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THE EU COHESION POLICY AND HEALTHY NATIONAL DEVELOPMENT: MANAGEMENT AND PROMOTION IN UKRAINE

Editors

Nataliia Letunovska,
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Anna Rosokhata



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**THE EU COHESION POLICY AND
HEALTHY NATIONAL
DEVELOPMENT: MANAGEMENT AND
PROMOTION IN UKRAINE**

Monograph

Edited by Nataliia Letunovska, Liudmyla Saher, Anna Rosokhata

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The monograph focused on the specifics of the principles of the EU Cohesion Policy implementation. The authors conducted an analysis of the economic, ecological and social aspects of the integration of the EU experience into the state policy of Ukraine. The monograph summarizes approaches to the restoration of the country and healthy development. Particular attention is paid to the issues of health care system management, the trends and prospects of achieving the state of resilience of the medical and social provision system of the population in the context of the impact of COVID-19 on the national economy. The experience of using marketing and innovative technologies in the context of healthy national development is summarized.

The monograph is generally intended for government officials, entrepreneurs, researchers, graduate students, students of economic, medical, and other specialties.

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reproductive age, it is extremely necessary to carry out measures aimed at prevention, timely diagnostics and treatment of infectious and inflammatory diseases of the genitourinary system. Ensuring reproductive health at the proper level is one of the priorities and values of European civilization, so the promotion of a healthy approach to life is one of the ways of European integration of Ukraine.

4.7. Urogenital inflammatory diseases in women of reproductive age as a cause of an unhealthy start of children's life: Ukrainian and European research

Maternal and child health is the most important medical and social problem in the world. Modern scientific research of the world's leading specialists has shown (Sekikubo et al., 2020; Sureshababu et al., 2021) that fetus and newborn adaptive reserves depend to a greater extent on case of maternal diseases during pregnancy, especially infectious diseases, which can definitely lead to pathology of various organs and systems in fetus, defects in immune response, metabolic problems and affect life expectancy. Recently interest to the problems of perinatal nephropathy has increased, as many kidney diseases in elder children have their origins in the antenatal and intranatal periods. No pathological condition in pregnant woman affecting the fetus leaves the kidneys intact (Gomi et al., 2015; Kazemier et al., 2016).

Epidemiological studies demonstrate that in the first year of life, nephropathology is more often diagnosed in boys, and from the second year of life and throughout childhood, girls suffer from this pathology more often (Budnik, 2019).

The non-specificity of clinical symptoms of perinatal nephropathies, the hidden onset and torpid course of pathological process, the low informativeness, technical complexity, invasiveness of many existing methods in studying newborn's kidney functions complicate in-time diagnosis of perinatal renal pathology and contribute to chronic pathology, development of chronic kidney disease and formation of chronic renal deficiencies just in childhood (Govindarajan et al., 2022; Henderson et al., 2023).

The increase in the incidence of newborn's kidney pathology is associated with an increase in the frequency of chronic urogenital

inflammatory diseases in the mothers, which can manifest as cystitis, pyelonephritis, salpingo-oophoritis, endometritis, asymptomatic bacteriuria, etc. (Albright et al., 2015; Minassian et al., 2013).

The occurrence of urogenital infection in women during pregnancy or before remains a problem for doctors for many years. It is known that about 40% of women during pregnancy have episodes of urogenital infection, the development of which can be attributed to following factors: female anatomical and physiological features, represented by a short and large urethra, closeness of urethra to the rectum; violation in urodynamics caused by hypotonia and dyskinesia of urinary tract due to an increase in the concentration of estradiol and progesterone, an increase in concentration of glucocorticoids; mechanical compression of ureters in the second half of pregnancy by an enlarged uterus and dilated ovarian veins; weakening of urethral sphincter at the end of pregnancy; a change in the properties of urine, which is manifested by an alkaline reaction due to bicarbonaturia as reaction on increased rate of glomerular filtration, etc. Also urodynamic disorders caused by obstructive causes, neurogenic disorders, vesicoureteral reflux, foreign bodies (stents, stones) and a number of concomitant diseases (renal failure, immunosuppressive state, anemia, etc.) are the factors that complicate the course of urogenital infection. Therefore, two main factors contribute to the occurrence and development of urogenital infection, especially pyelonephritis, in pregnant women and they are an infectious focus in the body and a violation in urodynamics of urinary tract (Bruxvoort et al., 2020; Sureshbabu et al., 2021; Xu et al., 2017).

In women who suffered from cystitis, urethritis or acute pyelonephritis in childhood, gestational pyelonephritis is often registered, which, according to statistics, escalates in one third of such pregnant women. Researchers have established that the kidneys function with great stress during pregnancy, because remove metabolic products of the woman herself and the fetus (Archabald et al., 2009; Hooton et al., 2013; Kulkarni et al., 2013).

There is a variety in causative agents of urogenital infection, in particular pyelonephritis (Al-Orphaly et al., 2021; Gajdacs et al., 2019; Li et al., 2019). The etiology of gestational pyelonephritis is directly related to the obligate and facultative microflora of gastrointestinal and urogenital tracts (Gharaghani et al., 2021; Kroken et al., 2018; Subashchandrabose et al., 2015). The most frequent causative agents of pyelonephritis are gram-negative bacteria (*Escherichia coli*, *Proteus mirabilis*, *Proteus vulgaris*,

Klebsiella pneumoniae, *Enterobacter* spp., *Serratia* spp., *Pseudomonas aeruginosa*) (Newman et al., 2017; Nicolle et al., 2019; Scavone et al., 2015; Subashchandrabose et al., 2015; Yuan et al., 2021) and gram-positive bacteria (*Streptococcus pyogenes*, *Enterococcus faecalis*, *Staphylococcus aureus*) (Deutch, 2017; Nallapareddy et al., 2011). Their importance increases significantly in case of nosocomial infection. *Candida albicans* and *Blastomyces* can act extremely rarely as pathogens (Gharaghani et al., 2021). Microbial associations are detected in more than 20% of pregnant women with pyelonephritis (Bruxvoort et al., 2020; Montagut et al., 2021).

There are three main mechanisms of pyelonephritis. From the site of infection via hematogenous (descending) way microorganisms in the form of infected emboli enter the kidney glomerular layer, glomerular capillaries and small terminal vessels. Via lymphogenic route the infection penetrates from the genitals and intestine. Transurethral (ascending) way with vesicoureteral reflux, which is observed directly during pregnancy (Al-Orphaly et al., 2021; Gajdacs et al., 2019; Li et al., 2019).

It is found that the course of gestational pyelonephritis caused by gram-negative microorganisms (Chathley et al., 2016; Li et al., 2019; Scavone et al., 2015), especially in the form of a mixed infection, is the most severe with bacterial shock and septicemia (Albright et al., 2015). Bacterial shock often develops with the start of antibacterial therapy according impaired urine outflow (Ailes et al., 2016; Committee Opinion No. 717, 2017; Sekikubo et al., 2017). Administration of antimicrobial drugs causes massive death of microorganisms (Ekwealor et al., 2016; Gu et al., 2022), and violation of the outflow of urine from the upper parts of urinary tract contributes to accumulation of endotoxins and their entry into the blood due to the occurrence of pelvic-renal reflux.

A serious problem of pyelonephritis in pregnant women is that the infectious process in kidneys is accompanied by great changes in the body's immune system, which affect the course and progression of the disease. There is a significant infiltration of kidney parenchyma by polymorphonuclear leukocytes, T- and B-lymphocytes, plasma cells together with inhibition of the functional activity of neutrophils, natural killer cells and disruption in immunoregulatory mechanisms of immune response (Kline et al., 2012; Lacerda et al., 2020).

Among the non-specific protective factors, the most important role in the immune protection of the body against infectious agents belongs to phagocytosis. Insufficient phagocytic activity of neutrophils is the most important factor in pathogenesis of urogenital inflammatory diseases

(Kroken et al., 2019; Mortimer et al., 2017). When phagocytosis is disturbed, there is persistence of bacteria that cause inflammatory changes in kidneys. Defects of phagocytic protection in kidneys infectious and inflammatory diseases are considered as one of the conditions for development of chronic inflammation. Information about the state of humoral immunity in chronic pyelonephritis in the stage of exacerbation during pregnancy is contradictory, but most international experts note that the active stage of pyelonephritis is accompanied by a decrease in B-lymphocytes content. A decrease in the level of immunoglobulins (IgG and IgA) in the peripheral blood is considered an immunodeficiency that requires correction. With chronic pyelonephritis in pregnant women, the content of other humoral indicators of protection also changes: lysozyme [1], complement, circulating immune complexes. In women with frequent relapses of chronic pyelonephritis during pregnancy, in addition to low indicators of T cells in the general pool and their functional activity, a deficiency of certain subpopulations of lymphocytes is noted. At the same time, a decrease in immunoregulatory index is observed due to an increase in the number of cytotoxic T cells. The above mentioned allows us to conclude that there is a deficiency of quantitative and functional indicators of the T-chain of immunity in exalation of chronic pyelonephritis during pregnancy. As the cause of cellular immunity suppression some scientists name the previous immunodeficiency, which increases during disease in pregnancy, especially in the third trimester; others consider that the defects in phagocytosis, when the slow elimination of bacteria leads to antigenic hyperstimulation, suppress cellular link of immunity. Prolonged inflammatory process leads to sclerosing of kidney tissue, impaired kidney concentration ability. It is possible to develop hypertension and kidney failure (Bookstaver et al., 2015; Nielubowicz et al., 2010), which can cause the development of various complications in pregnancy and childbirth.

Women with chronic inflammatory diseases of the genitourinary system often develop various complications during pregnancy and childbirth (Kumar et al., 2022). These complications may be placental insufficiency, fetal distress, intrauterine fetal development delay, intrauterine infection of fetus, premature birth, premature rupture of fetal membranes, etc. (Tsyupa, 2018).

Chronic infectious and inflammatory diseases of genitourinary system in mothers are factors that damage fetus and newborn kidneys. The conducted studies indicate the frequent development of an infectious-inflammatory process in kidneys in such newborns, which is explained by

the morpho-functional immaturity of this organ and immaturity of local immunity (Khalesi et al., 2014; Kazemier et al., 2015; Sorokina et al., 2018).

Maternal chronic inflammatory diseases of the genitourinary system cause dysfunction of immune system, development of systemic inflammation and kidney damage in newborn (Pedersen et al., 2019). Maternal endotoxemia in *Escherichia coli* experimentally induced infection of urinary system leads to proteinuria, excessive collagen deposition and development of sclerotic changes in the kidneys (Farias et al., 2020). Maternal infectious-inflammatory process in genitourinary system can act as one of the factors that damages embryogenesis of kidneys at organ, tissue and subcellular levels. Studies have shown an increase in case number of kidneys and urinary tract congenital abnormalities among children exposed to such maternal pathology in utero (Arima et al., 2018).

The presence of pyelonephritis in pregnant woman is accompanied by inflammatory changes in placenta, development of intrauterine infection and manifestations of endogenous intoxication with hypoxic and toxic damage in fetus kidneys (Schneeberger et al., 2013; Smaill et al., 2015). In addition, antimicrobials prescribed treatment of pregnant women are dangerous for the child's future (Sihra et al., 2018). It has been established that the frequency of nephropathy in children born from mothers who suffered with pyelonephritis during pregnancy is in 20 times higher than in the general population (Mortimer et al., 2017; Pathak et al., 2013).

The results of Ukrainian and European research indicate that chronic inflammatory diseases of mother's genitourinary system are a damaging factor that leads to development of kidney pathology in children at various stages of ontogenesis. In order to prevent the development of nephropathology in children, it is absolutely necessary to carry out, firstly, measures directed to prevent the development of urogenital inflammatory diseases in women of reproductive age, and secondly, in-time detection and treatment of the specified pathology in this category of persons.

The modern strategy in prevention and treatment of urogenital infection of pregnant women involves a multidisciplinary approach with the involvement of specialists from various fields. Increasing the effectiveness of therapy in women with urogenital infection will contribute to the comprehensive management of woman at all stages of pregnancy and will include the optimization of antibacterial therapy (Guo et al., 2018; Widmer et al., 2015), the restoration of urine passage in development of

urinary tract obstruction and prevention of fetoplacental insufficiency formation.

The rational construction of antibacterial therapy means taking into account the indications for its appointment, the sensitivity of pathogen isolated from the urine, the safety profile of drugs, the time of initiation and duration of treatment, namely the application of all the principles of prescribing antimicrobial drugs (Juralowicz et al., 2020; Shrestha et al., 2019).

Adherence to algorithm of women examination, dynamic observation from early gestation, in-time inpatient examination and complex treatment depending on the severity of the disease, prevention of relapses, as well as prevention and treatment of pregnancy complications will contribute to an optimistic prognosis regarding the healthy start of child's life (Moore et al., 2018; Sathiananthamoorthy et al., 2019).

The use of preventive technologies in modern medical practice helps to avoid fetus infection, but the influence of pathogen's virulence factors on development of pathological process in tissues of various organs is an urgent problem.

The course and outcome of infectious process are determined by a complex of interactions between causative agents of urogenital infection and macroorganism, and the mechanism of chronicity is determined by pathogen's heterogeneous properties, routes of infection and is related to host immune system, on correct functioning of which directly depends an outcome of disease both in mother and in child.

A practical solution to this problem can be implemented only with a comprehensive and in-depth study of features in interactions of components of "mother-placenta-fetus" system and the creation of an algorithm for necessary diagnostic procedures and a system of preventive measures to avoid development of intrauterine kidney pathology, and for this it is necessary to study the risks of pathological process in fetus using an interdisciplinary approach: to study the state of microbiome in pregnant women, factors of pathogenicity and virulence in urogenital pathogens and the impact on development of pathological process in fetus, determination of kidney-specific enzymes, the state of cellular and humoral immunity, cytokine balance and many other indexes.

Thus, the presence of chronic inflammatory diseases of the genitourinary system in pregnant woman is an unfavorable background in course of pregnancy, on which the possibilities of adaptative mechanisms are reduced or limited, various complications of pregnancy arise and fetus

kidneys morpho-functional state changes. And this in future will lead to development of various kidney pathologies. In order to prevent the development of kidney pathology in children, to carry out in-time diagnostic and treatment measures, an urgent question today is understanding of key pathophysiological mechanisms of influence of various negative factors during the intrauterine period when nephrogenesis occurs.

4.8. The impact of COVID-19 on the national economy: trends and prospects for achieving the state of resilience of the medical and social welfare system of the population³

The outbreak of the new virus occurred in December 2019 in China, from where it began to spread to all continents. On March 11, 2020, WHO stated that COVID-19 as a global pandemic. It changed the socioeconomic development of the world's countries, the medical and social welfare of the population, economic, institutional-political, financial-budgetary and education. Due to quarantine restrictions and lockdowns, the economic growth of most countries has slowed down significantly.

Many pharmaceutical campaigns changed their vector of development in the direction of inventing an effective vaccine that would avoid catastrophic economic and social consequences. For example, China's economic growth slowed to 4.5% in the first quarter of 2020, down from 6% in the fourth quarter of 2019. Stock market indices fell in America, Europe and the countries of the Asia-Pacific region. Oil prices fell significantly, which was due to a reduction in demand for it, in particular from China, as one of the main importers. A slowdown in the development of the metal market was observed: in mid-January 2020, it "slugged" by 7.1%. The copper index fell by 10.4%, nickel by 8.7%, tin by 8.2%, zinc by 7.3%, lead by 4.6%, and aluminum by 3.5%. A shortage of products and components from China, the basis for the production of complete products of foreign companies, began to be felt. The revenues of

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