 ± 3.16%).

After birth, 92/126 (73.02 ± 3.95%, $p = 0.3\cdot10^{-11}$) of preterm infants were diagnosed with infant respiratory distress syndrome (IRDS) and / or 74/126 (58.73 ± 4.39%, p = 0.01) asphyxia at birth, with clinical and laboratory and instrumental confirmation. Besides, 43/103 (41.75 ± 4.86%) newborns were shown to have hypoxic-ischemic impairment of the central nervous system and 23/126 (18.25 ± 3.44%) of children were somatically healthy - these were children at gestation age of 32.28 ± 0.95 weeks.

Clinical examination of preterm children did not reveal specific signs of myocardial dysfunction. It showed microcirculatory disorders in the form of marble hue of the skin in 69/103 (66.99 ± 4.63%, p = 0.000005) newborns, perioral cyanosis in 29/103 (28.16 ± 4.43 %), tachypnea in 66/103 (64.08 ± 4.73%, p = 0.0002), participation of auxiliary muscles in the act of respiration in 28/103 (27.18 ± 4.38%) patients. These clinical signs more often testified to the presence of respiratory disorders and microcirculatory disorders secondary to perinatal damage to the central nervous system.

Auscultation of the heart showed systolic noise in the 2nd–3rd intercostal space to the left of the sternum in 37/126 (29.37 ± 4.06%) preterm children which intensity depended on the presence of patent arterial duct, its diameter, as well as the time course of IRDS and the mean pressure in the pulmonary artery.

According to Leone A, Ersfeld P. et al. (2012) the "late preterm infants" are a special group for the development of medical complications at the stage of postpartum adaptation [8], which is important for assessing and identifying the features of hemodynamic adaptation in the neonatal period.

The study involved examination of 118/244 (48.36 ± 3.2%) "late preterm" newborns at gestation age from $34^{0/7}$–$36^{6/7}$ weeks. Multiple pregnancy was observed in 29/88 (32.95 ± 5.01%) women, of whom 28/29 (96.55 ± 3.39%, p = 0.000001) had twins, one woman had triplets. Pathological pregnancy occurred in 68/88 (77.27 ± 4.47%, ð = $0,5 \cdot 10^{-11}$) women. Moreover, 24/88 (27.27 ± 4.75%) of women had premature rupture of membranes and 12/88 (13.64 ± 3.66%) had preeclampsia. Antenatal distress and fetal development delay syndrome were recorded at the same frequency, namely 4/88 (4.55 ± 2.22%) of pregnant women, and the same frequency was associated with placental dysfunction and abnormal changes in the amount of amniotic fluid (oligohydramnios, polyhydramnios) in 6 / 88 (6.82 ± 2.69%). Placenta previa was observed in 4/88 (4.55 ± 2.22%) mothers. The threat of preterm delivery was registered in 40/88 (45.45 ± 5.31%) mothers.

Extragenital pathology was diagnosed in 60/88 (68.18 ± 4.97%, p = 0.000007) women. Chronic infectious pathology was the most common, namely chronic pyelonephritis in 18/88 (20.45 ± 4.3%) and chronic tonsillitis in 2/88 (2.27 ± 1.59%); exacerbation of bronchial asthma occurred in two women. Endocrine pathology (primary medically compensated hypothyroidism, obesity) was found in 8/88 (9.09 ± 3.06) mothers. Pregnancy in patients with anemia was observed in 7/88 (7.95 ± 2.88%) of mothers. One woman had a past history of acute lymphoblastic leucosis. Varicose disease of the lower extremities occurred in 6/88 (6.82 ± 2.69%) women. Cardiovascular diseases (arterial hypertension, secondary cardiomyopathy, congenital heart defect, heart rhythm disorders and vegetative-vascular dysfunction) were observed in 25–88 (28.41 ± 4.81%) mothers. A statistically significant relationship was found between the presence of cardiac pathology in a mother and the presence of 27/67 (40.30 ± 5.99%, p = 0.024) of myocardial dysfunction in a child in the early neonatal period. Each third woman (28/88 (31.82 ± 4.97%)) had a comorbidity of somatic pathology, which complicated the course of pregnancy.

According to the results of the clinical and instrumental examination, 30/118 (25.42 ± 4.01%) of "late preterm" infants had clinical problems such as IRDS, in 21/30 (70.0 ± 8.37%, p = 0.007), moderate degree of asphyxia during labor in 10/30 (33.33 ± 8.61%, p = 0.03) children, and 5/30 (16.67 ± 6.8%) newborns had a delay in intrauterine development.

"Late preterm" infants were not found to have specific signs of cardiovascular maladaptation. The most common were clinical signs typical for IRDS and asphyxia during labor. Auscultation detected systolic noise in 109/118 (92.37 ± 2.44%, p = 0.00001) newborns, of whom 91/118 (77.12 ± 3.87%, p = $0,3 \cdot 10^{-36}$) in a.pulmonale due to the presence of patent arterial duct and / or minimal physiological reverse flow in the pulmonary arterial valves.

Doppler echocardiography showed that the formation of diastolic function of the heart ventricles in healthy full-term neonates occurs during the first week of life. Parameters of diastolic flow in newborns in the early neonatal period have a phase redistribution: with the prevalence of early diastolic filling and a moderate increase in the ratio of early and late transmitral flow for the left ventricle; with predominance of the atrial component for the right ventricle [4].

Myocardial dysfunction was registered in 105/126 (83.33 ± 3.32%, p = $0.7 \cdot 10^{-24}$) of preterm children. Extragenital pathology in a mother was shown to be associated with an increase in the percentage of myocardial dysfunction incidence in newborns to 89.39 ± 3.79% versus 76.67 ± 5.46%, p = 0.046 children born from healthy women. Clinically important is the fact that the risk of developing myocardial dysfunction in children whose mother had a risk of abortion was 57/105 (54.29 ± 4.86%, p = 0.01). Diastolic dysfunction of the heart ventricles was recorded most commonly, in 80/105 (76.19 ± 4.16%, p = $0.3 \cdot 10^{-12}$). In 45/105 (42.86 ± 4.83%) of newborns, a violation of the systolic function of the right ventricle (mainly in children at gestational age from 24 to 31 weeks) was diagnosed in infants with respiratory distress, severe asphyxia during labor or prosthetic repair of external breathing function. Systolic dysfunction of the left ventricle was diagnosed in 16/105 (15.24 ± 3.51%) of prematurely born children.

Doppler echocardiography showed myocardial dysfunction in 67/118 (56.78 ± 4.56%), "late preterm" newborns, statistically more often in in those born from mothers with extragenital pathology (51/67 (76.12 ± 5.21%, p = $0.1 \cdot 10^{-7}$)). Diastolic dysfunction was found in 63/118 (53.39 ± 4.59%) of the "late preterm" neonates: left ventricular in 25/63 (39.68 ± 6.16%) and biventricular in 38/63 (60.32 ± 6.16%). The left ventricular systolic dysfunction was detected in 12/118 (10.17 ± 2.78%) newborns and right ventricular in 34/118 (28.81 ± 4.17%).

High incidence of diastolic dysfunction can be attributed to the fact that type 1 myocardial dysfunction (delayed relaxation) is more typical for fetal heart ventricles. Its presence can be explained by the systemic intrauterine functioning of the right ventricle in the absence of a hemodynamic load on the left ventricle [10]. Our independent studies have found that a neonatal myocardium in a premature baby shows features of the diastolic function of the heart ventricles, which is typical for the fetus until postconceptual age of 39–41 weeks. In future, the diastolic function in preterm infants is normalized and does not differ from the normal values of full-term infants by the rate and time parameters.

Systolic dysfunction of the heart ventricles was detected in newborns with respiratory disorders and / or asphyxia secondary to insufficient hemodynamic adaptation of the left ventricle to the load.

After discharge from the perinatal center at the age under 12 months of the actual age, 93 children were examined, of whom 61 were preterm and 32 were healthy children of the control group. They underwent follow-up examination: in the interval of 1 month, 3, 6 and 12 months of actual age. Given the fact of premature birth, morphofunctional immaturity, the time of stabilization of diastolic function in prematurely born children and "late preterm infants" was different from that of newborn babies. Rate and time indices were found to normilize in 46/61 (75.41 ± 5.51%, p = 0.1·10-6) prematurely born children from 5-6 months of actual age, indicating the normalization of diastolic function, in 15 / 61 (24.59 ± 5.51%) children to 6–8 months of actual age.

Hemodynamically significant open arterial duct was diagnosed in 17 children with extremely low and very low birth weight. All patients in this group were found to have disturbances in the diastolic function of the left and right ventricles of the heart by the type of delayed relaxation. In 10/17 (58.82 ± 11.94%) patients, spontaneous obliteration of the duct occurred at the end of the third month of life (from 31 to 68 days of life) with gradual normalization of the diastolic function of the ventricles in the heart at the age of 6-8 months of actual age.

Open oval window functioning was established in 100% of newborns in the neonatal period: the diameter in Group 1 children was 2.7 ± 0.5 mm, Group 2 and 3 – 3.5 ± 0.3 mm, Group 4 - 3.5 ± 0.4 mm. Spontaneous closure of open oval window in newborn infants occurred up to 6 months of life in 10/32 (31.25 ± 8.19%) and 12/32 (37.5 ± 8.56%) children up to 1 year. Spontaneous closure of open oval window in prematurely born children under one year of age occurred in 21/61 (34.43 ± 6.08%). The study showed that the size of open oval window did not depend on gender, weight at birth, gestation period.

Conclusions:

1) The peculiarities of the development of diastolic function of the heart ventricles in prematurely born children included diastolic dysfunction by the type of delayed relaxation, which is typical for the fetus, until the child reaches the postconceptual age of 39-41 weeks.

2) Normalization of the diastolic function of the heart ventricles occurred in 46/61 (75.41 ± 5.51%, $p = 0.1 \cdot 10^{-6}$) prematurely born children to 5–6 months of actual age, in 15/61 (24.59 ± 5.51%) children to 6-8 months of actual age.

3) Spontaneous closure of open oval window up to the age of 1 year occured in 22/32 (68.75 ± 8.19%, p = 0.009) full-term newborns and in 21/61 (34.43 ± 6.08%) preterm infants.

4) Hemodynamically significant patent arterial duct in 58.82 ± 11.94% of children spontaneously closes during the first three months of life.

5) The incidence of myocardial dysfunction in newborns from mothers with extragenital pathology increased to 89.39 ± 3.79% versus 76.67 ± 5.46%, p = 0.046 children born from healthy women.

6) The presence of extragenital pathology in mothers, including cardiovascular disorders, is a risk factor for the development of cardiovascular diseases in preterm children, which requires dynamic monitoring and monitoring of hemodynamic status for timely correction of the revealed changes.

Conflict of interest. No conflict of interest.

References

1. Noah Hillman, Suhas G. Kallapur, Alan Jobe. (2012). Ðhysiology of transition from intrauterine to extrauterine life. Clin Perinatol. 39(4): 769-783. doi: 10.1016/j.clp.2012.09.009.

2. Bobby Mathew, Satyan Lakshminrusimha. (2017). Persistent Pulmonary Hypertension in the Newborn. Children, 4, 63. 14 ð.; doi:10.3390/children4080063.

3. Boichenko A.D., Senatorova A.V., Honchar M.A., Kondratova Y.Iu. (2014). Typû dyastolycheskoi dysfunktsyy zheludochkov serdtsa u novorozhdennû kh v rannyi neonatalnû i peryod. Mezhdunarodnû i zhurnal pedyatryy, akusherstva y hynekolohyy. 5(3). 10–17.

4. Boichenko A.D. (2015). Systolichna ta diastolichna funktsii miokarda u novonarodzhenykh u rannii neonatalnyi period. Aktualni pytannia pediatrii, akusherstva ta hinekolohii. 1(15). 11–13.

5. Koert De Waal, Nilkant Phad, Anil Lakkundi, Peter Tan. (2017). Post-transitional adaptation of the left heart in uncomplicated, very preterm infants. Cardiology in the Young. 27(6), 1167–1173. doi.org/ 10.1017/S1047951116002687;

6. Escourrou G., Renesme L., Zana E., Rideau A., Marcoux M.O., Lopez E., ... Flamant C. (2017). How to assess hemodynamic status in very preterm newborns in the first week of life? Journal of Perinatology, 37(9), 987–993.

7. Amir Kugelman, Andrew A. Colin. (2013). Late preterm infants: near term but still in a critical developmental time period. Pediatrics., 132(4), 741–751.

8. Leone A., Ersfeld P., Adams M., Schiffer P.M., Bucher H.U., Arlettaz R. (2012). Neonatal morbidity in singleton late preterm infants compared with full-term infants. Acta Paediatr.;101(1): e6.

9. Willem P. de Boode, Yogen Singh, Samir Gupta, Topun Austin, Kajsa Bohlin, Eugene Dempsey, Alan Groves, Beate Horsberg Eriksen, …. Afif El-Khuffash. (2016). Recommendations for neonatologist performed echocardiography in Europe: Consensus Statement endorsed by European Society for Paediatric Research (ESPR) and European Society for Neonatology (ESN). Pediatric Research. 80(4), 465–471.

10. Fàtima Crispi, Brenda Valenzuela-Alcaraz, Monica Cruz-Lemini, Eduard Gratacós. (2013). Ultrasound assessment of fetal cardiac function. Australas J Ultrasound Med. 16(4), 158-167. doi: 10.1002/ j.2205-0140.2013.tb00242.x

PECULIARITIES OF HIGHER PSYCHOLOGICAL FUNCTIONS AND EMOTIONAL SPHERE IN PATIENTS WITH DEMENTIA OF VARIOUS TYPES ASSOCIATED WITH SUICIDAL RISK

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Abstract. The study involved 208 patients with dementia who were divided into three groups according to the type of dementia: 75 patients with Alzheimer's disease, 73 patients with vascular dementia and 60 patients with the mixed type of dementia. In each group, patients were divided into the main group (in which high suicidal risk (SR) was determined) and the control group (without signs of suicidal risk).

The aim of the study was to assess the influence of disturbances of higher psychological functions and emotional-volitional sphere on the formation of suicidal behavior (SB) in patients with different clinical types of dementia.

On the basis of clinical, pathopsychological, neuroimaging examination of patients we determined clinical and psychopathological peculiarities associated with high risk of suicide. The state of the following spheres of the psyche was determined: thinking, memory, will, emotions, attention, speech, perception, motor sphere.

Thus, it was established that torpidity of thinking, pseudomania and micromania, prevalence of hypomymia and hypothyroidism, inhibition of speech, attention fatigue and emotional disorders in the form of depressive affective manifestations are typical for patients with high risk of suicide. The patients of the control group without the signs of suicidal behavior have difficulties in planning and organization of activity, differed in psychomotor agitation, severity of fixative amnesia, and difficulty concentration.

The obtained data should be considered for diagnosis and prevention of suicidal behavior in this patient population.

Key words: thought disorder, memory impairment, attention disorder, perceptual disturbance, speech disturbance, emotions, vascular dementia, mixed dementia, dementia in Alzheimer's disease.

Introduction. According to statistics, from 5 to 25% of elderly people suffer from dementia. In absolute terms, it is at least 30 million patients in the world [1].

The semiotics of mental disorders in dementia includes a wide range of psychopathological disorders, namely cognitive, emotional and behavioral symptoms. Usually cognitive symptoms (higher mental, higher cortical, higher brain functions) include memory, intelligence, thinking, praxis, gnosis (perception), attention, speech. The impression of these mental functions causes violation of the processes of perception of the environment and social interaction of patients with dementia [2, 3, 4].

Non-congenital mental disorders in patients with dementia most commonly include depression, anxiety, agitation, aggression, insomnia and vagrancy [1–5].

About 40% of patients are known to have suicidal thoughts at the initial stages of dementia. Some authors prove the involvement of cognitive impairments to suicidal behavior. So the level of memory in elderly patients who committed suicide

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was lower than in patients with depression without suicidal manifestations [6]. In accordance with the concept of stress-diathesis, the basis of suicide is the cognitive (mental) control impairment, deficit of social functioning and impulsiveness [7, 8].

So far, modern literature has not adequately covered the mechanisms of the influence of higher mental functions and emotional sphere disorders on the formation of suicidal behavior in patients with vascular and degenerative dementia.

2.Purposes, subjects and methods:

2.1. Purpose was to study the influence of higher mental functions and emotional-volitional sphere disorders on the formation of suicidal behavior (SB) in patients with various clinical types of dementia.

2.2. Subjects & Methods. The study involved 208 patients who underwent clinical-psychopathological and neuroimaging examination in Sumy Regional Clinical Psychoneurological Dispensary, Sumy Regional Clinical Hospital for Veterans of War, Geriatric Boarding House, Sumy City Hospital No.4. The patients were divided into three groups according to the type of dementia: 75 patients with Alzheimer's disease, 73 patients with vascular dementia and 60 patients with mixed type of dementia. In each group, the patients were divided into the main group (which determined high suicide risk (SR)) and the control group (without the signs of suicidal risk). Thus, in the group of patients with Alzheimer's disease the main group composed 36 patients, the comparison group – 39 patients; in vascular dementia, 39 people were included in the main group and 34 in the comparison group; in mixed dementia, 30 patients composed the main group and 30 patients – the comparison group.

The diagnosis was established in accordance with the ICD-10.

Specification of clinico-psychopathological structure of higher mental functions was carried out following to the assessment of thought disorders, mnestic processes violations, emotional-volitional sphere and speech disorders, processes of attention and perception disturbance in different types of dementia taking into account the features of suicidal risk (SR) in these pathologies.

All thought disorders in accordance with the clinical classification (Sidorov P.I., Parniakov A.V., 2000) were divided into two groups: quantitative (pathology of the associative process) and qualitative (pathology of judgments and inferences).

Associative process pathology included violations of tempo, mobility and purposefulness of thinking, and pathology of judgments and inferences – intrusive thoughts, valuable and delusional ideas, as well as the ability to plan and organize activities.

Statistical processing of the results was performed with the Student's criterion and Fisher's exact test.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. Statistical comparative analysis of thought disorders among patients with high SR in different types of dementia showed that the violation of the tempo of thinking in the form of its acceleration was more pronounced among patients with mixed dementia compared with patients with Alzheimer's disease ($p \le 0.025$, DK = 8.57, MI = 0.74). The study also showed that by mental mobility in patients with vascular dementia prevailed the detailed thinking compared to Alzheimer's disease ($p \le 0.01$, DK = -3.75, MI = 0.50) and mixed dementia ($p \le 0.001$, DK = 6.64, MI = 1.20), in which stiff thinking prevailed (($p \le 0.01$, DK = 4.03, MI = 0.47) and ($p \le 0.05$, DK = -3.36, MI = 0.30) respectively). Violation of the purposefulness of thinking in the form of disintegration of thought was more pronounced in patients with mixed type of dementia compared to vascular dementia ($p \le 0.05$, DK = -4.15, MI = 0.34).

Comparative analysis of speech impairment in patients with high SR in different types of dementia allowed to establish that the number of patients with stereotyped oral speech was greater in Alzheimer's disease than in vascular dementias ($p \le 0.025$, DK = 4.15, MI = 0,43). It was also established that the number of patients with sensory aphasia prevailed in Alzheimer's disease ($p \le 0.025$, DK = 4.15, MI = 0.43) and in mixed dementia ($p \le 0.005$, DC = -5.29, MI = 0,81) in comparison with vascular dementia, and patients with optic-amnestic aphasia prevailed in mixed dementias than in vascular dementia ($p \leq 0.01$, DK = -2.65, MI = 0.34).

Comparative analysis of volitional disorders among patients with high SR in different types of dementia was also conducted. It was found that the severity of the hypobulia distinguished patients with Alzheimer's disease compared to patients with vascular and mixed dementia (($p \leq 0.005$, DK = -2.27, MI = 0.36) and ($p \leq 0.00025$, DK = 3,68, MI = 0.82) respectively), among which there were more patients with hypobulia (($p \leq 0.025$, DK = 4.42, MI = 0.43) and ($p \leq 0.05$, DK = -4, 31, MI = 0.41) respectively) and echopraxia (($p \leq 0.01$, DK = 6.02, MI = = 0.75) and ($p \leq 0.025$, DK = -5.56, MI = 0.60) respectively). The number of patients with parabulia and parakinesia was higher in mixed dementia than in Alzheimer's disease (($p \leq 0.01$, DK = -5.19, MI = 0.66) and ($p \leq 0.0001$, DC = -11, 58, MI = 2.16) respectively). In vascular dementia, the number of patients with parakinesia was lower compared to patients with mixed dementia ($p <0.01$, DK = -4.15, MI = 0.51), but the number of patients with psychomotor agitation was greater than with Alzheimer's disease ($p \leq 0.005$, DK = 7.43, MI = 0.94).

The expressed hypomimia was typical for patients with Alzheimer's disease and mixed dementia as opposed to patients with vascular dementia (($p \leq 0.001$, DK = 4.68, MI = 0.82) and ($p \leq 0.025$, DC = -3.48, MI = 0, 38) respectively). The inhibition of libido was more pronounced in patients with Alzheimer's disease compared to patients with vascular and mixed types of dementia (($p \leq 0.0001$, DK = 10.20, MI = 3.72) and ($p \leq 0.0001$, DK = 4,80, MI = 1.29) respectively. It should be noted that in the mixed type of dementia, the number of patients with inhibited sexual desire was greater than in vascular dementia ($p \leq 0.025$, DK = -5.40, MI = 0.51).

Statistical comparative analysis of violations of the emotional sphere in the main group in different types of dementia was performed to understand the influence of SR in different types of dementia on the emotional sphere. It showed that the feeling of exhaustion was higher in patients with mixed type of dementia than in Alzheimer's disease ($p \leq 0.005$, DC = -3.01, MI = 0.50) and vascular dementia ($p \leq 0.05$, DK = -1.60, MI = 0.16). Emotional lability was the most pronounced in vascular dementia ($p \leq 0.005$, DK = -3.84, MI = 0.61), and the lability of the emotional sphere was more inherent to patients with mixed type of dementia than to patients with Alzheimer's disease ($p \leq 0,05$, DK = -2,90, MI = = 0,31). Patients with Alzheimer's disease differed from patients with vascular dementia with a higher severity of depression ($p \leq 0.01$, DK = 1.81, MI = 0.24), anxiety ($p \leq 0.05$, DK = 2.22, MI = 0.25) and melancholia ($p \leq 0.01$, DK = 2.72, MI = 0.33).

The comparison of patients with high SR in different types of dementia made it possible to establish that fixative and progressive amnesia was more pronounced in patients with Alzheimer's disease (($p \leq 0.01$, DK = -2.78, MI = = 0.38) and ($p \leq 0.005$, DK = -2,27, MI = 0,36) respectively) and mixed dementia (($p \leq 0,005$, DK = 3,14, MI = 0,51) and ($p \leq 0,01$, DK = 2,20 , MI = 0,34), respectively) in comparison with vascular dementia. The tendency to describe the events that have never occurred in the life of patients (confabulations) was more typical for patients with vascular dementia compared to patients with Alzheimer's disease ($p \leq 0.025$, DK = 4.22, MI = 0.48).

Clinico-psychopathological analysis of perceptual disturbances allowed to establish some typical peculiarities, characteristic for patients with SR in different types of dementia.

Thus, it was established that the symptoms of depersonalization were more pronounced in mixed type of dementia compared with vascular dementia ($p \leq 0.05$, DK = -3.36, MI = 0.30) and Alzheimer's disease ($p \leq 0.025$, DK = 4.77, MI = = 0.53), and the symptoms of derealization were more pronounced in Alzheimer's disease and mixed dementia than in vascular dementia (($p \leq 0.05$, DK = -2.49, MI = 0.27), and ($p \leq 0.05$, DC = -2.49, MI = 0.27) respectively). Patients with vascular dementia had less pronounced agnosias compared with Alzheimer's disease ($p \leq 0.05$, DK = -2.39, MI = 0.22) and visual hallucinations compared to mixed dementia ($p \leq 0.05$, DK = -3.48, MI = 0.38).

Thus, the analysis of clinical and psychopathological structure of higher mental functions and emotional sphere in patients with suicidal risk in various types of dementia allowed to determine the clinical diagnostic criteria of

Table 1

Clinical diagnostic criteria for patients with high SR in different types of dementia

Indices		Patients with vascular dementia	Patients with Alzheimer's Disease	Patients with mixed dementia
		Diagnostic coefficient (DC)		
Thought disorder	Inhibition	2.41	1.14	1.58
	Circumstantial thinking	-	-	2.30
	Delusions of self-effacement	8.95	9.89	-
	Delusions of self-blame	-	5.79	-
Emotional sphere disorders	The feeling of despair	1.79	3.55	5.56
	The feeling of hopelessness	3.51	2.78	9.03
	The feeling of helplessness	-	-	2.76
	Depressed mood	2.00	4.82	2.79
	Asthenia	4.18	-	-
	Inner agitation	-	3.08	-
	Apathy	-	2.85	3.01
	Anxiety	-	2.57	-
	Melancholia	-	4.68	8.13
	The feeling of guilt	-	3.11	-
	Exhaustion	-	-	3.01
Volitional disorders	Hypomimia	-	2.72	6.02
	The reduction of volitional process	-	1.60	-
	Decreased interest	-	1.75	-
	Inhibition of autokinesia processes	-	2.17	-
Speech disturbance	Bradylalia	2.21	3.11	2.79
Attention disturbance	Exhaustion	1.17	1.96	1.46
	Poor attention	-	3.60	-

patients with high SR in different types of dementia (*table 1*).

4. Conclusions. Table 1 shows that the main clinical and psychopathological disorders in patients with high SR in various types of dementia are mental retardation, delusions of self-blame and self-effacement, predominance of hypomimia and oligothymia, decrease of tempo of speech, attention fatigue and numerous violations in the emotional sphere, which are mainly expressed by depressive affective manifestations. Patients in the control group had difficulty in planning and organizing activities, psychomotor agitation, the severity of fixative amnesia and difficulty concentration.

The obtained data should be taken into account when performing differential diagnostics of patients with SR in different types of dementia.

Referenses

1. World Health Organization. Suicide prevention (SUPRE). Geneva. Switzerland URL. 2007. Retrieved from: http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/.

2. Yakhno, N.N., Zakharov, V.V., Lokshina, A.B. and others. (2011). Dementia: a guide for doctors. Moscow: Medpress-information. P. 272.

3. Mikhailova, N.M., Roshchina, I.F. (2013) Ethical aspects of dementia of late age: problems and solutions. Clinical and special psychology, 2, 36–42.

4. Zakharov, V.V., Voznesenskaya, T.G. (2013) Neuropsychiatric disorders: diagnostic tests. Moscow: MEDPress-Inform. P. 320.

5. Kozyolkin, O. A., Sikorska, M.V., Vizir, I.V., Neryanov, Yu.M. (2015) Dementia: teaching aids. Zaporozhye: [ZSMU]. P. 90.

6. Mudrenko, I.G. (2018) Clinical phenomenology of suicidal behavior in dementia of different types. Science Rise: Medical Science, 1(21), 38–44.

7. Mudrenko, I.G. (2017) Factors of suicidal behavior in patients with dementia. Medical psychology, ¹ 3 (47), 53–57.

8. Mudrenko, ².G. (2017) Pharmacological correction of depressive symptoms in patients with different clinical variants of dementia. Ukrainian Journal of Psychoneurology,25 (92), 49–54.

NEW APPROACHES TO THE TREATMENT OF PATIENTS WITH SEBORRHEIC DERMATITIS

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Abstract. The article presents results of complex treatment of 55 patients with seborrheic dermatitis (SD) at the age of 26–48 years. Patients with SD are divided into two groups, homogeneous by age, sex, clinical forms, severity, laboratory parameters. Patients of group 1 in the cold period of the year (November-March) were administered cholecalciferol (vitamin D3) and synbiotic (combined probiotic) DermaPro in the background of complex traditional therapy. Patients of group 2 received only traditional treatment. Clinical remission and significant improvement were detected in group 1 patients (88.2%) more often compared with the similar result in group 2 patients (52.4%). Relapses of the disease were detected in 23.6% of patients in group 1 and 50.0% in patients in group 2 within one year. The appointment of patients with SD cholecalciferol and DermaPro led to an increase levels of 25(OH)D by 81.5% and cathelicidin LL-37 by 78.4%, normalization and improvement of gut microbiota in 88.2% of cases. The use of traditional therapy resulted in only normalization and improvement of intestinal biocenosis in 28.5% of patients.

Key words: vitamin D3, probiotic, clinical and laboratory efficacy, treatment, seborrheic dermatitis.

Introduction. Seborrheic dermatitis (SD) is a common chronic inflammatory skin disease associated with increased secretion of sebum, a change in its qualitative composition. Yeast-like fungi Malassezia spp. is supposed to be the main cause of SD, however, the amount of these lipophilic microorganisms is often within normal limits on the skin of patients [1, 2]. Genetic predisposition, hormonal status change, gastrointestinal tract and the nervous system diseases, dysfunction of the epidermal barrier may provoke the disease [3, 4].

New therapeutic technologies which allow to reduce rapidly the sign of the SD main symptoms (itching, skin lesions and scales, redness, plaques and hair loss) have emerged during the last decade. Medicines containing topical glucocorticosteroids, antifungal and antimicrobial substances, zinc pyrithione, selenium sulphide and others are used in treatment most often [5, 6]. When carrying out complex treatment, the availability of the body with vitamin D, the state of innate immunity and the gut microbiota of the patients have not been taken into account until now. The prognosis of some patients remains unfavorable, which is caused by insufficient effectiveness or resistance to traditional therapy, frequent recurrence, despite the successes achieved in the treatment of dermatosis. The search for new approaches to treatment continues, as these issues are an actual problem.

2. Purposes, subjects and methods:

2.1. Purpose. The purpose of the present study was to estimate the effectiveness of SD patients' therapy which is held using vitamin D and a probiotic containing Lactobacillus ramnosus GG.

2.2. Subjects. The study included 55 patients with SD at the age of 26-48 years (35 men and 20 women). Patients didn't have concomitant diseases at the stage of exacerbation or decompensation, primary hyperparathyroidism. Patients didn't take antifungal drugs, corticosteroids, anticonvulsants, vitamins within the last three months. All patients voluntarily signed informed consent to participate in the study.

Patients showed a variety of clinical SD signs, caused by the localization and type of the rashes, the prevalence of the skin process. The disease's

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severity degree was established on the base of the SDASI calculations (Seborrheic Dermatitis Area Severity Index [7]. In average SDASI was 10.3±1.6 points among the patients. Exacerbation of dermatitis occurred in 76.4 % of cases in autumn and winter, the disappearance of rashes or significant improvement in 85.4 % of patients in summer. 67.3 % of patients showed insufficient intake of foods rich in vitamin D (sea fish, eggs, milk). Associated diseases of the GIT and hepatobiliary system were diagnosed in 52.7 %, clinical manifestations of dysbiosis in 65.4 % of patients (discomfort or mild aching, blunt regular abdominal pain, flatulence). Laboratory signs of large intestine dysbiosis (decrease in the number of bifidobacteria and lactobacilli, aerobic E. coli typical, an increase in the number of saprophytic and opportunistic bacteria – epidermal staphylococcus, enterobacter, cytrobacter, yeast-like Candida fungi) were detected in 100 % of patients.

2.3. Methods. Patients with SD are divided into two groups. The group 1 consisted of 34 patients (24 men, 10 women), the average age was 36.4 ± 2.2 years, SDASI - 10.6 ± 1.8 points. The group 2 consisted of 21 patients (11 men, 10 women, the average age was 37.5 ± 2.5 years, SDASI – 10.1 ± 1.7 points. Both groups of patients were homogeneous by age, sex, clinical forms, severity, laboratory parameters.

Patients of the group 1were prescribed colecalciferol (vitamin D3) in the cold period of the year (November-February) and synbiotic (combined probiotic) DermaPro on the background of complex traditional therapy. Ñolecalciferol was taken at a dose of 2000 IU once a day during 6 weeks with vitamin D deficiency (level of 25(OH)D in the range of 51–74 nmol/l). The medicine was recommended at a dose of 3200 IU once a day during 8 weeks with a transition to 2000 IU for 2 weeks in case of vitamin D deficiency (level of 25(OH)D less than 50 nmol/L). The patients took DermaPro for one capsule during 14–21 days (taking into account the degree of dysbiosis). The Patients of the group 2 received only traditional treatment – oral antihistamines (levocetirizine, phencarol), vitamins of group B (vitamin B6, biotin, Neurovitan), antifungal drug itraconazole (in case of widespread and resistant to therapy), topical corticosteroids, topical inhibitors calcineurin, shampoos with antiproliferative, antifungal, keratolytic components.

Clinical and laboratory results were compared after the treatment with various methods in order to study the effectiveness of the therapy. The results of the treatment were assessed using the following clinical criteria: clinical recovery, significant improvement, improvement, no effect. The determination of the level of 25(OH)D and cathelicidin LL-37 in serum was carried out by the method of enzyme immunoassay. The standard bacteriological method of faeces examination was used to assess the state of the intestinal microflora.

The obtained data were processed with the determination of the arithmetic mean (M), the standard deviation (δ) using the STATISTICA for Windows 5.5 software system. Differences between groups were established using the ANOVA test and Mann-Whitney U. The criterion for statistical reliability of the findings was the value p <0.05.

The study was conducted according to the international bioethical standards.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. The clinical results (*table 1*) established that the clinical remission was 2.7 times more frequent among the patients of the group 1 (38.2%) than among the patients of the group 2 (14.3%). Significant improvement took place more often with the patients who received the therapy with vitamin D3 and probiotic (52.9%) than those who got the traditional therapy (38.1%). Improvement was more often registered in group 2 (33.3%) comparing to the same indicator in patients of the group 1 (accordingly, 8.8%). The therapy was

Table 1

Results of the treatment of patients with seborrheic dermatitis by various methods

Results of the treatment	Patients, groups	
	1, n = 34 abs. / %	2, n = 21 abs. / %
Clinical remission	13 / 38,2	3 / 14,3
Significant improvement	17 / 50,0	8 / 38,1
Improvement	4 / 11,8	7 / 33,3
Lack of effect	–	3 / 14,3
Total	34 / 100,0	21 / 100,0

ineffective only for the patients of the group 2 (14.3%). Positive results were achieved in 100.0% of patients in group 1 and 85.7% among the patients in group 2. However, clinical remission and significant improvement were more often determined among the patients who were treated according to the developed method (88.2%), comparing with the similar results among the patients who received the traditional therapy (52.4%, respectively).

Regression of the main clinical symptoms of Seborrheic dermatitis under the influence of therapy occurred after different times. The more rapid disappearance of subjective and objective manifestations of dermatosis was revealed in patients who received supplemental vitamin D3 and probiotic. Shorter time to regression of erythema and scaling in patients of the group 1 (5.1 ± 0.5 and 6.3 ± 0.7 days, $p < 0.05$) comparing to the patients of the group 2 (9.4 ± 0.9 and 10.1 ± 1.0 days) attracts the attention. Analysis of the decrease in SDASI in patients of different therapeutic groups also revealed the advantage of the developed differential treatment. Reduction of SDASI in 4.2 times was noted in patients of the group 1 (main), while in the group 2 – in 1.7 times.

Observation of patients within one year after treatment revealed relapses of the disease in 8 (23.6%) patients of the group 1 and 11 (50.0%) patients in the group 2.

The patients of the group 1 experienced a significant increase in serum 25(OH)D level ($p < 0.05$) after treatment reaching the target level (75–150 nmol/l, according to the guidelines for Central European countries [8]) and cathelicidin LL-37 ($p < 0.05$), whereas in the patients of the group 2 – the values of both indices practically did not change (*table 2*).

on the qualitative and quantitative composition of the intestinal microbiota of the complex approach with additional use of cholecalciferol and DermaPro. It was expressed in restoring the level of obligate microflora to reference values, reducing the number of facultative, eliminating pathogenic microbes. In patients of the group 2, intestinal dysbacteriosis persisted in most cases (71.4%), the indices improved or normalized in patients with the first degree of dysbiosis in the background of a diet. The use of therapy with vitamin D3 and synbiotic led to normalization or significant improvement in the quantitative and qualitative composition of the gut microflora in most patients.

The results of the study indicate that patients with seborrheic dermatitis require the appointment of vitamin D3 and a synbiotic, which not only increased the effectiveness of therapy and the rapid regression of clinical manifestations (a decrease of SDASI by more than 75%), but also the normalization of most laboratory indicators. All patients tolerated the treatment well.

Detection of anti-inflammatory and immunosuppressive activity of vitamin D has opened up new possibilities for the therapeutic use of this substance and its analogs for the control of inflammatory skin diseases supposedly associated with hyperproduction of cytokines (psoriasis, atopic dermatitis, urticaria, scleroderma) [9, 10, 11]. Data on the use of vitamin D in patients with SD don't exist in the available literature, although in 92.3% of patients a deficiency / insufficiency of the vitamin (at 20% in practically healthy individuals) was detected [12]. The choice of the optimal dose of vitamin D3 depends on the initial concentration of 25(OH)D in the blood. Calculation of the daily dose of vitamin D3 was carried out depending on the initial concentration of 25(OH)D according to the scheme developed by Garland et al. (2011) [13]. The doses fully satisfied the recommendations of the International Endocrinology Society.

Table 2

Dynamics of vitamin D status and innate immunity in patients with seborrheic dermatitis during the treatment

Parameters	Patients, groups	
	1, n=34	2, n=21
25(OH)D, nmol/l	53.06±4.30* 96.29±7.18	57.33±4.50 63.15±5.11
Cathelicidin LL-37, ng/ml	18.1±1.9* 32,3±2,7	19.2±2.1 21,4±2,2

Note: the numerator indicates pre-treatment indicators, the denominator indicates after treatment; differences are significant between the indices in the group for $p < 0.05$ – *.

Comparative analysis of the results of the study of faeces on intestinal dysbacteriosis in patients with SD after the treatment (*table 3*) showed the most pronounced corrective effect

Table 3

The state of the intestinal microbiota in patients with seborrheic dermatitis in the course of treatment

Parameters	Patients, groups	
	1, n=34 abs. / %	2, n=21 abs. / %
Dysbacteriosis of the intestine	4 (11.8)	15 (71.4)
Normalization of intestinal biocenosis	24 (70.6)	2 (9.5)
Improvement of bacteriological parameters	6 (17.6)	4 (19.1)

One of the "nonclassical" effects of the D-hormone, along with the inhibition of cellular proliferation and angiogenesis, an anti-inflammatory effect, is the stimulation of the production of antimicrobial peptides (cathelicidins, defensins) [14]. To date, it is believed that the role of vitamin D in the pathogenesis of allergic diseases is due to its regulatory effect on the immune system, participation in antimicrobial protection and the barrier function of the skin and mucous membranes [15, 16]. The appointment of colecalciferol in patients with seborrheic dermatitis confirms the modulating effect of vitamin D on the functioning of innate immunity on the basis of a significant increase the level of LL-37 in the blood of patients by a factor of 1.8.

Probiotics acquire great importance in the treatment of seborrheic dermatitis, taking into account their normalizing effect on the state and balance of intestinal microflora, immunity and immune response - modulation of the Th1 / Th2 response, inhibition of Ig E synthesis, stimulation of Ig A production, antimicrobial peptides, macrophages and so on [17, 18]. High importance and leading positions in the number of communities of symbiotic microorganisms of "healthy" people of all age groups of lactobacillus led to a choice for correction of dysbiotic disorders in SD of the DermaPro synbiotic [19].

The drug consists of a probiotic (lactobacillus) and a prebiotic (fructo-oligosaccharide). Lactobacillus rhamnosus GG, included in the preparation 1.5 billion CFU, prevent the proliferation of pathogenic microorganisms in the intestine and help restore the balance of useful microflora, eliminate dysbiosis and normalize digestion, immune response. It should also take into account the normalizing effect of vitamin D on the state of the intestinal microflora [20].

The obtained results of the research allow us to state that the use of vitamin D3 (cholecalciferol) and synbiotic DermaPro in the complex treatment of diabetes is an effective and safe method of therapy.

Conclusions:

1. The use of vitamin D3 and synbiotic in the treatment of SD contributed to an increase in the effectiveness of complex therapy – remission and significant improvement were noted in 88.2%, relapses in 23.6% of patients compared to those in patients receiving only traditional therapy (52.4 % and 50.0 %).

2. The appointment of patients with SD cholecalciferol and DermaPro led to an increase in blood levels of 25(OH)D by 81.5% and cathelicidin LL-37 by 78.4%, normalization of gut microbiota in 88.2% of cases.

3. The use of drugs that have a normalizing effect on the vitamin D status and the level of cathelicidin LL-37 of blood, intestinal microbiocenosis is a new pathogenetic grounded approach to the therapy of patients with SD.

References

1. Kornishova, V. G., Mogileva, Ye. Yu. (2012). Seboreynyy dermatit (obzor) [Seborrheic dermatitis (review)]. Probl med mikol, no 3, pp. 3–11.

2. Paulino, L. C. (2017). New perspectives on dandruff and seborrheic dermatitis: lessons we learned from bacterial and fungal skin microbiota. Eur J Dermatol, 27(S1), 4–7.

3. Dessinioti, C., Katsambas, A. (2013). Seborrheic dermatitis: etiology, risk factors, and treatments: facts and controversies. Clinics in Dermatol, 31(6), 343–351.

4. Bakardzhiev, I., Argirov A. (2017). New Insights into the etiopathogenesis of seborrheic dermatitis. Clin Res Dermatol Open Access, 4(1), 1–5.

5. Clark, G. W., Pope, C. M., Jaboori, K. A. (2015). Diagnosis and treatment of seborrheic dermatitis. Am Fam Physician, 91(3), 185–190.

6. Chowdhry, S., Gupta, S., D'souza, P. (2017). Topical antifungals used for treatment of seborrheic dermatitis. J Bacteriol Mycol Open Access, 4(1). doi: 10.15406/jbmoa.2017.04.00076.

7. Baysal, V., Yildirim, M., Ozcanli, C., Ceyhan, A. M. (2004). Itraconazole in the treatment of seborrheic dermatitis: a new treatment modality. Int J Dermatol, 43(1), 63–66.

8. Holick, M. F., Binkley, N. C., Bischoff-Ferrari, H. A., Gordon, C.M., Hanley, D. A., Heaney, R. P., … Weaver, C. M. (2011). Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab, 96(7), 1911–1930.

9. Bekirova, E. Yu. (2013). Vliyaniye vitamina D na sintez tsitokinov indutsirovannymi mononuklearnymi leykotsitami u patsiyentov psoriazom s D-defitsitom [Influence of vitamin D on the synthesis of cytokines induced by mononuclear leukocytes in patients with psoriasis with D-deficiency]. Tavrich mediko-biol vestn, vol. 16, pp. 22–24.

10. Bell, D.S. (2011). Protean manifestations of vitamin deficiency, part 2: dificiency and its association with autoimmune disease, cancer, infection, astma, dermopathies, insulin resistans, and type 2 diabetes. South Med S, 104, (5), 335–339.

11. Polat, M., Uzun, Ö. (2014). Vitamin D in dermatology. Open Access Dermatology, 2(1), 9.

12. Narozhnaya, M. V. (2017). Obosnovaniye primeneniya vitamina D v lechenii seboreynogo dermatita [Substantiation of the use of vitamin D in the treatment of seborrheic dermatitis]. Dermatovenerol Kosmetol, 3(3), pp. 292–299.

13. Garland, C. F., French, C. B., Baggerly, L. L., Heaney, R. N. (2011). Vitamin D supplement doses and serum 25-hydroxyvitamin D in the range associated with cancer prevention. Anticancer Res, 31(2), 607–611.

14. Pigarova, Ye. A., Pleshcheva, A. V., Dzeranova, L. K. (2015). Vliyaniye vitamina D na immunnuyu sistemu [The effect of vitamin D on the immune system]. Immunol, vol. 36, no 1, pp. 62–66.

15. Maylyan, E. A., Reznichenko N. A., Maylyan, D. E. (2017). Ekstraskeletnyye effekty vitamina D: rol' v patogeneze allergicheskikh zabolevaniy [Extracellet effects of vitamin D: a role in the pathogenesis of allergic diseases]. Nauchnyye vedomosti Seriya Meditsina. Farmatsiya, no 5(254), pp. 22–33.

16. Roider, E., Ruzicka, T., Schauber, J. (2013). Vitamin D, the cutaneous barrier, antimicrobial peptides and allergies: Is there a link? Allergy Asthma Immunol Res, 5(3), 119–128.

17. Butel, M. J. (2014). Probiotics, gut microbiota and health. Med Mal Infect 44(1), 1–8.

18. Sanchez, B., Delgado, S., Blanco-Míguez, A., Lourenco, A., Gueimonde, M., Margolles, A. (2017). Probiotics, gut microbiota, and their inluence on host health and disease. Mol Nutr Food Res, 61(1), 17–32.

19. Vaughn, A. R, Notay, M., Clark, A. K., Sivamani, R. K. (2017). Skin-gut axis: The relationship between intestinal bacteria and skin health. World J Dermatol, 6(4), 52–58.

20. Ly, N. P., Litonjua, A., Gold, D. R., Celedón, J. C. (2011). Gut microbiota, probiotics, and vitamin D: interrelated exposures influencing allergy, asthma, and obesity? J Allergy Clin Immunol, 127(5), 1087–1094.