I. РАВНОСТОЙНИ НА МОНОГРАФИЧЕН ТРУД НАУЧНИ ПУБЛИКАЦИИ

Глави от книги на международни издателства:


Vitamin B12 is a water soluble vitamin and important micronutrient with critical role in DNA, protein and lipid synthesis. It is responsible for one-carbon metabolism and cell division of nervous and hematopoietic cells. Among its various functions, the role as immunomodulator in cellular immunity, especially in elevating the number of CD8+ cells and NK cells attracts scientific interest. Many alternative anticancer and antiinflammatory treatments involve use of B12 together with other vitamins and nutrients, but still the scientific information is too obscure and insufficient. Controversial data link tumorigenesis with either increased or decreased B12 blood levels in different types of cancer. Dietary intake and additional supplement with the vitamin do not protect against cancer risk, but the dominant opinion is to integrate B12 as part of rational and healthy nutrition to ensure proper function of the immune system. This chapter will review in brief the most important facts for vitamin B12 functions and properties. We will try also to present in concise way the human immune system and the exact role of B12 in immune activity with emphasis on the questionable participation of vitamin B12 in the process of carcinogenesis and its significance as anticancer immunotherapy.


Tuberculosis (TB) and HIV/AIDS infection are one of the most ubiquitous and deadliest communicable diseases in the world. They cause millions of deaths each year and are recognized as major threats for public health worldwide. The corresponding pathogens (*Mycobacterium tuberculosis* and HIV) share overlapping epidemiology – they affect low-income countries and place an immense burden on their feeble health care systems. Over the last decades, the natural history of both diseases has changed: in addition to devastating single HIV and TB infections, the coinfection with both pathogens has emerged and has spread in pandemic scale. When present as dual infection in an individual, *Mycobacterium tuberculosis* and HIV potentiate each other and kill in cooperation the host. TB is the leading cause of death in HIV-positive patients and in turn HIV infection is the strongest risk factor for the development of new or reactivation of dormant TB disease. Both pathogens (as single or dual infection) provoke a robust
immune response in the infected host but the immune system does not achieve to eliminate the infectious agent(s). The failure of immune defense results in vulnerable immune balance between the micro- and the macroorganism and often ends up in a fatal outcome.

**Публикации в международни списания с импакт фактор (Thomson Reuters):**


Syphilis is a sexually transmitted disease with continuously rising rates among European countries. The vertical (mother to child) transmission is an important way of dissemination, often leading to stillbirth and permanent impairment of the newborn. We present a retrospective cross-sectional analysis of 2702 pregnant women tested for syphilis seropositivity. During the study period (2009-2013) non-specific and specific treponemal antibodies were detected in 15 pregnant women (0.56% of sample size with 95% confidence interval (CI) 0.28-0.84). Our results showed a lack of correlation between syphilis seropositivity and age, ethnic origin, or pregnancy trimester of the mother. The only factor found to influence syphilis seropositivity was the mother’s place of residence – rural inhabitants had significantly higher risk for syphilis infection when compared to urban inhabitants, with a seropositive proportion of 1.08% versus 0.36%, respectively.


The aim of the present study was to assess the prevalence of hepatitis B surface antigen among pregnant women in Varna Region, Bulgaria. During the period 2009-2013, an average prevalence of 2.26% (95% CI 1.75, 2.91) was measured in a total number of 2700 samples. Analysis demonstrated that rural residence and minority ethnic origin are important risk factors for hepatitis B infection among pregnant women with relative increase in the prevalence of 2.40 (95% CI 1.46, 3.94) and 2.43 (95% CI 1.46, 4.05) when compared with urban residence and ethnic majority origin respectively.


The response of *Saccharomyces cerevisiae* to arsenic involves a large ensemble of genes, many of which are associated with glutathione-related metabolism. The role of the glutathione S-transferase (GST) product of the *URE2* gene involved in resistance of *S. cerevisiae* to a broad range of heavy metals was investigated. Glutathione peroxidase activity, previously reported for the Ure2p protein, was unaffected in cell-free extracts of an *ure2Δ* mutant of *S. cerevisiae*. Glutathione levels in the *ure2Δ* mutant were lowered about threefold compared to the isogenic wild-type strain but, as in the wild-type strain, increased 2–2.5-fold upon addition of either arsenate (AsV) or arsenite (AsIII). However, lack of *URE2* specifically caused sensitivity to arsenite but not to arsenate. The protective role of
URE2 against arsenite depended solely on the GST encoding 3'-end portion of the gene. The nitrogen source used for growth was suggested to be an important determinant of arsenite toxicity, in keeping with non-enzymatic roles of the URE2 gene product in GATA-type regulation.


Growth of Saccharomyces cerevisiae ure2Δ mutant strain was investigated in the presence of diverse oxidant compounds. The inability of the strain to grow on a medium supplemented with H₂O₂ was confirmed and a relationship between diminishing levels of glutathione (GSH) and peroxide sensitivity was established. Data for the lack of significant effect of URE2 disruption on the cellular growth in the presence of paraquat and menadione were obtained. The possible role of Ure2p in acquiring sensitivity to oxidative stress by means of its regulatory role in the GATA signal transduction pathway was discussed. It was suggested that the susceptibility of ure2Δ mutant to the exogenous hydrogen peroxide can result from increased GSH degradation due to the deregulated localization of the γ-glutamyl transpeptidase activating factors Gln3/Gat1. The important role of Ure2p in in vivo glutathione-mediated reactive oxygen species (ROS) scavenging was shown by measuring the activity of antioxidant enzymes glutathione peroxidase, superoxide dismutase (SOD) and catalase in an URE2 disrupted strain. A time-dependent increase in SOD and catalase activity was observed. More importantly, it was shown that the ure2 mutation could cause significant disturbance in cellular oxidant balance and increased ROS level.

7. Zamfirova D., Todorova T. T., Hristozova Ts., Nedeva T., Michailova L., Kujumdzieva A. (2003) Influence of glucose repression on antioxidant enzyme system in mutant strain Hansenula polymorpha DOG R13, Biotechnology & Biotechnological Equipment, 17(2) (ISSN 1310-2818; IF 0.055; цитирана 3 пъти)

A mutant of the methylotrophic yeast Hansenula polymorpha DOG R13 was studied during cultivation on methanol and glucose. DOG R13 with constitutive methanol oxidase and peroxisome biosynthesis was obtained after UV treatment of the parent strain CBS 4732. The ability to grow on 2-deoxy-D-glucose suggested that this strain is less sensitive to glucose repression which was proved in our experiment. For that purpose the methanol oxidase (MOX), a key enzyme in the methanol metabolism and catalase (CAT) and superoxide dismutase (SOD) involved in the antioxidant enzyme system were assayed during different conditions of growth. The parent strain Hansenula polymorpha CBS 4732 was used as a control. During cultivation on methanol, high activity of the three enzymes was detected. Transfer of methanol grown culture to a medium with high glucose concentration (YNB + 10% glucose) caused significant decrease of MOX activity, especially in the parent strain. The antioxidand enzymes SOD and CAT showed different tendency. SOD activity remained high, while CAT activity followed the dynamic of MOX and decreased. This was less in DOG13 compared with the parent strain. During derepression a moderate increase of MOX was determined, although the absence of inducer methanol. SOD activity remained high during this process and CAT was elevated compared with the repressed culture. These findings were proved with the fine structure
analysis, showing typical peroxisomes and their morphology at different cultivation conditions.

Публикации в международни списания с SJR фактор (Scopus):


Hepatitis A virus (HAV) infection is an acute, self-limited liver disease transmitted usually through the faecal-oral route via person-to-person contact. Bulgaria has intermediate HAV endemicity with higher susceptibility among adults and recurrent outbreaks. As HAV infection is strongly related to human movements and represents a significant risk to travelers and migrants, as well as to local population receiving these groups, we set out to analyze the epidemiological data on hepatitis A in five of the largest tourist border regions of Bulgaria located in its eastern part: Varna, Shumen, Dobrich, Burgas and Yambol. We reviewed retrospectively all reported cases of acute hepatitis A in the eastern regions of Bulgaria over a 7-year period between 2008 and 2014. A total of 2879 newly infected patients were registered during the study period, the number varying widely: from 190 cases in 2014 to 923 in 2012. The average incidence of HAV was higher in the southeastern regions than in the northeastern regions (55.30%00 vs 15.04%000 respectively, p < 0.0001). The most affected age group in all regions was the 5-9-year olds (p < 0.0001) and males were significantly more susceptible to HAV (p = 0.02). Hepatitis A is still a major public health problem in Bulgaria; there is a significant difference in the incidence of the disease between the regions in the south-east and those in the north-east and between the different age groups and sexes.

Публикации в международни списания без импакт фактор:


The recent outbreak of Ebola viral disease in West Africa was the largest ever recorded in human history. Thousands of people lost their lives or families, three entire countries have totally collapsed and will need decades to restore their economics and health systems. Now, when recapitulate the last two years, we need to providethe correct answers of why and how this outbreak happened. It’a time to give a new meaning to our nature-deteriorating activities threatening in many cases our own health and well-being.

II. НАУЧНИ ПУБЛИКАЦИИ, СВЪРЗАНИ С ПРИСЪЖДАНЕ НА ОНС „ДОКТОР”

Дисертационен труд:


Glutathione S-transferases (GSTs) represent a family of detoxification enzymes that play an important role in toxicant resistance in both prokaryotic and eukaryotic organisms. Their
action is a crucial component of cellular responses to environmental pollutants, carcinogens, drugs, and products of oxidative stress. Members of the family can act as peroxidases, isomerases or thiol transferases. In addition, some GSTs plays a role in the modulation of cellular signal transduction, most notably inhibiting two of the major regulatory cascades in the eukaryotic cells, GATA regulation in yeast and JNK signaling in mammals.

The first yeast GST on which the present thesis has focused, Tef4p, is a homologue of elongation factor EF1Bγ. Yeast elongation factor 1 comprises subunits EF1A, EF1Bα, and EF1Bγ. Unlike EF1A and EF1Bα, neither homologue of EF1Bγ (encoded by TEF3 and TEF4) is essential for yeast. In this work, sensitivity to As(V), H₂O₂ and CDNB, as well as decreased glutathione levels were observed for the tef4Δ mutant, indicating a possible role of Tef4p in arsenate, oxidant and organohalogens detoxification. In contrast, the tef3Δ mutant was not sensitive to these toxic compounds. These phenotypes of tef4Δ mutant could be explained by two alternative hypotheses: (1) Tef4p is a GST with enzymatic activity, or (2), Tef4p plays a yet unknown role in glutathione metabolism. However, attempts to complement the phenotypes of the tef4Δ mutant with an expression vector containing a copy of the TEF4 gene were unsuccessful and, we were unable to confirm that the observed phenotype was a direct result of TEF4 disruption. Future work should therefore involve the isolation and purification of Tef4p and Tef3p as recombinant proteins, in order to assess the pertinence of these two hypotheses.

The other yeast GST, investigated in this work, the protein Ure2 of Saccharomyces cerevisiae is a GST homologue with multisubstrate glutathione-dependent peroxidase activity. It is also a precursor of the yeast prion [URE3], and is a major negative regulator of the GATA transcription factors. In this work, we have presented evidence that Ure2p is also required for the detoxification of trivalent arsenic in S. cerevisiae. The protective role of Ure2p against arsenite is determined by the C-terminal domain of the protein, which displays GST similarity and determines GATA factor regulation role. This raises the question as to whether this effect derives from enzymatic Ure2p action (as GST) or, alternatively, from the direct or indirect GATA-type regulation of one or more genes whose products are implicated in the arsenic stress response. The data presented in this thesis suggest that Ure2p is implicated in arsenite transport by regulating the expression of FPS1 gene (coding for the main arsenite transporter) in yeast. The previously reported glutathione peroxidase activity of Ure2p, the decreased level of reduced glutathione in the ure2Δ mutant, as well as the inhibitory function of Ure2p in the expression of enzyme for non-preferred nitrogen assimilation do not seem to have an effect on arsenic sensitivity of the disruption mutant. GATA transduction has been implicated in glutathione degradation since GATA factors and Ure2p regulate the expression of the CIS2 gene which encodes γ-glutamyl transpeptidase, the first enzyme in glutathione degradation. The resulting decreased glutathione content in the ure2Δ mutant thus probably determines the observed sensitivity of the ure2Δ disruption mutant to hydrogen peroxide. The results presented here raise intriguing questions regarding the GST-dependent regulation of cellular signaling. Previously, URE2 disruption mutants have been shown by others to be sensitive to a broad series of toxic agents (Al, As, Cr, Se, Cd, Ni, Co, Cu, Fe, Ag, Hg, H₂O₂, diamide, cumene hydroperoxide and t-butyl hydroperoxide). These toxicants are GST substrates, so that the sensitivity of ure2Δ mutant argues in favor of Ure2 being a glutathione S-transferase. Nevertheless, studies so far have not unequivocally distinguished whether the ure2Δ mutant phenotype is a direct or indirect effect of the absence of expression of URE2. Our data demonstrate that the effect of URE2 disruption
to arsenic and peroxide resistance is a result of the loss of the negative Ure2p regulation of Gat1p and/or Gln3p transcription factors, which are pleiotropic regulators and possibly involved in arsenic and peroxide detoxification. The exact GATA regulation mechanism of arsenite uptake in yeast remains, however, to be clarified. Which of the known GATA factors are implicated in this regulation? Another interesting question is the nature of the primary signal event. While the mechanism of Ure2/GATA factor interaction has been clarified, the mechanism of signal transmission upstream of formation of the complex Ure2p-Gln3 is still unknown. Importantly, arsenite transport is a newcomer in GATA regulated processes in S. cerevisiae. This not only expands the scope of GATA regulated processes far beyond nitrogen assimilation, but also raises the question “How such different physiological processes can be fine-regulated using one mechanism?”.

Публикации, представени за придобиване на ОНС „Доктор“:

11. Todorova T. T., Vuilleumier S., Kujumdzieva A. V., (2007) Role of glutathione S-transferases and glutathione in arsenic and peroxide resistance in Saccharomyces cerevisiae: a reverse genetic analysis approach, Biotechnology & Biotechnological Equipment, 21/3 (ISSN 1310-2818; SJR 0.131; цитирана 8 пъти)

Glutathione S-transferases (GSTs) define an enzyme family of multifunctional proteins with important roles in cellular detoxification of exogenous and endogenous compounds. The availability of the complete genome sequence and of disruption mutants for all genes/ORFs of Saccharomyces cerevisiae facilitates genome-wide experimental approaches for the detailed understanding of eukaryotic detoxification pathways. In this work, the role of glutathione metabolism and in particular the specific requirement for GSTs for adaptation to oxidative and arsenic stresses in S. cerevisiae was evaluated by screening of a wide selection of genespecific disruption mutants from the EUROSCARF collection.

III. НАУЧНИ ПУБЛИКАЦИИ, НЕСВЪРЗАНИ С ПРИСЪЖДАНЕ НА ОНС „ДОКТОР”

Публикации в международни списания:


Mumps is a viral childhood infection that is vaccine-preventable. The applied routine vaccination is safe and highly effective in reducing disease incidence. The purpose of the present work is to investigate the epidemiology of mumps in Varna region from 2011 to 2015. We performed a retrospective analysis using report data of Regional Health Inspectorate – Varna for the period 2011-2015. During the specified 5-year period a decrease in incidence rate of epidemic mumps has been observed in Varna. Disease affected all age groups (124 cases in total), but the incidence rate was the highest in 5-9-year-old (37 cases) followed by the group of children of 1-4 years of age (27 cases in total). Cases have been recorded during all months of the year but peaks were registered in November (18 cases), February (17 cases) and May (17 cases). To minimize the susceptible population and to eliminate the disease, high MMR (measles-mumps-rubella) vaccine coverage must be maintained in the society.
Territorial inequality in health-care services is an important problem worldwide. A complete study of the correlation between the inequalities and the territorial disproportion of the health services is required, as this will ensure a scientifically based model for improvement of the access to health services. The aim of the current work is to analyze the patients’ satisfaction with the territorial distribution of medical-diagnostic services and to prepare a cartogram of the observed differences in the northeastern region of Bulgaria. Between July and September 2015 we studied 502 patients from 30 municipalities situated in Northeastern Bulgaria about their opinion for the number of accessible medical diagnostic laboratories. We also drew a visual presentation of the spatial distribution of medical diagnostic laboratories in the region. Laboratories in Northeastern Bulgaria are unequally distributed and mainly concentrated in the regional centers and larger towns. Accordingly, most of the patients living up to 3 km from a medical diagnostic laboratory were satisfied from the number of available labs, while people living 3-10 km apart thought that laboratories are not enough. The main reason for health inequalities in Bulgaria is the territorial imbalance between health care units. The increased need of health care and social assistance requires new resources to provide laboratory services via mobile lab offices and home visits. A better infrastructure of the outpatient health care in Northeastern Bulgaria and new players in the lab service market will assure equal access and favorable concurrent environment.

With the continuously growing number of people using online sources for health information and services, the concept of eHealth is progressively developing and it is a high-priority topic for the European Union. The absence of centralized internet-based eHealth platform in Bulgaria results in deficiency in the information exchange among physicians and other healthcare providers. The question about the readiness and the attitude towards the eHealth concept among all participants in the healthcare system in Bulgaria still remains to be clarified and the purpose of the current study is to assess the opinion of healthcare providers and consumers about the electronic way of receiving laboratory test results. We also try to explore the existing preference trend in relation to the socio-demographic characteristics of the studied population. In the current work, we investigated the needs and recommendations of 1039 patients, laboratory staff and out-of-hospital general practitioners in Northeastern Bulgaria (regions of Varna, Dobrich and Shumen). The results show that laboratory results are preferred in electronic form and there is a significant need for better online communication between different participants in the healthcare system. In this context, we also summarize a model for improvement in the interaction among healthcare providers. The actual opportunities for online communication provoke active participation of all players in the health service market and require a novel model of communication among healthcare providers.

The prevalence of cytomegalovirus (CMV) infections is between 50% and 85% in adults in different parts of the world. Its epidemiology varies on socioeconomic and age groups. The present retrospective study has been performed to determine the seroprevalence of CMV among the population in North-Eastern Bulgaria. For the period 2003–2015, the prevalence of individuals with antibodies to CMV was estimated, using indirect enzyme-linked immunosorbent assay (ELISA) to detect virus-specific IgG and IgM. The population sample included 7879 randomly chosen hospitalized patients of both sexes and different ages. The total seroprevalence of CMV was determined to be 78.4% (CI 95% 77.5; 79.3), and the relative proportion of acute CMV infections 22.9% (CI 95% 21.9; 23.7). The proportion of CMV IgG and IgM by sex and by age was also analysed. The results of the study reveal that CMV infection is highly prevalent among the population and occurs mainly in the first years of life.


Pertussis is an acute infectious disease, caused by *Bordetella pertussis*. Although an effective vaccination program exists in many countries, it is a wide-spread and highly contagious infection. In Varna Region, *B. pertussis* infection affects different age groups, but the incidence rate is highest in infants under 1 year (12 cases in total), following the group of children at 0-9 years of age (9 cases in total). During the period 2009-2014, a significant decrease in the immunization covering was detected, mainly due on irregular vaccine supply and anti-vaccination movement among parents.


Methicillin-resistant *Staphylococcus aureus* (MRSA) are bacteria, responsible for severe and hard-to-manage infections in human. They are resistant to beta-lactam antibiotics – penicillins (methicillin, dicloxacillin, nafcillin, and oxacillin), cephalosporins and carbapenems, but can also be resistant to the new-generation MRSA-active cephalosporins (such as ceftaroline) or other groups of antibiotics, including aminoglycosides, macrolides, clindamycin, amphenicols, quinolones and tetracyclines. MRSA bacteria are pandemic and are often isolated in medical practice and nosocomial infections. The MRSA detection is a challenge to any clinical microbiology laboratory and demands implementation of strict protocols for active screening. While more expensive molecular techniques have the potential of offering highly sensitive and rapid results, the cultural methods require longer time but can achieve a comparable sensitivity for lower price.

Zika virus (ZIKV) is an arbovirus from *Flaviviridae* family, genus *Flavivirus*. Like most of the viruses which belong to the *Flavivirus* genus, it replicates in and is transmitted by mosquitoes. Unlike other arbovirus infections including dengue and chikungunya, Zika virus causes a relatively mild disease. The most common symptoms of ZIKV are mild fever, arthralgia, myalgia, headache, asthenia, abdominal pain, oedema, lymphadenopathy, retro-orbital pain, conjunctivitis, and cutaneous maculopapular rash, which last for several days to a week. Although 80% of the cases with ZIKV are asymptomatic, severe complications such as microcephalia and GBS may be observed. This explains why ZIKV is more dangerous than it was thought to be and why it rapidly evolves in unexpected challenge for the international and national public health authorities.


Extended-spectrum beta-lactamase (ESBLs) producing bacteria are microorganisms which have the ability to hydrolyze β-lactame ring of a large part of the antibiotics, commonly used to treat bacterial infections including urinary tract infections. The aim of this study is present the epidemiology of childhood urinary tract infections caused by ESBL-producing strains in Varna, Bulgaria. A total of 3895 urine samples of children patients (aged 0 to 18 years) were examined during the period 2010-2012 for presence of ESBL-producing bacteria. Six percent of the tested urinary samples were positive for ESBL production. All of the isolates were resistant to ampicillin, piperacillin, cephalothin, cefprozil, cefuroxime, ceftriaxone, ceftazidime, levofloxacin, cefaclor, but were were sensitive to meropenem and imipenem. Cephalosporins and penicillins are the most used antibiotics in Bulgaria, but they should be very precisely prescribed in medical practice, because otherwise preconditions for maintaining high share of ESBLs are created.


*Listeria monocytogenes* may cross and proliferate in the placenta and cause severe infections during pregnancy. In pregnant women, listeriosis usually occurs during the third trimester, when cell-mediated immunity is reduced. Common results are abortion, stillbirth, intrauterine and/or neonatal infections. The patient described here was a newborn male, delivered by urgent cesarean section after chorioamnionitis in 33 weeks' gestation. Soon after the birth, the baby became high oxygen doze dependent with signs of pulmonary insufficiency. The blood tests have shown decreased level of lung perfusion and ventilation, significant hypoxemia and hypercarbia. *Listeria monocytogenes* was isolated from ear secretion, while blood culture and other peripheral samples were negative. The baby was discharged on the 20-th day of his birth with weight of 2000 g and normal lung and heart function. On follow-up visits at the clinic, he showed normal neurological status, cognitive function and vital signs.
Bulgaria is a country of moderate endemicity for hepatitis B infection with 3-7% of the general population chronically infected with the virus. Since 1991, an obligatory vaccination has been implemented for all healthy newborns. As a result, twenty years later, hepatitis B prevalence is significantly reduced but viral hepatitides still represent an important public health problem that needs to be addressed especially in some ethno-religious and regional groups. No recent published data are available about hepatitis B circulation in Bulgaria and in its Eastern part particularly. In the current study, we analyze the epidemiological data on hepatitis B cases in easternmost Bulgarian regions and try to determine the possible risk, which the infection poses to public health in these regions. We performed a retrospective analysis (2008-2014) using epidemiological data from the National surveillance system for hepatitis B notification. The incidence of acute hepatitis B in all considered regions has been durably decreasing for the last seven years: while in 2014 its total value was 9.69%000, in 2014 it reached a minimal rate of 3.09%000. We found that young individuals in their 20s years (the borderline generation before and after implementation of mandatory vaccination) are most vulnerable to hepatitis B. South regions are also more affected by hepatitis B infection when compared with regions on the North. We reported a stable downward trend in the incidence of hepatitis B infection in all studied regions of Bulgaria. This result can be directly linked with the presence of effective vaccination program at national level.

Epstein-Barr (EBV) is a widespread virus which can be detected in more than 90% of world population. Primary EBV infection during adolescence and adulthood results in infectious mononucleosis, while in children it is usually asymptomatic. EBV is responsible for different malignant forms of B-cell or epithelial cancers, such as Hodgkin’s and non-Hodgkin’s lymphoma, Burkitt’s lymphoma, post-transplant lymphoproliferative disorders, nasopharyngeal carcinoma, hairy leukoplaikia and HIV-associated lymphomas. Evidence exists that an infection with EBV is also linked with a higher risk of hepatocellular and gastric cancers, as well as autoimmune diseases. EBV shows two alternative life cycles – latent and lytic. After the primary infection, the virus remains in the B lymphocytes in latency, while the lytic infection takes place predominantly in the epithelial cells and can last for months with constant virus release in saliva and nasopharyngeal secretion. Unlike other herpes viruses, the development of oncological diseases is linked with the latent cycle, as a result of the immune response failure to control latently infected cells. With the present work we try to concisely review the current knowledge about mechanisms of EBV pathogenesis in humans and to summarize recent findings in the field.
and is considered to be uncommon rare pathogen for both immunocompetent and immunosuppressed individuals. Currently, pulmonary infections caused by *Mycobacterium peregrinum* are unusual and diagnosed only in limited number of cases. Here, we present a clinical case of elderly man (72 years) with 1 month history of non-specific respiratory symptomatic. The patient was without underlying immunosuppressive condition or lung disease. Chest X-ray demonstrated persistent pleural effusion, opacities and cavitations in the right lobe. One of the sputum cultures grew a rapidly growing mycobacterium and the isolated strain was found to be *Mycobacterium peregrinum* as identified by molecular genetic detection (PCR and DNA strip technology). To our knowledge, this is the third case in the world to report *Mycobacterium peregrinum* as a possible causative agent of pulmonary infection.


*Mycobacterium gordonae* is a slow growing mycobacterium usually found in soil, tap water, and as laboratory contaminant. It is occasionally implicated in different infections in immunosuppressed patients. In contrast, there have been few case reports of active infection in immunocompetent individuals. We report a case of a 46-old immunocompetent patient with long-term cough and poor expectoration. A computed tomography of the chest revealed punctiform lesions and fibrosis formation in the upper right lobe. It did not show any infiltrate in lung parenchyma. *Mycobacterium gordonae* was definitively diagnosed by genetic method. After antituberculosis treatment the toxic infectious syndrome was overcome. *Mycobacterium gordonae* is reported to cause clinically significant nontuberculosis infection in both immunocompetent and immunosuppressed individuals. *Mycobacterium gordonae* is hardly diagnosed with traditional laboratory methods, but the latest molecular techniques allow successful isolation and identification of slow growing *Mycobacterium gordonae*.


Hepatitis B (HBV) and hepatitis C viruses (HCV) are highly contagious and important occupational hazard for health workers. Dental practice often includes direct contact with patients’ body fluids and exposure at high degree to potentially HBV and HCV infected materials and instruments. The purpoe of this study is to investigate the level of knowledge about hepatitis B and C infections and the attitude towards hepatitis B virus vaccination among Dental Medicine students. A cross-sectional survey was conducted among 96 students of Faculty of Dental Medicine, Medical University of Varna in March, 2015. The questionnaire contained 22 questions divided into 4 major sections. SPSS ver.16 software package was used for statistical data processing. Most of the participants (82.3%) considered hepatitis B and C as serious diseases and had positive attitude towards HBV vaccination (75%). Almost 90% considered that dental practice could enhance the risk of infection with HBV and HCV. Unfortunately, only 57.4% of students knew their vaccination status and 13.9% had checked HBV antibodies level. The majority of respondents demonstrated a high level of knowledge of HBV and HCV infections. All
participants were aware about the risk of potential HBV and HCV transmission in their future practice and anticipated applying preventive measures at work. However, deeper information about HBV vaccination and checking anti HBs titer is still needed among dental students, as well continuous target education in the field.


Mammalian transmissible spongiform encephalopathies are uncommon and irreversible diseases caused by prions. Prions lack nucleic acid and can self-propagate by converting normal cell protein to isomeric prion form. In the pathogenesis of these diseases a long variable incubation period occurs, followed by progressive appearance of severe clinical symptoms and death. A major knowledge in the field of prions comes from studies on a functionally unrelated protein of yeast Saccharomyces cerevisiae – [URE3], which in normal state (Ure2p) possesses a variety of regulatory and enzymatic functions. Ure2p is a cytoplasmic homodimeric protein with structural homology to glutathione S-transferases and crucial role in nitrogen metabolism, oxidant protection and heavy metal resistance in yeast. In this work, we discuss the role of Ure2p to provide valuable information about protein infectivity, prion structure and functions.

27. Цанкова Д., Цанкова Г., Тодорова Т. Т., Ерменлиева Н., Добрев Б. (2016) Микрофлора на устната кухина при пациенти с фиксирани ортодонтски апарати – литературен обзор. Варненски медицински форум, 5(S3) (ISSN 2367-5519)

Устната микрофлора е сложна система, в която резидентната микрофлора се намира в динамично равновесие с постъпващите отвън патогени и хранителни елементи. Това равновесие може да бъде нарушено от редица фактори, сред които и наличието на фиксирани ортодонтски апарати, затрудняващи поддържането на добра хигиена на устната кухина и натрупване на зъбна плака. Целта на настоящия обзор е да се обобщат литературните данни относно влиянието на фиксираните ортодонтски апарати върху микрофлората на устната кухина. Някои проучвания съобщават за промяна в качеството и количеството на оралната микрофлора след ортодонтско лечение, например увеличено количество на Streptococcus mutans, Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, участващи в развитието на пародонтит. Това налага при пациенти с продължително носене на фиксирани ортодонтски апарати да се провежда микробиологично изследване на оралната микрофлора с цел превенция на развитието на възпалителни процеси в устната кухина.

28. Ерменлиева Н., Тодорова Т. Т., Цанкова Г., Георгиева Е., Янакиея Т., Велкова М., Ростамлоо М., Николова Д., Цанкова Д. (2016) Ботулинов невротоксин – биохимични аспекти и механизм на действие (литературен обзор). Варненски медицински форум, 5(S3) (ISSN 2367-5519)

Ботулиновият невротоксин (BoNT) е една от най-силените биологични субстанции, познати на човечеството. Продуцира се от спорообразуващи анаеробни бактерии
**Clostridium botulinum**, които причиняват заболяването ботулизъм. BoNT блокира освобождаването на невротрансмитера ацетилхолин, провеждащ нервните импулси до мускулните влакна. По този начин токсинът косвено предизвиква мускулна паразла. Тази негова животозастрашаваща способност обаче се оказва изключително ефективна при терапия на редица заболявания, свързани с аномална хиперактивация на мускули и жлези, естетически корекции на глаберални бръчки и други. Известни са девет серотипа на BoNT, наименувани с латинските букви от A - Н (BoNT-C е разделен на два типа), като типовете А, В, Е и F причиняват ботулизъм при човека. Според някои автори са изследвани и изолати от хора, съдържащи BoNT-G. Изследват се и редица нови направления в медицинската практика, където BoNT може да се приложи ефективно: детска церебрална параплиза, хронични анални фисури, урологични смуления и други.

29. Ерменлиева Н., Костадинова Цв., Георгиева Е., Мехмед Х., Асенова В., Петрова М., Цанкова Г., Цанкова Д., Тодорова Т. Т. (2016) Препарати, съдържащи ботулинов невротоксин и приложението им за естетически цели (литературен обзор). Варненски медицински форум, 5(S3) (ISSN 2367-5519)

Ботулиновият токсин (BoNT) е една от най-токсичните биологични субстанции, известни за човечеството. Представлява невротоксин, продуциран от бактерии от род *Clostridium*, причиняващи заболяването ботулизъм. Появата на бръчки по лицето се дължи не само на стареене на кожата. Някои бръчки и неестетически изражения на лицето са резултат от свръхактивност на лицевата мускулатура. Успехът при приложението на BoNT като селективен депресор на активността на скелетната мускулатура води до широкото му приложение при изглаждането на бръчки. На световния пазар съществува разнообразие от продукти, съдържащи BoNT за козметично приложение, които са получили одобрение от регулаторните органи или са в процес на разработка. Към момента Botox® дава дял от 85% от световния пазар на продукти, съдържащи BoNT. Други продукти на световния пазар с по-ограничено приложение са Dysport®, Xeomin®, Myobloc®, Prosigne® и други. По данни на редица изследвания приложението на BoNT се отличава с висока ефективност и безопасност. Нежеланите ефекти са рядкост и са обратими. Най-сериозните неблагоприятни ефекти са временно слабост (паразла на близката мускулатура), времена птоза на горния клепач или челото (1-3% от пациентите). Параплиничния ефект след инжектиране с BoNT е със средна продължителност три месеца. За поддържане на ефективността са необходими допълнителни приеми на BoNT-препарат на равни интервали.

30. Ерменлиева Н., Цанкова Г., Тодорова Т. Т., Костадинова Ц., Георгиева Е. (2016) Детекция на полирезистентни ESBL-щамове. Едно от предизвикателствата пред съвременната медицина, Мединфо, 10 (ISSN 1314-0345)

Поради просто та устройство бактериите са размножават в рамките само на няколко минути. Така те бързо и адекватно се приспособяват към заобикалящата ги среда. Тези от тях, които заради промяната в генотипа (мутации) преживяват атаката с антибиотици, предават генетичните си качества на следващите поколения или могат да разменят променената вече генетична информация с други
бактериални щамове. Възникването, разпространението и селекцията на резистентни бактерии застрашават човешкото здраве, защото:

- Инфекциите с резистентни бактерии водят до нарастване на заболяемостта и смъртността на пациентите, както и до увеличаване на продължителността на болничния престой на хоспитализираниите такива.
- Антибиотичната резистентност често води до отлагане на подходяща антибиотична терапия.
- Неподходящата или отложената антибиотична терапия при пациенти с тежки инфекции може да доведе до нежелан изход и дори до тяхната смърт.

31. Тодорова Т. Т., Цанкова Г., Георгиева Е., Лодозова Н. (2015) Епидемиология на заболяванията от варицела в Област Варна през първата половина на 2015, Варненски медицински форум, 4(3) (ISSN 2367-5519)

Варицелата (пещенка) е широко разпространено инфекциозно заболяване, причинявано от Varicella Zoster Virus (VZV). Вирусът атакува предимно малки деца (на възраст 5-10 години), но всички възрастови групи, независимо от пол или националност са уязвими. В държави, с въведена задължителна имунизационна програма, епидемиологията на варицелата се променя значително, като се редуцират както заболяваемостта, така и възможните усложнения, хоспипализации и смъртни случаи при деца и в общата популация. За съжаление, в България, както в повечето Европейски страни, задължителна имунизация срещу VZV не съществува. Поради огромната контагиозност, дължаща се на високо основно peпродуктивно число от 12-18, близо 100% от българската популация се заразява с варицела в даден момент от живота си. Това често довежда до сериозни усложнения и инвалидизация. Целта на настоящето изследване е да проучи настоящия епидемиологичен взрив на варицела в страната, и в частност във Варна. Броят на заболяванията, отчетени през януари е 315, броят им значително започва да намалява през май и достига минимум през юни. Епидемията обхваща повече от 1431 лица в Област Варна, като следва бимодално разпределение с пик през януари и април. Област Варна е една от най-големите области в страната с висока гъстota на населението, по-голяма част, от което е урбанизирано. Следователно, рискът от заразни заболявания е много висок. Това е причината, областта да бъде една от най-засегнатите от настоящата варицелна епидемия.

32. Цанкова Д., Цанкова Г., Костадинова Ц., Тодорова Т. Т. (2015) Въздействие на меда от манука върху някои бактерии от микрофлората на устната кухина, Варненски медицински форум, 4(3) (ISSN 2367-5519)

Използван в древната медицинска практика за лечение на рани, пептични язви, бактериални гастроентерити и офталмологични инфекции, днес медът отново е въведен като средство в модерната медицина. Той има и своиства, свързани с лекуването на периодонтит и гингивит. Антимикробното действие на меда от манука се счита, че се дължи изцяло на осмотичния ефект на високото му захарно съдържимо. Медът може да разруши биофилма на P.gingivalis. Някои изследвания показват, че броят на P.gingivalis, L.acidophilus и S.mutans значително намалява след консумация на мед. Освен това медът не само спира растежа на бактериите от
зъбната плака, но също така намалява и количеството на произведената киселина, което пречи на бактериите да произвеждат декстран. Друго проучване показва, че оралното приложение на прополиса намалява загубата на кост от алвеоларния израствък, предизвикана от периодонтит при плъхове. В заключение може да се каже, че медът или неговите компоненти, добавени към продуктите за поддържане на оралното здраве, могат да имат ефект в превенцията и лечението на периодонтита.

33. Цанкова Г., Тодорова Т. Т., Георгиева Е., Лодозова Н. (2015) Възможна специфична профилактика на ротавирусни инфекции при новородени, Варненски медицински форум, 4(S3) (ISSN 2367-5519)

Ротавирусните инфекции са най-честата причина за тежък остър гастроентерит при кърмачета и деца в ранна детска възраст, като засягат 95% от неваксинираните деца на възраст до 5 години. В страните от Европейския съюз всяка година от ротавирусни инфекции боледуват почти 3 600 000 деца. В България по данни на НЦЗПБ за първите 6 месеца на 2015 г. са регистрирани 612 ротавирусни гастроентерити. Основният метод за контрол на ротавирусните инфекции е въвеждане на задължителни или препоръчителни ваксинални програми при деца до 6-месечна възраст. След проведени широкомасштабни проучвания през 2006 г. срещу ротавирусни гастроентерити за приложение са одобрени две живи перорални ваксини: Rotarix и RotaTeq, които се различават по антигенна структура и имунизационна схема. Масовата имунизация с тях е въведена в 49 страни, сред които САЩ, Австралия, Великобритания, Белгия, Норвегия. У нас от януари 2010 г. с Наредба №15 за имунизациите в Република България прилагането на ротавирусните ваксини е включено в списъка на препоръчителните имунизации. Важен елемент от борбата с ротавирусните инфекции е разработване и внедряване на Национална програма за контрол и лечение на ротавирусни гастроентерити за периода 2015-2019 г.

34. Цанкова Г., Костадинова Цв., Лодозова Н., Георгиева Ем., Тодорова Т. Т. (2014) Оценка на имунния статус на жени в детеродна възраст срещу вируса на рубеола във Варненска област, Варненски медицински форум, 3(S4) (ISSN 2367-5519)

Рубеола е остро инфекциозно заболяване, което се причинява от Rubella virus. Характеризиращ се с леко протичане при децата и широко епидемично разпространение. Въпреки, че рубеолата е позната отдавна, интересът към нея и социалното й значение нарастваат след 1941 г., когато офталмолог Норман Макалистър Грег установява, че вирусът може да предизвика различни увреждания на плода, известни като конгенитален рубеолен синдром (КРС). След въвеждане на противорубеолната ваксина броят на децата с конгенитален рубеолен синдром рязко намалява, но докато има страни с ендемично разпространение, той ще продължава да бъде проблем за общественото здравеопазване. Целта е обобщаване и анализиране на данни от проведено серологично проучване за наличие на защитни антитела към рубеолния вирус при жени в детеродна възраст в град Вarna и областта. Проучването обхваща 710 жени на възраст от 18 до 40 години. Серологичното изследване е извършено с китове VIR-ELISA anti Rubella IgG за количествено определяне на анти-рубеолни антитела от клас IgG. От всичките 710 изследвани лица 41 (5.77%) са серонегативни към рубеолния вирус.
Възрастовото разпределение на серонегативните проби показа, че най-висок е относителният дял на незащитените (6.63%) сред жените на възраст от 21-30 години. Разпространението на рубеолния вирус в някои страни по света, увеличената миграция на хора, наличието на незащитена популация от жени в детеродна възраст, тежките увреждания на плода налагат определянето на титъра на специфичните IgG антитела да се въведе като задължително изследване още при първото посещение на бременната в женската консултация.

35. Тодорова Т. Т., Тачева Д., Владимиров Я. (2008) Зависимост между стандартните семенни показатели и ДНК фрагментацията на сперматозоиди при пациенти с репродуктивни проблеми, Репродуктивно здраве, 15 (ISSN 1312-6180)

През последните години, анализът на ДНК уврежданията на сперматозоидите придобива все по-голямо значение за клиничната практика, като предоставя важна информация в редица случаи на неизяснен чрез конвенционалния семенен анализ мъжки стерилитет. Цялостта на ДНК в сперматозоидните ядра е от критична важност за правилното предаване на генетичната информация в поколението, като всяка повреда или нарушение в структурата на сперматозоидната ДНК и хроматин могат да доведат до тежки форми на мъжки стерилитет. В настоящето изследване е проследена зависимостта между стандартните параметри на семенния анализ и процента на ДНК фрагментация на семенните проби при 45 пациента с репродуктивни проблеми.

Публикации в сборници от научни прояви на български език:

36. Ерменлиева Н., Георгиева Е., Цанкова Г., Тодорова Т., Костадинова Ц. (2016) Инсинерация – основан подход при третиране на медицински отпадъци, Доклади от четвъртата студентска научна конференция "Екология и околната среда", Шумен 2016, том 3 (ISSN 2367-5209)

Генерираните от лечебни и здравни заведения медицински отпадъци са потенциални носители на инфекциозни елементи. Тяхното управление е комплексен въпрос, който има голямо обществено значение за здравето на населението и благосъстоянието на околната среда. Има различни физични, химични и включващи използването на радиация методи за стерилизация на болнични отпадъци, като всеки от тях се отличава с характерни особености и приложение. В световен мащаб изгарянето (инсинерацията) на медицинските отпадъци се наложил като подход за третирането им с най-добрите показатели – пълно обезвреждане на опасните отпадъци, намаляване на теглото и обемът им, голяма производителност. Процесите на гореене, обаче, са свързани и с отделянето на емисии в околната среда и в този смисъл при експлоатацията на съоръженията е необходимо да се спазват стриктни изисквания за контрол на замърсятелите и горивните процеси.

37. Ерменлиева Н., Георгиева Е., Тодорова Т., Костадинова Ц., Цанкова Г. (2016) Микровълнова стерилизация и стерилизация с електронен лъч – иновативни технологии, в подкрепа на конвенционалните методи за управление на медицински отпадъци, Доклади от четвъртата студентска научна конференция "Екология и околната среда", Шумен 2016, том 3 (ISSN 2367-5209)
Инсинерацията се е наложила като най-ефективен и рентабилен метод за обезвреждане на медицински отпадъци (МО) във всички проучени страни по света. Инсталациите са мащабни и скъпо струващи, но имат много голям капацитет, висока продуктивност, обезвреждат напълно МО и намаляват обема им до 95%. Недостатък в технологията са емисиите от диоксини, фурани и други замърсители, които се отделят като отпадни газове във въздуха при процеса на горене. Технологичният прогрес в съвременното общество предлага някои алтернативни и по-екологосъобразни методи за надеждно обезвреждане на медицински опасни отпадъци. Микровълновата стерилизация и стерилизацията с електронни лъчи са едини най-съвременните подходи, отличаващи се с високата си ефективност. Чрез тях се постига пълно обезвреждане на инфекциозни болнични отпадъци и минимална вреда за околната среда. Добре е те да се познават добре от всички експерти в областта на третирането на опасни МО и здравните работници.

IV. УЧЕБНИЦИ И УЧЕБНИ ПОМАГАЛА

Учебни материали за електронно обучение:


The potential use of human stem cells and especially of embryonic stem cells for research and therapy has created major ethical and political debates in Europe. Since Dolly was cloned in 1997 and human embryonic stem cells first successfully cultured, stem cells and stem cell transplantation have however suddenly become the topic of intense scrutiny from the public, politicians and bioethicists. The sudden interest in stem cells has mainly been caused by ethical worries about the production and use of human embryonic stem cells or stem cells produced by cell nuclear replacement. This critical interest has to some extent spilled over into all other areas of stem cell research.

The question whether it is ethically defensible to do research on embryonic stem cells can be described as a conflict between different values, between different actors' rights and obligations, or between the short- and long-term interests of different groups. On the one hand, there is interest in new knowledge that can lead to treatment of hitherto incurable diseases. On the other hand, when this research involves the use of human embryos, it raises the question of ethics and moral. Opinions on the legitimacy of experiments using human embryos are divided according to the different ethical, philosophical, and religious traditions in which they are rooted. EU Member States have taken very different positions regarding the regulation of human embryonic stem cell research. This confirms that different views exist throughout the European Union concerning what is and what is not ethically defensible.

The European debate regarding human stem cell research is fragmented, with many disparate institutions and other bodies having their say. A number of European states have signed up to a Convention controlling this area. The European Union itself currently does not regulate the field of stem cell research, but the European Parliament has suggested that it should.
There are significant differences in national attitudes towards specific techniques and areas of research. In particular, human embryonic stem cell research has recently provoked intense public and political debate. As the life sciences and biotechnology develop, they contribute considerably to securing welfare on the personal and societal levels as well as to creating new opportunities for our economies. At the same time, the general public is increasingly concerned about the social and ethical consequences of these advances in knowledge and techniques as well as about the conditions forming the choices made in these fields.

V. ПУБЛИКУВАНИ РЕЗЮМЕТА ОТ УЧАСТИЯ В НАУЧНИ ПРОЯВИ


Lyme disease (Lyme borreliosis) is a transmissible infection, common in the Northern hemisphere. It is caused by a group of spirochetal bacteria known as *Borrelia burgdorferi sensu lato*. The aim of the present work is to investigate the incidence rate of borreliosis in different regions of Bulgaria and to outline the burden it poses to public health. Number of confirmed Lyme disease cases was derived from the National surveillance database of the National Center of Public Health and Analyses. Incidence rates at national and regional levels were calculated using the official annual estimates of the National Statistical Institute for the total population number in each region for the corresponding year. Statistical analyses were performed with “R commander” software with significance of p < 0.05. The incidence rates of borreliosis showed a stable trend for the last 5 years in Bulgaria – the mean 5-year annual incidence was 6.2 (2011-2015). Despite this stability at national level, Lyme disease was highly variable at regional level with incidence rates varied from 0 to 49 per 100000 inhabitants (for 2015). Several regions showed significantly higher endemicity for the disease. Socio-demographic factors were not found to be important for Lyme disease frequency while geographic location in the north part of the country is a significant risk factor for it. Lyme disease is a serious health risk in Bulgaria especially in its Northern part – regions Gabrovo, Razgrad and Targoviste are the most vulnerable for higher incidence of the disease.


Botulinum neurotoxin (BoNT) is one of the most poisonous biological substances known to mankind. The toxin is produced by the spore-forming anaerobic bacteria *Clostridium botulinum*, which causes botulism. The aim of our literature review is to summarize the scientific data about the clinical uses of botulinum neurotoxin. The search for articles was conducted in PubMed; including articles published in English after 1990. They should report human observational studies presenting the following keywords: “Botulinum neurotoxin” or „preparations containing botulinum neurotoxin”. BoNT blocks acetylcholine release – the principal neurotransmitter of the nerve impulses to muscle fibers. Thus indirectly causes muscle paralysis. This life-threatening ability, however, turns out to be extremely effective in the therapy of a number of diseases associated with hyperactivation of the muscles and glands – dystonia, urine incontinence, aesthetic corrections of glabellar wrinkles and others. A number of new directions in the medical practice—cerebral palsy, chronic anal fissures, urological disorders and others – are currently under study for
successful application of BoNT. On the world market there are a variety of products containing BoNT for cosmetic purposes, which received regulatory approval or are under development. Currently Botox® gives a share of 85% of the global market of products containing BoNT. Other products on the world market but with limited application are Dysport®, Xeomin®, Myobloc®, Prosigne® and others. The application of BoNT is distinguished by high efficiency and safety. Side effects are rare and reversible. Due to that fact BoNT may have clinical usage in various medical fields.


Bulgaria is a country of moderate endemicity for hepatitis B infection with 3-7% of the general population chronically infected with the virus. Since 90s of 20th century an obligatory vaccination have been implemented for all healthy newborns, but hepatitis B infection is still an important public health problem that needs to be addressed especially in some particular age and socio-demographic groups. No recent published data are available about HBV epidemiology in Bulgaria and in its Eastern part particularly. In the current study, we analyze the epidemiological data on HBV incidence in five regions in Eastern Bulgaria (Burgas, Dobrich, Shumen, Varna and Yambol) and try to determine the possible risk, which HBV infection poses to public health in these regions. The number of cases of acute viral hepatitis B in all considered regions has been durably decreasing for the last seven years, reaching a minimal incidence rate of 3.09‰ in 2014. Young individuals in their 20s years (the last generation in Bulgaria without mandatory vaccination) have been found to be most affected by hepatitis B infection.


*Listeria monocytogenes* may cross and proliferate in the placenta and cause severe infections during pregnancy. In pregnant women, listeriosis usually occurs during the third trimester, when cell-mediated immunity is reduced. A common results are abortion, stillbirth, intrauterine and/or neonatal infections. Two forms of neonatal infection exist: early-onset sepsis (acquired *in utero*) and late-onset meningitis (acquired through vaginal transmission).

The patient was a newborn male, delivered by urgent cesarean section after chorioamnionitis on 02 June 2013 in a small private hospital in Varna. Six hours later he was transferred to our hospital with hypotonia and weak, not rhythmic breathing with lots of crackles. After the admittance, the baby became high oxygen doze dependent with signs of pulmonary insufficiency. The blood tests have shown decreased level of lung perfusion and ventilation, significant hypoxemia and hypercarbia. After 48 hours, the baby was extubated, passed the period after ventilation without complications and started to eat independently. *Listeria monocytogenes* was isolated from ear secretion, while blood and CSF cultures were negative. The baby was discharged on the 20-th day of his birth with weight of 2000 g and normal lung and heart function. To date, he has normal neurological status, cognitive function and vital signs.

Epstein-Barr (EBV) is a widespread virus which can be detected in more than 90% of world population. Primary EBV infection during adolescence and adulthood results in infectious mononucleosis, while in children it is usually asymptomatic. EBV is responsible for different malignant forms of B-cell or epithelial cancers, such as Hodgkin’s and non-Hodgkin’s lymphoma, Burkitt’s lymphoma, post-transplant lymphoproliferative disorders, nasopharyngeal carcinoma, hairy leukoplakia and HIV-associated lymphomas. Evidence exists that infection with EBV is also linked with a higher risk of hepatocellular and gastric cancers, as well as autoimmune diseases. EBV shows two alternative life cycles – latent and lytic. After the primary infection, the virus remains in B lymphocytes (latent infection) and its genome localizes in the nucleus under the form of circular episome. The lytic infection takes place predominantly in the epithelial cells and can last for months with constant virus release in saliva and nasopharyngeal secretion. Unlike other herpes viruses, development of oncological diseases is linked with the latent cycle, as a result of immune response’s failure to control latently infected cells. At least 5 viral genes are involved in the process of malignization and especially in blocking tumor-suppressive cell mechanisms. With the present study we aimed to review the current knowledge in mechanisms of EBV pathogenesis in humans.


The objective of our study is to assess the level of depression among patients with rheumatoid arthritis and ankylosing spondylitis in Bulgaria. We also try to find the degree of correlation between depression levels and the activity and duration of the disease. A cross-sectional study among 140 people living with rheumatoid arthritis and ankylosing spondylitis was conducted from May 2015 to July 2015. The following instruments were used: Beck Depression Inventory (BDI) and Routine Assessment of Patient Index Data3 (RAPID3). The relationship between variables was assessed using chi-square test with significance level of p < 0.05. Almost 66% of all studied individuals living with rheumatoid arthritis and ankylosing spondylitis experienced some level of depression. This is directly related to the activity and duration of the disease. Depression among patients with rheumatoid arthritis and ankylosing spondylitis is a major health problem. Our study shows the need for assessment of depression levels in such patients. We also recommend conducting further studies on the prevalence of depression and depressive symptoms in people living with rheumatoid arthritis and ankylosing spondylitis and screening for the presence of comorbid depression and its timely treatment.


Syphilis is a sexually transmitted disease, caused by the spirochaete Treponema pallidum. During the course of pregnancy it may lead to serious fetal disorders and to intrauterine
The study comprises 2702 pregnant women. The syphilis screening was performed on blood samples by ELISA (Enzyme Linked Immunosorbent Assay), VDRL (Veneral Disease Research Laboratory) and TPHA (T. pallidum haemagglutination assay). The specific treponemal antibody was detected in 27 pregnant women by using ELISA, in 15 pregnant women by VDRL and in 16 women by TPHA. Our results showed no significant relation between the age of the patient, pregnancy trimester and the susceptibility to the disease. In contrast, the ratio positive/negative samples was three-fold higher in the group of women from rural regions compared to those of urban origin. Serological syphilis screening with different methods is necessary for better protection and prevention of possible congenital transmission and habitual abortions. The insufficient number of physicians in rural regions and therefore the limited accessibility to health care is pertinent for higher syphilis prevalence in less urbanized regions.

8. Todorova T. T., Vuilleumier S., Kujumdzieva A. V. Sensitivity of *Saccharomyces cerevisiae* GST mutants to arsenate, XI конгрес на микробиолозите в България, Варна, 5-7.10.2006

Arsenic is a toxic metalloid present in natural and polluted industrial environments. It is a human carcinogen but is also used in treatment of acute promyelocytic leukemia and protozoan parasitic diseases. When mammals are exposed to arsenate, it is reduced to arsenite either by the PNP arsenate reductase or MMA(V) reductase, a member of omega class of glutathione S-transferases (GST). The later enzyme catalyzes the conjugation of the electrophilic toxic compounds with the –SH group of glutathione (GSH), therefore playing a critical role in xenobiotic elimination. Based on sequence, substrate specificity, structure and immunological properties, GSTs have been grouped into eight distinct families. In contrast with mammals, plants and even bacteria, little is known about GSTs of yeasts and fungi but they seem to be especially diverse both structurally and functionally. In this study we have taken a systematic genetic approach to study the potential role of GSTs in arsenate toxicity in *Saccharomyces cerevisiae*. A search in *Saccharomyces* Genome Database reveals the presence of 11 genes and ORFs with homology to GST, which single disruption mutants were tested for their sensitivity to arsenate. The mutant, disrupted for the gene *TEF4*, coding for translation elongation factor EF1γ (GST homologue) was studied. A hypersensitivity of this mutant to AsV has been found, indicating a possible participation of Tef4 protein in arsenate detoxification.

9. Тодорова Т. Т., Тачева Д., Петрова Д., Дубровина М., Топалова Д., Владимиров Я. Ранното делене на ембриона: важен фактор, определящ жизнеспособността и потенциала за развитие на човешките бластоцисти, XII национален конгрес по стерилитет, контрацепция, хормонозаместителна терапия и гинекологична ендоскопия с международно участие, Боровец, 17-20.03.2011

В последните години все по-голяма популярност придобива един алтернативен метод за селекция на ембриони, основаващ се на времето на тяхното първо делене до 2-клетъчен стадий. Ембрионите, които достигат 2-клетъчен стадий на 25 час след инсеминирането се означават като ‘ранно-делящи’ се, докато тези, които не са разделени на 25 час – като ‘късно-делящи’ се. Трансферираните ранно-делящи се ембриони имат по-добър потенциал за имплантация и успешна бременност. В
нашата практика, при трансфер на 2 или 3 ден са регистрирани значително повече клинични бременности при пациенти с ранно-делящи се ембриони в сравнение с пациенти с късо-делащи се ембриони. С настоящето проучване, ние развиваме стратегията за селекция на ранно-делящи се ембриони до стадий на бластоцит култивиране. Ембриони от 273 двойки са изследвани за ранно делене на 25 час и за формиране на бластоцит на 5/6 ден от култивирането. Получените резултати показват, че ембриони недостигнали до 2-клетъчен стадий на 25 час след инсеминирането имат двойно по-висок риск от стопиране на развитието си при ин витро култивиране, докато бластоцитите, развили се от ранно-делащи се ембриони имат по-висок шанс за успешна имплантация след трансфер.

10. Тодорова Т. Т., Тачева Д., Горанова Т., Дубровина М., Владимиров Я. Ранното делене на 25 часов след IVF и ICSI като параметър за селекция на ембриони, Х национален конгрес по стерилизитет, контрацепция, хормонозаместителна терапия и гинекологична ендоскопия с международно участие, Несебър, 23-26.04.2009

Често използван и достъпен метод за селекция на ембриони с високо качество за трансфер е оценка на морфологията на ембриона. В настоящата работа се предлага метод за оценяване жизнеността на ембриона въз основа на времето на първото клетъчно деление на честотата на забременяване. Ембрионите, които достигат 2-клетъчен стадий на 25 час след инсеминирането се означават като ‘ранно-делящи’ се. Значително повече клинични бременности са регистрирани при пациенти с ранно-делащи се ембриони, в сравнение с пациенти с късо-делащи се ембриони. Не е наблюдава статистическа разлика по отношение на другите ключови параметри, което подчерта съществената роля на ранното делене на ембриона за осъществяване на бременност при асистираните репродуктивни методи.

11. Горанова Т., Тодорова Т. Т., Тачева Д., Дубровина М., Владимиров Я. ДНК фрагментация на сперматозоидите като индикатор за изхода от АРТ, Х национален конгрес по стерилизитет, контрацепция, хормонозаместителна терапия и гинекологична ендоскопия с международно участие, Несебър, 23-26.04.2009

Връзката между ДНК фрагментацията на сперматозоидите и мъжкия инфертилитет е тема на много проучвания от последните години, но все още резултатите са противоречиви. Настоящото изследване беше проведено с цел да се изясни прогностичната роля на ДНК фрагментацията при АРТ. Проучването установи, че съществува статистически значима корелация между процента на ДНК фрагментация и риска от спонтанен аборт (p < 0.05). Връзка на останалите клинични показатели с ДНК фрагментацията не беше доказана. Когато сравниме пациентите с Normozoospermia, установихме корелация между ДНК фрагментацията и риска от спонтанен аборт при пациенти, подложени на ICSI процедура, но не и при тези претърпели стандартна IVF процедура. Проучването ни потвърди прогностичната стойност на ДНК фрагментационния анализ за изхода от АРТ и показа, че за двойки, при които мъжът е с Normozoospermia и висок процент на сперматозоидите с ДНК фрагментация, по-подходяща е IVF процедурата.