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BOOK OF ABSTRACTS ЗБОРНИК РЕЗИМЕА



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MAIN TOPICS

Actual epidemiological respiratory infectious disease problems
Epidemiology of non-infectious mass diseases
Current parasitoses
Fungal infections: prevention, diagnostics and therapy
Microbiology today
Environment and health
Nutrition and health
Socio-medical aspects of health
Motivating the local community in health promotion

GLAVNE TEME

Savremeni epidemiološki problemi respiratornih zaraznih bolesti
Epidemiologija masovnih nezaraznih bolesti
Aktuelne parazitoze
Gljivične infekcije: prevencija, dijagnostika i terapija
Mikrobiologija danas
Životna sredina i zdravlje
Ishrana i zdravlje
Socijalno-medicinski aspekti zdravlja
Mobilizacija lokalne zajednice u promociji zdravlja

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A. PLENARNA PREDAVANJA
A. PLENARY LECTURES

EKONOMSKA KRIZA I NJEN UTICAJ NA ZDRAVLJE -
GRČKA TRAGEDIJA
**THE ECONOMIC CRISIS AND ITS IMPACT ON HEALTH -
THE GREEK TRAGEDY**

Eleni Jelastopulu

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First of all allow me to express my cordial thanks to the Organizing Committee and of course to Prof. Biljana Kocić for the invitation to participate in your 47th Days of Preventive Medicine here in Nis. It is a very great honour for me to open your congress and I wish to take this opportunity to underline that the invitation you have extended to me symbolises the unbreakable links between Serbia and Greece and I look forward to strengthen our friendship and create collaborations between our faculties.

So I bring greetings from Greece, which continues to bear the effects of the economic crisis, which certainly extend to the health care system and the health status of the Greek population.

The debt crisis continues to threat Greece, although in May 2010, the European Union (EU) and the International Monetary Fund (IMF) approved a 110 billion euro loan package to the Greek government in return for promises of spending cuts to sharply reduce the Greek public deficit. The plan, negotiated by German Chancellor Angela Merkel and Greek Prime Minister George Papandreou, was intended to cover the borrowing needs of the Greek government through 2013. In spite of this rescue package and another, 130 billion euro package in March 2012, the debt crisis in Greece continues.

Now, in its fifth year of recession and operating within severely constricted fiscal limits, the country is undergoing a massive and unprecedented process of changes and structural reforms, in large part driven by the terms of Greece's loan agreement with the European Commission, European Central Bank and the IMF (International Monetary Fund), also known as the Troika, and its Economic Adjustment Programme.

In the health care system the implication of the crisis have to be seen in two levels:

First, in the actual process of **delivery of health services**, that is, coverage of the population, operational and functional problems in delivery of preventive, curative and rehabilitative services, financial cuts and restrictions in the provision of services and of course on matters of quality of health care.

Second are the implications on the **health status of the population** which is reflected in the deterioration of quality of care, and is manifested in higher levels of morbidity, suicides, physical and mental disorders and other health conditions and diseases.

In my talk I will concentrate mainly on the second level of implication that is issues and evidence on the impact on health status of the population, after giving you some basic information about the Greek health care system and the required reforms by the Troika.

Economic crises have been shown to have a negative effect on health status through declines in public spending and household income. Both have sharply declined in Greece, and the effects of the crisis and austerity on health have been marked. Since the onset of the crisis several studies have been published investigating the effects on public health, and I will present the latest available information and data illustrating Greece's experience from the restrictive policies during the economic crisis.

The IMF's loans to Greece came with "conditionalities", which include privatization of state-owned enterprises, liberalization of markets and imposition of public spending ceilings, including health and education, with the assumption that these policies will trigger economic growth and eventually improve the chance that loans will be paid back.

Consistent with these broader policies, between 2010 and 2012 the Greek Ministry of Health started restructuring the Greek Health Care System, which is a mixed system of public-sector and private-sector services with a tripartite structure: A tax-funded National Health System, multiple public sickness funds based on occupations, and an unregulated private for-profit health care market.

The Greek Ministry of Health has adopted a wide range of market-oriented "reforms" such as austerity measures including curtailing of government health spending and reductions in the salaries of health professionals working in the public sector, restrictions on access and privatization schemes including introduction of copayments for outpatient services of public hospitals, closures and mergers of public hospitals' beds and clinics and contracting with private insurance companies for services delivered by public hospitals.

A new public sickness fund, the EOPYY (National Organization for the Provision of Health Care Services), which merged the 4 largest sickness funds in the country, led to substantial reductions in social insurance health benefits, as well as increased copayments for drugs and diagnostic tests. The foundation of EOPYY answers the long awaited separation between the administration of pensions and health care. However significant administrative and financial management problems hamper the Organization's effective and efficient operation.

A third main category of reforms can be summarized as deregulation of private health services, including removal of restrictions on private hospitals, such as legislative controls concerning the expansion of these hospitals' infrastructure or limitations concerning the establishment of laboratories, medical centers, and dialysis units by entrepreneurs.

The determinant role of economic and social conditions on population health is well documented from epidemiological research, showing associations with increased suicide, homicide, male cardiovascular disease, alcohol abuse, and communicable disease mortality, as well as increased morbidity and mental disorders incidence.

These associations between economic crises and health can result in an increased need for services especially among vulnerable groups such as the unemployed, the uninsured and immigrants. Decreased household income and purchasing power (because of unemployment and reduction of real wages) can lead to reduced health expenditures by households, decreased consumption of private health services, and increased utilization or demand of services in the public sector. In light of such observations, restrictive public health policies in Greece predictably will result in a deterioration of the population's health status.

While it will take several years for the full effects of the crisis in Greece on population health to be fully assessed, key indicators have already significantly deteriorated. In relation to population health, the first effects of the crisis have been noted in self-reported health, mental health including suicides, in infectious diseases and in oral health.

Studies of self-rated health using a pre-crisis benchmark found an increase in the prevalence of people reporting their health as bad and very bad, and linked this development to the economic crisis (1). In addition, a significant increase in people reporting unmet medical and dental need was noted (2,3).

Mental health is an area that is particularly vulnerable to rapid economic fluctuations, and the first available data reveal worrisome trends (4) According to the study of Marina Economou, the one-month prevalence of major depression was found to be 8.2% in 2011; as compared to the corresponding rate in 2008, which was 3.3%. This rise was significantly associated with economic hardship. Mainly young people, married persons, individuals with financial distress (Index of Personal Economic Distress (IPED)) and people who use medication displayed increased odds of suffering from major depression in 2011.

Marina Economou's findings show a profound and detrimental influence of the economic crisis on the mental health of the Greek population, and especially on the prevalence of major depression. This is of primary concern, if one takes into consideration that depression constitutes one of the main contributors to disease burden and disability worldwide.

In addition, a further survey found a 36% increase between 2009 and 2011 in the number of people reporting suicidal ideation or suicidal attempts in the month before the survey, with a higher likelihood for those experiencing high economic distress (5). The proportion of respondents who reported suicidal ideation was 6.7% in 2011 versus 5.2% in 2009. A significant increase in the prevalence of suicidal ideation was observed in men (7.1% vs. 4.4%), in respondents aged 55–64 years (7.2% vs. 1.9%), in married (7.3% vs. 2.3%), in respondents who used psychotropic medications (22.7% vs. 4.5%) and in those who had sought help from a mental health professional (17.3% vs. 8.3%).

The first available official data on suicides also reveal a worrying increase. In the last years, the number of Greeks that commit suicide has been raised dramatically. The number of suicides increased by nearly 27 percent in 2011 compared to 2010, and by 45% compared to 2007, which was the last year before the start of the economic crisis in Greece.

According to estimates of the non-governmental organization “Klimaka”, based on data released by the Hellenic Statistical Authority (ELSTAT) and the World Health Organisation (WHO), 477 suicides were reported in Greece in 2011 (393 men and 84 women). This number is not only the highest in the last 50 years, but the number of women committing suicide shows a dramatic rise of 105 percent compared to 2010.

Including suicide attempts, the number climbs up to nearly 1000 in 2011 or more than 3,000 in the last three years. Based on its own research the NGO Klimaka remarked some days ago at the occasion of the World Suicide Prevention Day on 10 September that the number of suicides had continued to rise through 2012 and 2013 and that there are strong indications of a further “very large rise” in these past two years.

The region with the highest official suicide rate for 2011 was Crete, with 6 suicides per 100,000 inhabitants, followed by Peloponnese (with 5.7), East Macedonia and Thrace (with 5.4) and West Greece (with 5.3 respectively), while in North Aegean and Central Macedonia the lowest suicide rates have been reported.

The NGO “Klimaka” estimates that in fact the number of people taking their own lives in Greece is much larger than those reported, while there is no data on non-fatal suicide attempts, which is estimated to be 20 to 30 times more than the recorded suicides.

And in fact, according to data from the Research Institute of Mental Health at the University of Athens, the incidence of suicides in Greece has almost doubled the last three years, from 3.4 suicides per 100,000 inhabitants in 2009 to 6.5 in 2011.

The suicide prevention Hotline received in 2012 more than 4000 phone calls, i.e. 4 times more than previous years, most of which focusing on social and economic problems, while a few years ago, the incoming phone calls focused on issues of mental health. 35% of people calling Klimaka's Hotline are unemployed, followed by self-employed and pensioners.

Nearly 50% addressing Klimaka's suicide prevention hotline are the potential victims themselves, 25% are the indirectly concerned, i.e. relatives, friends or partners of the victims and about 17% state authorities such as police or internet users noticing postings of suicidal behaviors.

Infectious diseases have been shown in many studies to spread in periods of economic turmoil. According to researchers at the Hellenic Center for Disease Control and Prevention, our country has been suffering a disproportionately high morbidity and mortality burden of different large-scale epidemics since the beginning of the economic crisis.

For example, Greece ranked 4th among 30 European countries in deaths from the outbreak of the Novel A (H1N1) influenza virus, showing one of the highest mortality rates in Europe with about 13 deaths per million population. Major outbreaks were also observed in West Nile Virus infections, documented for the first time in Greece in 2010, with estimated human cases more than 25,000. During 2011, WNV human infections were reported for a second consecutive year and a new geographic pattern spread of this virus was noticed, suggesting that WNV is established now in Greece and its transmission will continue to occur in the future, not only in Greece, but also – as you can see -in the neighboring countries, such as Serbia (6).

As further consequences of the public health budget-cutting by more than 40% in order to meet the targets set by the Troika, Greece experienced a malaria epidemic in the last four years - the largest in the last 40 years. Malaria was eliminated from Greece in 1974, and is now brought back not only by infected visitors and migrants (as it sometimes happens in the rest of Europe) but is being transmitted from person to person within the country. Between January and October 2012, Greece has reported a total of 70 cases of malaria. This is the first time since 1974 that malaria is locally transmitted in Western Europe and the reason for it are the drastic cutbacks in municipal insecticide spraying schemes to combat mosquito borne diseases.

The economic crisis and associated adjustment policies have affected the health of mainly vulnerable groups. The most striking finding relates to the HIV outbreak in our country. Regarding the HIV infections, a significant increase occurred in the period from 2009-2012.

More specifically, in 2012 a total of 1180 new HIV infections were reported to the Hellenic CDC. Among them, 85% were males and 15% were females. Speaking in incidence, a total of 11 cases of HIV infection per 100,000 population were reported in 2012, which is the highest figure ever recorded in the HIV/AIDS reporting system (7).

The main driver for this increase is the group of injecting drug users. In 2011, the number of reported HIV infections amongst people who inject drugs showed an unprecedented increase, which continues in 2012. More detailed, the reported number of HIV infections among IDUs jumped from 14 cases in 2010 to more than 200 cases in 2011 and doubled in 2012, reaching the number of 522 infected IDUs. This is the first time, since the HIV epidemic began in Greece that the annual reported number of HIV infections in IDUs comprised the majority

(44.2%) of all reports that have been received in 2012, and this is a result of cutting in half the needle-exchange program budgets.

These observed continuing upward trends and the changes in the characteristics of the HIV epidemic is directly linked to the crisis as funding available for HIV prevention and treatment services became limited. The distribution of both syringes and condoms dropped between 2009 and 2010. However, in response to the outbreak, the number of syringes distributed rose from 7 per injecting drug user per year in 2010 to 45 in 2012. While this seems a welcome increase, it is still well below the minimum of 200 recommended by the European Center for Disease Prevention and Control.

Further effects of the austerity measures are exemplarily the de-stocking of more than 200 essential medicines from some pharmacies as the state's drug budget was reduced and pharmaceuticals companies left the country.

Furthermore, since 2008 there has been a rise of more than 40% of people who report being unable to access healthcare, the majority concentrated in pensioners.

Infant mortality rates have risen 40% between 2008 and 2010.

Over 35,000 public health workers, nurses, and doctors have lost their jobs. Unemployment rates have hit 27% and youth unemployment has jumped to near 75% in some areas.

With little hope for the future, desperate people are turning to cheap, synthetic drugs and the use of anti-depressants has skyrocketed, adding costs to the healthcare system.

Several prevailing myths are commonly offered as alternative explanations for these devastating health outcomes in Greece instead of the imposed deep budget cuts starting in 2010. Three of them are:

The first myth: "Greece's healthcare system is excessive and inefficient." But there are just 5 hospital beds per 1,000 people, versus more than for example 8 beds per 1,000 people in Germany.

The second myth: "Greeks are lazy." But in 2011 the average Greek citizen worked more than 2000 (2,038) hours per year which is 600 hours more than the average German, according to the OECD.

The third myth: "Europe's bailout money is being squandered." But bailout money is not flowing in to support Greece's healthcare system -- it is instead circulating back to large international banks in Germany, France and the UK.

In their new book, "The Body Economic: Why Austerity Kills," economist David Stuckler and physician Sanjay Basu examine the health impacts of austerity across the globe. The authors estimate that there have been more than 10,000 additional suicides and up to a million extra cases of depression across Europe and the United States since governments started introducing austerity programs, in the aftermath of the economic crisis. In Greece, where spending on public health has been slashed by 40 percent, HIV rates have jumped 200 percent, and we have seen our first malaria outbreak since the 1970s and the West Nile Virus outbreak for the first time in our history, as mentioned before.

Unfortunately, governments continue to ignore the disastrous effects of the recent financial crisis on human health and have even exacerbated them, by adopting harsh austerity measures and cutting key social programs at a time when people need them most. In Greece, Troika's impositions and governmental mismanagement of financial strife has resulted in this grim array of human tragedies, from suicides to HIV infections, and other epidemics.

Today, Greece is the unhappiest nation in Europe, followed by Portugal, Italy and Spain, as data from the just released second “World Happiness report” are showing. And the end of the Greek tragedy is not to be seen yet.

The disappearance of smile from our faces reminds us every day that, in an effort to finance debts, ordinary people are paying the ultimate price: losing access to care and preventive services, facing higher risks of HIV and other sexually transmitted diseases, and in the worst cases losing their lives.

In this context, five priorities should be reconsidered by health policy makers, namely equitable access to services; greater empowerment of citizens in decision-making about the services they need and their treatment options; restructuring of the health care system towards a patient-centered, primary care system; greater decentralization and regionalization of decision-making and provision; and increasing the accountability of the health care sector.

There is also a need to rethink and to promote a public debate on the health budget not as a financial burden but as a developmental tool, with the need to address not only economic dimensions but also the welfare of citizens. In other words, resetting the social values underlying the health care system is a prerequisite for establishing a new paradigm for its sustainable development.

Coming to the end, there is an important question which we have to ask and which contains two issues: health policy and political decisions.

What is the health policy response to the crisis and how will we politically manage the implementation of these policies?

In dealing with this question we have to see the implications and consequences of the introduced changes within two perspectives:

First, within the perspective whether these changes that have been - or are to be taken lead to the goals and desired outcomes when implementing the required operational and structural reforms in the health system.

Second, and this takes a special interest in monitoring, analyzing and criticizing, whether the policy-making process in its final stage which is evaluation of the implemented actions or changes was effective and efficient. In other words, if the measures required in the Memorandum by the Troika, which were rather fiscal consolidation measures than really structural and operational reform changes achieved the desired outcomes. And the answer for Greece is a big “NO”.

Thus, the Greek health care system is an experimental ground for analyzing this dual approach to interventions and reforms during the economic crisis. After all, countries which are experiencing similar economic crisis can learn the same lessons from us.

Therefore, decision makers should design and implement the policies necessary to protect the health status of the population, the public health, and to narrow health inequalities in Greece and everywhere!

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B. SESIJA: SAVREMENI EPIDEMIOLOŠKI PROBLEMI RESPIRATORNIH ZARAZNIH BOLESTI

B. SESSION: ACTUAL EPIDEMIOLOGICAL RESPIRATORY INFECTIOUS DISEASE PROBLEMS

I PREDAVANJA PO POZIVU

I INVITED LECTURES

1. ACTUAL EPIDEMIOLOGICAL PROBLEMS OF THE RESPIRATORY INFECTIONS

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Abstract:

Respiratory infectious diseases represent significant public health problem worldwide. These diseases are caused by numerous previously known microorganisms, as well as recently recognized ones, identified by new diagnostic abilities. Conditions of life in modern society favour the spread of these agents and respiratory infections are therefore called diseases of modern society. Most significant results in control of respiratory infections have been achieved by immunization. Along with other well planned and organized measures, it may help in reducing the frequency of these conditions.

Key words: epidemiology, respiratory infections

Paper:

Objective

Objective of this paper is to describe actual epidemiological problems of the respiratory infections that already are or may pose significant public health threats to the population worldwide.

Methods

This review examines the state of knowledge on a given topic. Paper was based on review of selected scientific articles and reports of leading international organizations.

Results

Respiratory infections are the most frequent diseases in humans worldwide due to efficacy of air as a mode of transmission and conditions of life in modern society achieved by growth in urban population, tourism and international traffic.

Due to lack of efficacious measures directed to the air as a mode of transmission, only a small number of respiratory infections can be well controlled by immunization. However, properly planned and organized activities may help in reducing the frequency of other respiratory infections conditions. Such measures, including adequate surveillance and timely intervention are also needed in order to maintain low frequency or elimination of vaccine preventable diseases.

Despite decades of successful implementation of immunization programs and adopted elimination strategies of vaccine preventable diseases, an increase in morbidity of measles, rubella, pertussis and mumps has been registered in last few years (1,2). Measles outbreaks have occurred in a number of European countries with a tendency to become endemic. During 2010 and 2011, over 30.000 of cases were registered in European Union. In 2012 rubella outbreaks occurred in Romania and Poland with over 20.000 and 6.000 registered cases, respectively.

While in measles and rubella outbreaks the majority of cases occur in unimmunized, in mumps outbreaks previously immunized adolescents and adults represent the mostly affected population. This raised an issue of duration and quality of immune response after mumps immunization. Failure of immunization may be a consequence of absence of proper immune response after immunization or waning vaccine induced immunity over a period of years and another cause of outbreaks may be considered as incongruity in vaccine and circulation genotypes of mumps virus strain (3).

Increase in number of registered pertussis cases in countries with high immunization coverage is a result of waning of vaccine induced and naturally acquired immunity. Due to shift of disease towards older age groups, in settings without active surveillance pertussis frequently remains unrecognized (4).

Unfortunately, there are no vaccines for the majority of respiratory infections. That is why these diseases are present as endemoepidemic within the population. Although these diseases are caused by numerous microorganisms, over 2/3 are caused by viruses. There are over 200 antigenically different viruses that cause respiratory infections (5). Thanks to the advances in molecular technology, the list of viruses causing respiratory infections is constantly expanding revealing "new causative agents of old diseases"(6).

At the beginning of 21st century, SARS outbreak in Hong Kong indicated that respiratory infectious diseases still represent global health threat showing the potential of spread of infectious diseases through international travel to all parts of the world from one location. SARS was recognized as a new clinical entity in 2003. Due to a lack of specific prevention measures, reliable diagnostic tests and adequate causal therapy, outbreak was contained with measures known for centuries, such as quarantine. Through collaboration of experts and governments worldwide, rapid information flow, joint action of health authorities and by motivation of general public, SARS was put under control within only three months. Total of 8.096 cases and 774 deaths were registered (7). Etiological agent was isolated from sputum and lungs of patients and established as new human coronavirus (SARS-CoV).

This outbreak increased attention and put coronacviruses into the focus of experts which resulted in discovery of two new coronaviruses, NL63 and HKU1, related to respiratory illnesses in human. HCoV-NL63 was discovered in 2004 in a child with bronchiolitis in Holland (8), while HCoV-HKU1 was discovered in 2005 in a patient with chronic pulmonary illness in Hong Kong (9). Numerous research later on confirmed presence of these viruses in human population worldwide. These viruses were detected in 1-10% of cases of acute respiratory tract infections in patients of all age groups with different severity of illness including deaths in infants and small children, elderly and immunocompromised. Co-infections with another viral agent were also frequent in these findings.

Recently, another coronavirus was detected and named Middle East Respiratory Syndrome Coronavirus (MERS-CoV). It is similar with bat coronaviruses. It is somewhat different than other coronaviruses isolated from human biological samples. Till June 2013, total of 54 cases were registered. Majority of cases developed clinical picture of severe acute respiratory illness with 30 deaths registered. Most of the cases were registered among population of Saudi

Arabia, while minorities were international travellers visiting this country. Possibility of human to human transmission is an option due to confirmation of secondary cases among close family contacts, which were not travelling. Surveillance of contacts of cases among international travellers indicates small infectious dose and detection of cases with mild clinical picture implies possibility that some secondary cases remained unrecognized.

Human metapneumovirus (HMPV) was described in 2001 as a new respiratory pathogen (10). Virus was isolated from samples of respiratory secretion collected during 20 year period among acute respiratory infections cases of children in Netherlands. It was classified as a member of family Paramyxoviridae. Two genotypes were identified (A and B) with two subtypes in each (A1, A2, B1, B2). Severity of illness could not be related to a certain genotype. When diagnostic tests were developed, global distribution of these viruses was determined, as well as wide spectrum of clinical manifestations in patients of all age groups. HMPV are frequent causative agents of upper and lower respiratory tract infections in newborns and infants. In adults, clinical picture is most frequently mild with severe clinical course only in elderly, chronic and immune deficient patients. Infection is related to the exacerbation of asthma in children and COPD in adults. Seroprevalence studies showed presence of HMPV specific antibodies in over 90% of children below 5 years of age and almost 100% of adults indicating that primary infection occurs early in infancy.

Other viruses were identified in samples from human respiratory tract (6). Human bocavirus (HBoV) was described in 2005 and soon thereafter it was recognized as ubiquitous. Although the virus was related to respiratory tract infections, including pneumonia, it was detected in cases of gastroenteritis in children in the absence of respiratory symptoms. Findings suggest that HBoV may be a causative agent of acute gastroenteritis. It is possible that these symptoms may be a reflection of host's systemic response to the infection.

New human polyomaviruses KIV (detected in Karolynska Institute) and WUV (detected in Washington University) were identified in 2007 in children from respiratory tract specimens. Although the infection so far was not related to certain specific illnesses, further research is needed to determine whether the finding of these viruses in respiratory tract represents a consequence of pathogenetic mechanism or reflects a mode of transmission. This research bears important medical significance having in mind viral oncogenic potential in mammals (6).

Finally, influenza is the last well known communicable disease with pandemic potential. Beginning of the debate on possibility of new pandemic started after outbreak in poultry in Hong Kong in 1997 caused by highly pathogenic H5N1 subtype of influenza A. Virus was transmitted from wild birds and caused severe outbreak in poultry with high case fatality rate. Interest among experts for this outbreak was high due to the fact that 18 cases among humans with 6 deaths were registered at the same time during the outbreak in poultry. Soon outbreaks in poultry were detected worldwide following the path of migratory birds while number of cases among humans remained low without human to human transmission documented except in few secondary cases. However, spread of outbreaks in poultry and cases in humans were the initial reason for consideration of a possibility of new influenza pandemic due to the fact that simultaneous infection in humans with avian and human viruses may lead to recombination and appearance of a new subtype of influenza virus with pandemic potential. World Health Organization determined that the level of risk of new pandemic was high and gave recommendations to all countries to prepare for such an event. Despite the estimates that pandemic may start in South East Asia where outbreaks of avian flu in poultry and majority of human cases were present, pandemic spread started in Mexico and was caused by new H1N1 later known as swine flu. Since detection of the virus on 15 April 2009 and proofs of a new

variant that did not previously circulate in human population, only two weeks were passed till global surveillance was established, information regarding clinical characteristics provided, as well as characteristics of cases and risk factors in humans described. Measures were proposed in order to limit the global spread and manufacture of vaccines was initiated. In only 9 weeks pandemic spread to all continents.

Today, WHO once again warns on the possibility of spread of infection caused influenza A(H7N9), detected in several provinces in East China. Significance of exchange of information between health and veterinarian authorities, development of valid diagnostic tests and vaccines is crucial in order to properly follow the situation and to intervene in a timely manner (11, 12).

Conclusion:

Emerging and re-emerging respiratory infectious diseases are still and will be leading causes of illness and deaths in population worldwide.

New molecular technology and further advances will enable discovery of new etiological agents and possibility to determine epidemiological characteristics of illnesses they cause.

Vigilance must be maintained.

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2. RESPIRATORY VIRAL INFECTIONS: OLD VIRUSES, NEW VIRUSES, AND IMPORTANCE OF SPECIFIC TIMELY DIAGNOSIS

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Respiratory viruses are considered as the main cause of acute respiratory infections in humans, particularly in infants and children. Despite the fact that most of them cause benign and self-limited infections in immunocompetent adults, infections in children, elderly, immunocompromised individuals or persons with chronic underlying diseases are very often the cause of hospitalizations, mainly during the cold months of the year. Besides classical respiratory viruses, such as influenza viruses, respiratory syncytial virus, human rhinoviruses, parainfluenza viruses, adenoviruses, enteroviruses and human coronaviruses, other “new” viruses have been added to this list, such as human metapneumovirus, novel coronaviruses, human bocavirus (hBoV) and others.

Due to the limited sensitivity and specificity of classical virological techniques based on direct detection of virus in the clinical sample (viral culture, different antigen detection methods) and detection of immune response to the virus by serologic assays in paired serum samples, a considerable number of acute respiratory infections were not etiologically identified. Recent advances in molecular diagnosis have significantly improved diagnostic possibilities. Moreover, nucleic acids amplification techniques are the only available method for most “new” respiratory viruses because they do not grow or grow poorly in cell culture and for which no efficient antigen detection methods have been commercialized.

In 2008, the National Laboratory for influenza and other respiratory viruses of the Institute Torlak started with the introduction of *in-house* molecular techniques for influenza and other respiratory viruses. Up to now, real-time PCR test has been introduced in the routine diagnostic use for influenza viruses, respiratory syncytial virus, human rhinoviruses, parainfluenza viruses, adenoviruses, enteroviruses and human coronaviruses. Besides classical respiratory viruses, some other “new” viruses have also been added to this list, such as human metapneumovirus and novel coronavirus.

The introduction of molecular techniques made it possible to determine the aetiological diagnosis of viral respiratory infections in many clinically unclear cases and to avoid unnecessary antibiotic use, as well as it enabled the appropriate use of antiviral drugs. Establishing virological diagnosis is also of crucial importance to minimize the risk of nosocomial transmission and to provide epidemiological information for an early response in the prevention of infections.

3. PREVALENCE OF *STREPTOCOCCUS PNEUMONIAE* SEROTYPES CAUSING INVASIVE DISEASES IN SERBIA – “FILLING GAPS IN MAPS”

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Streptococcus pneumoniae is a major cause of invasive disease (bacteremic pneumonia, septicemia, and meningitis) in children and adults worldwide (1). Also it is a common cause of uncomplicated pneumonia, sinusitis, and acute otitis media. Pneumococcus annually kills more than 800,000 children under 5 years of age (2). Many of these deaths could be prevented with vaccination.

Major pneumococcal virulence factor is capsula. Capsular polysaccharides are highly heterogeneous. To date, 93 pneumococcal serotypes have been identified (3), although only approximately 10 of them are commonly the cause of invasive disease (1). Geographical and temporary differences of main serotypes of pneumococci have been widely reported.

Currently, there are two generations of pneumococcal vaccines. First is pneumococcal polysaccharide vaccine (PPV23), comprised of purified polysaccharides of 23 different serotypes, that is recommended for adults over the age of 65 and some high-risk patient populations, but its use in children is limited as polysaccharides are poorly immunogenic in infants and children. Therefore, new generation of pneumococcal vaccine have been developed. Second generation includes 7-valent, 10-valent and 13-valent pneumococcal polysaccharide conjugate vaccines (PCV 7, PCV 10, PCV 13) composed of seven, ten and thirteen different pneumococcal polysaccharides conjugated to a protein carrier. These vaccines successfully protect newborns and infants from invasive pneumococcal diseases (IPD), as well as some noninvasive (non-bacteriemic pneumonia, otitis media). However, after vaccine introduction, increase in non vaccinal pneumococcal types (NVT) has been reported, phenomenon designated as replacement of serotypes.

Both PCV7 and PCV10 pneumococcal conjugate vaccines are registered and recommended in Serbia, but not reimbursed, and the vaccine coverage is low thus far. Prior to the introduction of vaccines no study on seroepidemiology of invasive pneumococcal diseases (IPD) in our country had been conducted.

Serotyping of pneumococci is important task for the National Reference Laboratory (NRL) for Streptococci and Pneumococci, which was established at the Institute for Microbiology and Immunology, Faculty of Medicine Belgrade in 2008. Since NRL was not funded, serotyping could not be performed at the time. However, NRL started to collect pneumococcal isolates, thus making collection of invasive strains, whose number reached 106 in 2012th year. Isolates were mainly obtained from patients older than 50 ys (45%), while 29% were originated from children <5 ys. Fifty-two strains were isolated from blood, 36 from cerebrospinal liquid, 17 from pleural liquid and one from biopsy specimen. Antimicrobial susceptibility for all isolates was tested using Vitek 2 automated system (AST-P576). E-test (bioMerieux, France) was used to determine penicillin and erythromycin MICs. Interpretation of resistance category was done using CLSI standard (2012) (4). After receiving donated antisera (manufactured by Statens Serum Institute, Denmark), serotyping was performed by Neufeld Quellung reaction. A total of 98 pneumococcal isolates were successfully typed.

Overall 25 different serotypes were found. In children (<5ys) the distribution of pneumococcal serotypes was more homogenous than in adults > 50 ys - 11 different serotypes

in children versus 19 in adults. The most frequently encountered serotypes were 3, 19F and 14, followed by 6A and 23F. In children (<5 ys) the most prevalent serotypes were 19F (23%) and 14 (20%), while in adults (>50 ys) serotype 3 dominated (33%). PCV-7 and PCV-10 vaccine coverage in children (<5ys) was 63% and 80%, respectively, while in adults (>50 ys) it was 27% and 31%, respectively. The serotype distribution of invasive pneumococcal serotypes in our country is similar to the distribution reported from other European countries in the pre-vaccine era. (5).

All isolates were susceptible to carbapenems, vancomycine, fluoroquinolones and telithromycin. Resistance (intermediate category included) was found to penicillin (PEN=32,08%), 3rd generation cephalosporines (CTR=17.9%), macrolides (ERY=41.51%), tetracyclines (TET=33,02%) and chloramphenicol (CHL=8.49%). Macrolide and penicillin co-resistance was present in 24.5% of isolates. Resistance was significantly more common in pediatric isolates and serotypes than in those from adults.

We can conclude that, in this first report on seroepidemiology of IPD in Serbia, we found that the most common serotypes causing IPD were 3, 19F and 14. Penicillin and macrolide resistance was most common in serotypes 6A, 6B, 14, 19F and 23F, especially in strains isolated from children. Although we don't know yet the true burden of invasive pneumococcal diseases in Serbia, these results will help fill gaps in epidemiological map of IPD with data from our country.

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4. EPIDEMIOLOŠKE KARAKTERISTIKE I IMUNIZACIJA PROTIV OBOLJENJA IZAZVANIH PNEUMOKOKOM

4. EPIDEMIOLOGICAL CHARACTERISTICS AND IMMUNIZATION AGAINST DISEASES CAUSED BY PNEUMOCOCCUS

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Of all people with pneumonia, was the cause of 40% pneumococcus. This infection often present in childhood with age and pre-existing chronic diseases caused by pneumococcus (*Streptococcus pneumoniae*), which is a gram positive diplococcus with about 90 serotypes. Invasive disease (bacteremia, meningitis, pneumonia -bacterial) and non-invasive disease (otitis media, pneumonia non-bacterial) and associated with NTHi - invasive (meningitis, septicemia, pneumonia) and invasive disease (otitis media, pneumonia, sinusitis, bronchitis), a serious problem in the present medicine.

Pneumococcal infections are responsible for more deaths than any other bacterial infection that can be prevented vaccine. More than 50% of the deaths could have been avoided by the use of vaccines.

Invasive pneumococcal disease (IPD), which includes sepsis, meningitis and pneumonia bacterial leading vaccine-preventable cause of death in children under 5 years of age. Using data from an extensive literature review of studies through 156, 2009. the journal Lancet published a meta-analysis in which the estimates to pneumococcal disease annually worldwide causes 826 000 deaths in children under five godina. To represents approximately 11% of all deaths in this age group of children. Predisposition to the disease on the age, chronic diseases (cardiovascular diseases and lung), anatomic and functional asplenija, immunodeficiency and other factors (obesity, smoking, genetic heritage, malignancies, therapy-radiateit). extremely high risk was observed with chronically ill children: sickle-cell anemia 150/100.000, asplenija 250/100.000, solid malignancies 300/100.000, 420/100.000 HIV infection, and hematologic malignancies 500/100.000. The most common and common bacterial complication is the flu and measles. Lethality at any higher risk ranges from 25% (pneumonia) and 50% (pneumonia with bacteremia) and up to 60% (meningitis). Resistance to antibiotics reduces the effects of therapy.

Continuous improvement of pneumococcal vaccine gave good effects in recent years in developed countries and the United States and EU. Key goal of vaccination is to reduce pneumonia vaccine complications, bacteremia, hospitalization for pneumonia and death.

Reduces more than 35-45%, bacteriemia for more than 60%, hospitalization by 50% and death in patients at high risk.

II USMENA PREDAVANJA
II ORAL PRESENTATIONS

**1. EPIDEMIJA PAROTITISA U REPUBLICI SRPSKOJ 2011-2012
PAROTITIS EPIDEMIC IN REPUBLIC OF SRPSKA 2011-2012.**

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Epidemic parotitis is acute, viral, contagious, generalized disease which is commonly accompanied by swelling of parotid glands.

Aim of presentation: Presenting the epidemic of parotitis in Republic of Srpska during period of 2011. and 2012.

Material and methodology: Analysis of all reported –registered cases during two year period (2011. and 2012.). Descriptive method has been used. Analised data originated from official sources, reports from primary health care institutions, hospitals and laboratory results of reference laboratories.

Results and discussion: Total number of reported cases in parotitis epidemic in 2011.-2012. was 7.813.

Total number of female patients was 3.125, and for male patients that number was 4.688. Largest percent of patients were in the age group from 20 to 29 years -57.6%. 28.5% of registered cases were patients aged 15 to 19 years and only 6% of all cases were patients in the age group from 30 to 39 years.

Total number of hospitalized patients was 319.

Total number of patients with complications was 114, mainly with orchitis.

Significant number of patients were refugees, displaced persons and members of Roma population. Epidemic was present in all regions of Republic of Srpska.

Conclusion: Parotitis epidemic in Republic of Srpska was a result of omission in vaccination with MMR vaccine during the war period.

Keywords: parotitis, orchitis, MMR vaccine

2. VAKCINACIJA PROTIV SEZONSKOG GRIPA 2012/2013: NEŽELJENI EFEKTI KOD ODRASLIH VAKCINISANIH U REGIONALNOM ZAVODU ZA JAVNO ZDRAVLJE, SLOVENIJA

2. 2012/13 SEASONAL INFLUENZA VACCINATION: EVALUATION OF ADVERSE EVENTS AMONG ADULTS IMMUNISED AT A REGIONAL PUBLIC HEALTH INSTITUTE, SLOVENIA

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Objectives: While Slovenia is facing low and declining seasonal influenza vaccine uptake, all aspects that may influence the decision to get vaccinated are being analysed. Adverse events following immunization (AEFI) represent one of the implicated factors. We tried to investigate them in details beyond the scope of routine reporting by healthcare professionals, where minor events go usually unreported but are still a factor of concern for persons deciding to get vaccinated.

Materials and methods: Our study included all the adults who got vaccinated at our regional public health institute during the 2012/13 influenza season. A trivalent split-virion, inactivated vaccine from a single producer was used nationwide. Data were collected with a self-administered questionnaire 4 weeks after vaccine administration. The study population was divided in two groups based on age: Group 1 (18-59 yo); Group 2 (≥ 60 yo).

Results: Of 475 persons vaccinated at our institution 405 were willing to participate. Questionnaires were returned by 146 persons; 45% females and 55% males. AEFI observed respectively in Group 1 (n=50, median age=51 yr) and Group 2 (n=96, median age=71 yr) were: injection site reactions (32% and 15%); asthenia (10% and 0%); malaise (6% and 1.1%); headache (6% and 4.3%), arthralgia (6% and 5.4%) and myalgia (2% and 3.2%). No serious side effects were detected.

Conclusion: The observed AEFI are in line with the safety profile of the vaccine; predominantly local reactions with a lower occurrence in the elderly group. From preliminary data vaccination coverage in Slovenia is at 4.4% (16.8% ≥ 65 yo and 11% among healthcare professionals). Population perception of vaccine safety is still scarred by the 2009 pandemic season. In the search for novel approaches to tackle the problem of low uptake, data on a reassuring safety profile finds their place in activities aimed to enhance awareness with data-driven health information.

Key words: Influenza vaccines; Influenza; Vaccination; Adverse effects; Immunization

3. RESPIRATORY DISEASES IN MUNICIPALITY OF PROBISTIP IN 2011 YEAR

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Objective of the work:To show the condition of the respiratory diseases in municipality of Probishtip in 2011 year.

Method of the work: A descriptive-analytical method was used. The incidence is 1:100000 residents. **Results:** In the 2011 year in Probishtip, 3210 cases of respiratory diseases with incidence 19812/100000 were registered. The infections of the upper respiratory tracts are 2913 (incd.17983 /100000) while 297 on the lower respiratory tracts.(incidence 1833 /100000) Most patients with upper respiratory tract we have in the 7-week-171 cases. (incidence 1056 /100000) Largest number of infections on the lower respiratory tract are in the 2 week - 21 cases.(incidence 130 /100000) The age group 20-59 is most frequent among the upper (1147 cases) and lower (103 cases) respiratory tracts. Compared with R. Macedonia incidence in Probishtip in both upper and lower respiratory tract is lower. In R.Macedonia the most typical age group is 0-6 years, while in Probishtip is the age group 20-59 years.

Conclusion: In municipality of Probishtip in 2011 year, upper respiratory tract infections occur nine times more than the lower respiratory tract infections while most diseased are at the age group of 20-59 years.

Keywords: case, respiratory diseases, infection.

4. TREND I EPIDEMIOLOŠKE KARAKTERISTIKE TUBERKULOZE U NIŠAVSKOM OKRUGU

4. TREND AND EPIDEMIOLOGICAL CHARACTERISTICS OF TUBERCULOSIS IN THE NISAVA DISTRICT

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Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. It manifests mostly in the lungs, but it can affect other organs too. Only the patient suffering from pulmonary tuberculosis is contagious. The infection is not the same as the disease, because 10% of those who are infected get sick from tuberculosis.

The aim of this paper is to show the trend and epidemiological characteristics of tuberculosis in the territory of the Nisava District in the period from 2008 to 2012.

As material: were used records of contagious disease from the area of the Nisava District in the period from 2008 to 2012, the annual reports of IPH Nis and annual reports of the Department of Pulmonary Diseases and Tuberculosis in Nis. A descriptive epidemiological method was used.

Results: in the observed period there were 266 cases of pulmonary tuberculosis and extrapulmonary localization. Trend of disease is slowly declining and is $y = -0.2 + 53.8x$ and $R^2 = 0.0015$. The highest rate of disease has Doljevac Municipality - 178.74, and the whole Nisava District 67.80/100000 inhabitants. The rate of incidence of males is two times higher than the incidence of women (91.86:44.57). The highest rate of incidence is age 70-79 – 111.81. The highest number of patients - 10.90% was registered in August. 51.88% of TB patients originated from the rural area, 31.58% are pensioners and the unemployed, 25.94%, 84.21% were hospitalized, at 92.86% vaccination status was unknown or the report noted that the patient was not vaccinated. The success of vaccination ranged from 76.65% to 97.62% and depended on the availability of the vaccine on the market.

Conclusion: The effect of the risk factors, increasing living standards, vaccination, timely detection and proper treatment of TB patients should reduce morbidity and the further emergence of resistant bacilli to drugs.

Key words: tuberculosis, trend, epidemiology, vaccination

5. EPIDEMIOLOŠKE KARAKTERISTIKE RESPIRATORNIH OBOLJENJA U R.
MAKEDONIJI

**5. EPIDEMIOLOGIC FEATURES RESPIRATORY DISEASE IN THE REPUBLIC OF
MACEDONIA**

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The aim of this paper is to present epidemiological situation with respiratory disease in the Republic of Macedonia. Materials and methods. Data is used for movement of the respiratory disease from the P.H.I. Institute for public health - Skopje. The data refer to the period in 2012. Descriptive method of work is applied. Results. The largest recorded incidence of respiratory disease was recorded during the winter months, with an incidence in February of 4716.4/100000 for upper respiratory infections incidence from 1387.8/100000 to the lower respiratory tract. In relation to the age structure the largest number of patients is registered at the age group of 0-6 years, with most patients in March 30718 on the upper airway and 8085 in the lower respiratory tract. Conclusion. The high incidence of respiratory disease in the Republic of Macedonia indicates that one of the causal factors for their high incidence is the lack of specific protection of age structure until the age of 7, as well as resistance to a number of antibiotics as a result of uncontrolled intake during frequent infections.

Keywords: epidemiology, characteristics, respiratory, diseases, Republic of Macedonia.

III POSTER PREZENTACIJA
III POSTER PRESENTATION

1. EPIDEMIOLOŠKE KARAKTERISTIKE SEZONSKOG GRIPA U AP VOJVODINI U SEZONI 2012/13

2. EPIDEMIOLOGICAL CHARACTERISTICS OF FLU IN AP VOJVODINA DURING 2012/13 SEASON

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Objectives: The aim of this study was to analyze the epidemiological characteristics of influenza through surveillance of influenza during 2012/13 season.

Materials and methods: Data for the analysis were epidemiological surveillance of influenza through sentinel surveillance, virological surveillance and surveillance of severe acute respiratory distress infection/syndrome. Sentinel physician network consisted of doctors from the public sector, general practitioners, pediatricians and specialists in emergency medicine and pulmonologists from intensive care units. Supervision was the Institute of Public Health of Vojvodina, Novi Sad. Material of patients (nasopharyngeal swabs) was tested by PCR in the Institute of Public Health of Vojvodina.

Results: Opposite to pandemic season, when recorded intensity of clinical activity of the influenza virus (above of the intermediate threshold) was from 45th to 52th week of surveillance with the peak incidence at 50 th week (1090.3/100.000), in the next three seasons intensity of virus activity was above intermediate threshold in the period of 4 to 11 weeks (season 2010/11), of 11 to 13 weeks (season 2011/12) and of 5 to 11 weeks (season 2012/13) of surveillance.

Summarized results of virological surveillance of influenza, in the season 2012/13, include the largest number of confirmed cases was coincided with the highest activity of the virus influenza during sentinel surveillance of ILI. The largest number of patients was registered in the age group 5-14 years and lowest number of patients was in age group over 65.

The case definition ILI was the best applied in the age group 5-14 where was the highest percentage of confirmed influenza cases (83.7%) compared to the tested of suspected ILI cases.

Within virological surveillance, in the season 2012/13, out of total of 378 tested samples of patient material, infection was confirmed in 192 (51%) samples: influenza type B was confirmed in 51.6% (99/192), influenza A (H1N1)pdm09 in 33.3% (64/192), influenza A (H3N2) in 13.0% (25/192) and influenza A – not subtyped in 2.1% (4/192) samples.

The average age of 10 patients with fatal outcome during the season 2012/13 was 53.5 (range: 26 to 68 years), and dominant type with fatal outcome was influenza type B (40%). In the patients with fatal outcome, 60% cases were two comorbidities associated with influenza and 80% was acute respiratory distress syndrome.

Conclusion: The influenza virus is constantly present in a population with different intensity and prevalence type of virus. The disease is most frequently registered among vulnerable young adults, but fatalities due to influenza xere usually registered among the elderly population.

Key words: Influenza, sentinel surveillance, pandemic influenza, virological surveillance

ILI – *influenza like illnes*

C. SESIJA: GLJIVIČNE INFEKCIJE: PREVENCIJA, DIJAGNOSTIKA I TERAPIJA
C. SESSION: FUNGAL INFECTIONS: PREVENTION, DIAGNOSTICS AND THERAPY

I PREDAVANJA PO POZIVU
I INVITED LECTURES

1. DOKAZIVANJE RANIH LABORATORIJSKIH BIOMARKERA I NJIHOV ZNAČAJ ZA ISHOD INVAZIVNIH GLJIVIČNIH INFEKCIJA KOD NAS
1. THE PROVING OF EARLY LABORATORY BIOMARKERS AND THEIR SIGNIFICANCE TO THE OUTCOME OF INVASIVE FUNGAL INFECTIONS

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Fungi are very abundant organisms in the vicinity of people (~ 1.5 million species) and all the more important causes of the infection (mycosis). Mycosis caused by a relatively small number of fungi (~ 100 types), and pathological processes may be localized on the surface or in deep body organs and tissues (systemic mycosis or an invasive fungal infection/IGI). IGI is characterized by poor clinical course, difficult and late diagnosis, poor prognosis and frequent lethal outcome, but there are patients who are treated in tertiary institutions and who are at risk due to the underlying disease (high-risk patients VRP). The most important group of VRP persons : with hematological malignancies, organ transplant, bone marrow transplant, HIV infection, a congenital immunodeficiency, pulmonary disease, with abdominal surgery, burns, in intensive care units and novordencad. In approximately 80 % of all cases, the IGI causing fungi genera *Candida* and *Aspergillus* which cause invasive candidiasis (IC), and invasive aspergillosis (IA). During the period from 1980 to 2010. The determined a significant increase in the prevalence of IC (50 %) and IA (about 300%). In VRP incidence of IGI is an average of 30 % (3-48 % depending on the underlying disease and risk factors), and mortality is up to 50 % for IC, and up to 90 % for IA. Reducing mortality depends on early laboratory diagnosis and timely and appropriate treatment. Diagnosis based on proving the fungus in tissue and/or isolation of fungi, and the results of therapy antimycogram (AM) is of major clinical importance (proven IGI). However, this method is a low -sensitive and a negative finding is present in about 50 % of the samples. Also, the isolation of fungi is a slow method because of the biology of fungi and there, and the difficulty in obtaining a representative sample. " Cost-benefit " analysis showed that the use of antifungals, without laboratorjiske confirm I am, significantly higher treatment costs and increases the possibility of resistance of fungi. AM and resistance data are significant savings to the health care system by reducing and rational use of antifungal drugs which are the most expensive. Using conventional methods for the diagnosis of IGI, in addition to having the biggest " evidence " power, may determine non - *Candida* and non - *Aspergillus* species of fungi that cause IGI in 20% of cases, the most important are : *Fusarium* genus, the genus *Cryptococcus* fungi and class *Mucoraceae*. These methods, despite the fact that rare and late yielding positive results are also important for the detection of fungi in cases of their primary location in the sinuses and lungs, where they can spread and lead to the development of IGI. Due to the fact that early diagnosis and early treatment key factors in reducing mortality from IGI, today for the early diagnosis of IGI

proving increasingly important biomarkers such as antigens (Ag), and the DNA of fungi and/or specific antibodies (Ab) patients. Positive findings Ag mushroom galactomannan (GM), manana (MN), beta- D -glucan (BDG) and specific anti- Aspergillus and anti - Candida At, significantly increase the percentage of " probable " IGI and for initiating early "pre - emptive " therapy. Some of these tests, such as GM, have been approved by the FDA, and has been included as a criterion for the diagnosis of IA by Escort/MSG.

In the past the following objectives were achieved: (i) the introduction, improvement and standardization of new laboratory procedures, as a basis for timely and optimal treatment, and the long-term cost reduction therapy and mortality, (ii) the introduction of tests for the timely and effective diagnosis based on a combination of method of : proving a fungus in the tissues, the isolation, characterization and results of AM and on the basis of laboratory evidence of early biomarkers (triple test) : GM, MN, BDG, and/or a specific person suffering at (iii) introduction of the EORTC/MSG criteria ("proven,", "probable", and "possible "/T) for the diagnosis of IGI and implementation of European standards. Patients are monitored, where a negative finding biomarkers, are safe and free from IGI prophylaxis, thereby avoiding the unnecessary use of antimycotics. In case of positive findings of laboratory biomarkers, if the patient without treatment mortality is high, and the timely implementation of therapy highly correlated with the survival of these patients. Implementation of early laboratory biomarkers in patients at risk for IGI is of great importance for patient monitoring and timely and proper application antigljivcnih agents.

2. GLJIVICNI SINUSISTIS – DILEME U DIAGNOSTICI I TERAPIJI 2. FUNGAL SINUSITIS – DILEMMAS IN DIAGNOSIS AND THERAPY

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Beside the fact that fungal diseases of paranasal sinuses are relatively uncommon, their prevalence increased worldwide in last two decades¹. This pathological condition can be present in all ages². Inflammation of sinuses mucosae can be caused by bacteria, viruses or fungi. Development is favored by anatomical variations, allergic component, obstruction of drainage of any origin (polyps, benign malignant tumors, edema...), ciliary dyskinesia, smoking, immune deficit, pollution of the environment, etc. Wide variety of infections can be present and clinically can be presented as invasive or not invasive forms, but comparing with bacterial there are some basically differences. It can be said that between 13.5 and 28.5% of all maxillary sinusitis is fungal or mixed fungal and bacterial infections³. Bacterial sinusitis are everyday pathology in ambulance, they are not so difficult for diagnosis and can have allergic component like predisposing factor. In acute forms they has clinical picture which is clear. Fungal sinusitis, are rare, allergic component is consequence of infection and clinical signs are usually discrete in noninvasive forms. Incidence of fungal sinusitis is rising³, and reasons for this can be explained by broad use of antibiotics, rise of use of immunosuppressive drugs and better diagnostic procedures. Dark and humid space of paranasal sinuses is perfect surrounding for fungi.

Classification divides fungal rhinosinusitis into invasive and non-invasive (also called extra mucosal) forms, based on the presence or absence of microscopic evidence of fungal hyphae within the tissues (mucosa, blood vessels or bone), respectively³. Invasive forms are divided in three groups granulomatous invasive fungal sinusitis, chronic invasive fungal sinusitis and acute fulminant fungal sinusitis. Noninvasive forms are divided, fungal balls, allergic fungal sinusitis, eosinophilic fungal rhinosinusitis, superficial sinonasal colonization (saprophytic form), as well as semiinvasive (last two of noninvasive fungal sinusitis and semi invasive fungal sinusitis are object of discussion are they or not separate categories⁴. Fulminant invasive fungal sinusitis is rare infection present in patients with immunodeficiency especially in neutropenic patients and present life treating situation⁵. Usually are caused by *Aspergillus spp.*, in immunodefficient patients^{5, 6}. In this group also belongs invasive sinusitis caused by *Mucor* species which can have devastating effects on face. Granulomatous invasive fungal sinusitis and chronic invasive fungal sinusitis have extensive bone erosion, multiple sinus involvement, and major bulk of disease being intra-sinus rather than extra-sinus⁷. Fungal balls present noninvasive form which can be defined like non-invasive accumulation of dense fungal concrements in paranasal sinuses, mostly in maxillary sinus³. Allergic fungal rhinosinusitis is a benign and non-invasive sinuses disease related to a hypersensitivity reaction to fungal antigens. Tissue edema with chronic inflammatory disturbances of the respiratory mucosa is present⁸. It is obvious that clinical presentation of fungal sinusitis can be very different depending of type, primarily depending of invasiveness of infection. It can be asymptomatic to very intensive like in acute fulminant fungal sinusitis.

Diagnostic procedures include plain radiographies, CT and sometimes NMR. Plain radiography can give just basically data about infection and false positive results can be seen

often. For example difference between fungal balls and foreign body in maxillary sinuses are difficult to separate³. CT is one usually diagnostic procedure for invasive forms and fungal balls. Any extra sinuses progression needs CT procedure as diagnostic tool. Here, one of biggest dilemmas and problem can be present. Most often fungal balls can be replaced for tumorous formation and detail analysis of CT presentations are necessary⁹. Other diagnostic procedures include biopsy, fine needle biopsy, echosonography and microbiological procedures³.⁹. Big problems can be seen in cases of invasive sinusitis where it is necessary in short time to evaluate diagnosis in light of followed surgical procedure.

It is interesting that in cases of fungal balls as well as in all fungal sinusitis cultures are frequently negative, up to 50%³. *Aspergillus* are most present form. Besides *Aspergillus spp*, moulds genera *Fusarium*, *Bipolaris*, *Curvularia*, *Exserohilum*, *Drechslera*, *Helminthosporium* and *Alternaria* species can be present. Besides low level of identification, for therapeutically reasons it is important to isolate fungi and if it is possible to apply antifungal susceptibility testing *in vitro*. Therapeutically access is also in relation to type of infection. Acute invasive fungal sinusitis need intensive therapeutically approach. In invasive type of fungal sinusitis surgery is prompt and necessary therapeutically approach from beginning of disease no matter of sequel of such therapeutically approach¹⁰. Besides surgery intreatment of invasive fungal sinusitis liposomal amphotericin B have important role besides it's toxic and allergic reactions^{11, 12}. Besides opinion that endoscopic surgery can be used in treatment of invasive forms in combination of liposomal amphotericin B, dilemma arises about use of endoscopic versus classical surgical access¹³. Another dilemma is to use or not surgery in every case because there are cases in literature which are treated only with liposomal amphotericin¹⁴. Another dilemma arises according to orbital exenteration¹⁵. Limited surgical debridement and use of amphotericin B is described in some cases for treatment of invasive fungal rhinosinusitis with orbit involvement, without orbital exenteration¹⁶. It can be said that beside treatment, mortality rate in invasive fungal sinusitis is still very high up to 50% and intracranial progression or lack of surgical treatment upraise this rate¹⁰. Noninvasive fungal sinusitis do not demand prompt surgical action as it was in case of invasive ones. Allergic fungal sinusitis proven by high IgE level in blood is known for variety of treatment plans¹⁷. Some of them include immunotherapy, some combination of corticosteroid and immunotherapy and some combination of immunotherapy, surgery and corticotherapy¹⁸. However, surgical therapy takes first place with three goals, to eliminate allergic agent and break circle, to give good aeration of paranasal sinuses and to estimate good drainage¹⁷. Besides therapy which can sometimes be very aggressive, rate of relapses can be very high up to 100%¹⁷. When we speak about therapy of fungal balls, surgical approach is evidently on first place¹⁹. Functional endoscopic surgery is gold standard in this field, but classical surgical procedures like Caldwell-Luc approach are also described¹⁹ and for intracranial, or orbital progression of disease external approach is indicated²⁰. Big dilemma is to use or not medicament antifungal therapy with surgery or not. Some authors suggest to its use for reduce infection and to prevent relapses of infection²⁰. Other authors think that only surgical approach other functional endoscopic or classical Caldwell-Luc is sufficient therapeutically options^{3, 21}. This question will directly relate to patient's development of disease. Any bone destruction are indication for more aggressive therapeutically approach²⁰. Complications of fungal sinusitis are presented primarily by spreading of disease in nearby anatomical compounds, like is intracranial penetration or penetration in orbit. When we speak about invasive forms sequels of surgical therapy can be devastating, like is eye exenteration, maxillectomy, loss of enormous quantity of face soft tissue etc. For surgeons such defect is indication for complex reconstructive procedures, but with big question is face transplantation indicated or not. With their low incidence, diagnostic problems, different clinical presentation and different therapeutically accesses fungal sinusitis can be problems in everyday clinical

practice. Most important difference is to divide fungal from bacterial sinusitis, fungal sinusitis from tumors in this area and to see if invasive or non-invasive form is present, which will directly influence therapeutic access. Besides numerous controversies and dilemmas in diagnosis and therapy, basically therapeutic access can be definite according to clinical signs.

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3. PREVALENCIJA GLJIVIČNIH INFEKCIJA KOD DECE SA MALIGNITETOM 3. THE PREVALENCE OF FUNGAL INFECTION IN CHILDREN WITH MALIGNANCY

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ABSTRACT

Invasive fungal infections (IFI) are an important complication in hematologic malignancies and stem-cell transplantation (SCT). This infection are a significant problem for children whose immune system is not functioning properly. However, there are limited data characterizing IFI in children. The cumulative incidence of IFI was 6.9%; Fungal infections are associated with significant morbidity and mortality (1).

Four cases of IFI were diagnosed in 4 patients with cancer over the last 5 years at our department. Two patients have acute lymphoblastic leukemia (ALL), two acute myeloid leukemia (AML). The age was 9 to 18 years. Dignosis were confirmed by ultrasonography and Magnetic resonance imaging, diagnostic test galatomamanan.

Analysis showed that age at diagnosis older than 10 years, relapse of original disease, long-term administration of broad-spectrum antibiotics, and acute myelogenous leukemia (AML) were the risk factors for IFI. All patients with IFI received long-term antibiotic and corticosteroid therapy.

Conclusions: Fungal infections are becoming an increasing problem during intensive therapy of acute leukemia and malignant disease, and contribute to poor therapy outcome. The diagnosis of fungal infection during life is extremely difficult and frequently late. There is the need of a more precise diagnostic test that would provide earlier diagnosis. The knowledge of risk factors is helpful in the diagnosis and therapy of fungal infections. The suspicion of fungal infection in patients at risk justifies the introduction of antifungal therapy and contributes to better therapeutic outcome.

Keywords: malignant disease, invasive fungal infections.

Introduction

Invasive fungal infections (IFIs) continue to cause considerable morbidity and mortality in children with malignant disease and in haematopoietic stem cell transplant (HSCT).

Diagnosis of IFI is difficult. Therefore, physicians rely on a constellation of clinical signs, radiography, culture, histopathology and adjunctive tests to establish diagnosis. Children with malignant disease often have multiple co-morbidities, and understanding the current outcomes and prognostic variables is therefore important for overall management.

Yeasts and moulds are endogenous colonizers and ubiquitous inhabitants of the environment; the healthy human immune system appears well equipped to defend against invasive infection. However, in immunosuppressed patients, many yeasts and moulds become opportunistic pathogens (2).

However, the most common causes of IFI, can be divided into three groups: *Candida species*, *Aspergillus species*; and other moulds (*Zygomycetes*, *Fusarium species* and *Scedosporium species*) that are increasingly reported as important pathogens in HSCT recipients (3).

Factors that are important in contributing to children with malignant disease risk for IFI include recent: past and present immune function, impacted by cellular deficiencies and dysfunction associated with administration of pharmacologic agents, use of indwelling devices, such as intravascular (IV) catheters, and breakdown of physical barriers that normally impair systemic invasion (e.g. translocation of *Candida species* across the intestinal mucosa, and exposure to inhaled fungi during periods of risk).

Candida species are a common inhabitant of the human gastrointestinal (GI) tract and skin. Breaks in the integrity of skin and GI tract mucosal barriers such as occurs during mucositis, may lead to IC, particularly in the context of immunosuppression (2) Older studies, performed prior to widespread prophylactic use of azole drugs, showed that underlying patient age, acute graft-versus-host disease (GVHD), donor human leucocyte antigen (HLA) mismatch, duration of neutropenia, underlying disease and specific conditioning agents (such as high dose total body irradiation) contribute to patient risks for IC (4) Use of prophylactic azoles had decreased the attack rate and 1-year cumulative incidence of IC, although recent studies have reported a consistent low incidence of 'breakthrough' infection, especially in the highest-risk patient population. Most recent studies report incidence rates in 5% range, with risk factors including (GI)-tract colonization, cytomegalovirus (CMV) disease, and prior episodes of bacteraemia (5). Risks associated with GI tract breakdown are one of the Despite improvements in supportive care, IFI is still associated with a significant mortality rate and high health care costs. In studies published within the last decade, mortality rates in children with candidemia range from 19% to 31%. Invasive aspergillosis in children is associated with even greater mortality: 68% to 77%. A higher mortality rate is seen in those with greater degrees of immunosuppression, particularly after hematopoietic stem cell transplantation (6).

Currently, there are 4 classes of drugs for treatment of IFIs: polyenes, triazoles, echinocandins, and nucleoside analogues. Differing antifungal pharmacokinetics between children and adults were demonstrated, requiring dose modification. Significant differences in toxicity, particularly nephrotoxicity, were identified between classes of antifungal agents. Therapy needs to be guided by the pathogen or suspected pathogens, the degree of immunosuppression, comorbidities (particularly renal dysfunction), concurrent nephrotoxins, and the expected length of therapy (3, 5).

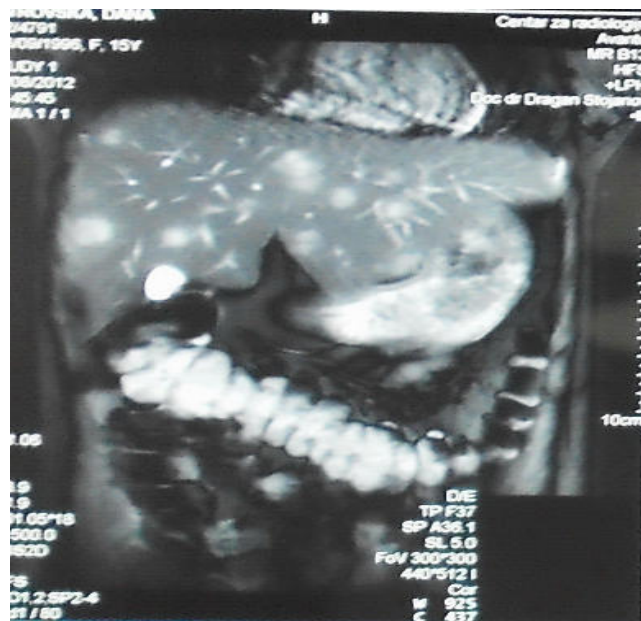
Results

Four cases of invasive fungal infections were diagnosed in 4 patients with cancer over the last 5 years at our department. Two patients have acute lymphoblastic leukemia (ALL), two acute myeloid leukemia (AML). The age was 9 to 18 years. Dignosis were confirmed by ultrasonography and Magnetic resonance imaging, diagnostic test galatomamanan.

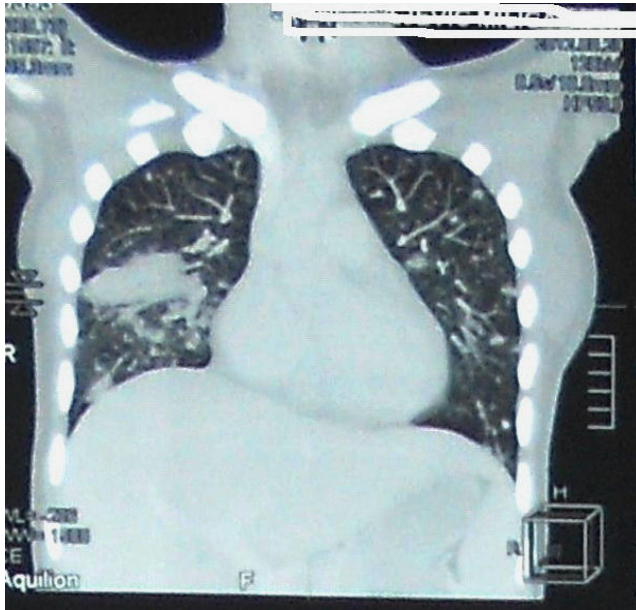
Analysis showed that age at diagnosis older than 10 years, relapse of original disease, long-term administration of broad-spectrum antibiotics, and acute myelogenous leukemia (AML) were the risk factors for IFI. All patients with IFI received long-term antibiotic and corticosteroid therapy (Table 2.)

Table 1. The infected lesions

The infected lesions	No of patient
LUNG	1
ENDOPHTHALMITIS	1
SINUSITIS	1
LIVER	2
KIDNEY	1
FUNGEMIA	2



Picture 1. Hepatosplenic candidiasis



Picture 2. Pulmonary aspergillosis

Tabela2. Risk faktor for IFI our patient

Patient	MS	DM	E DJ	AS
Malignant disease	AML	ALL	AML	ALL
Broad-spectrum antibiotics and corticosteroids	YES	YES	YES	YES
Neutropenia	YES	YES	YES	YES
Age	18	15	15	9
Diagnosis	Aspergillus galactomanan Ag + MSCT+	Galatommanan Neg- MR+	Galatommanan Neg- MR+	Candida mannan Ag +.
Infected lesion	Lung, sinusitis, endophthalmitis	Liver	Liver, kidney	Fungemia
better therapeutic outcome.	No	yes	yes	No
	died	alive	alive	died

Discussion

Invasive fungal infections continue to be associated with significant mortality and morbidity. Despite significant differences in pediatric antifungal pharmacokinetics, few adequately powered pediatric trials have been conducted to compare the efficacy and toxicity of different antifungal agents. Pediatricians often rely on adult data with results extrapolated to children. No consistent differences in treatment success or mortality rate have been demonstrated in comparative trials in patients with fever with neutropenia, candidemia, and invasive candidiasis. Insufficient evidence is available to recommend routine use of combination therapy for candidemia or aspergillosis. Additional research on antifungal agents in children to assess pharmacokinetics and toxicity of newer agents, relative efficacy, and cost is needed. (5).

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4. INVAZIVNA ASPERGILOZA KOD PEDIJATRIJSKIH HEMATOLOSKIH PACIJENATA

4. INVASIVE ASPERGILLOSIS IN PEDIATRIC HEMATOONCOLOGY PATIENTS

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Abstract

Invasive aspergillus infections are recognised a few decades ago. Improvement of various types of medical technologies resulted in a greater number of high risk patients for this infection. New methods of diagnostics and new drugs resulted in better survival rates. However, high index of suspicion and prompt inclusion of treatment, without waiting for fulfilling criteria of proved infection, are of paramount importance for optimal outcome. Along with this issue, clinicians have to bear in mind side effects of antimicotic drugs as well their price.

Key words: aspergillus, invasive infection, diagnosis, children

Invasive fungal infections during the last two decades are emerging threats in hematology patients and in patients treated with allogeneic bone marrow transplantation. One of the most frequent infections in this setting is caused by fungal species *Aspergillus*.

Aspergillus spp. are ubiquitous saprophytic molds, causing mainly a variety of pulmonary syndromes, but they could cause infections of paranasal spaces, central nervous system and skin. Although the most immunosuppressed patients are the most frequently affected, aspergillosis could be found in immunocompetent or minimally immunosuppressed persons.

There are several types of the pulmonary involvement, usually referred as invasive and noninvasive pulmonary aspergillosis. A clinical and radiological finding depends on the degree of immunosuppression and anatomical integrity of the lung parenchyma. Invasive forms are invasive pulmonary aspergillosis and chronic necrotic aspergillosis, while aspergiloma and allergic bronchopulmonary aspergillosis are noninvasive forms of aspergillus pulmonary disease.

Invasive pulmonary aspergillosis (IPA) is first described in 1953, but it is more frequent during the last two decades due to a more intensive chemotherapy regimens and increasing number of allogeneic bone marrow transplantations. In the setting of solid organ transplantation, especially vulnerable group are patients who underwent lung transplantation.

Besides immunosuppressed patients with low absolute number of granulocytes, invasive aspergillosis could be a problem in patients with functional defects of granulocytes such as chronic granulomatous disease. Patients at risk are also those suffering cystic fibrosis and low birth weight and premature infants.

Clinical picture of IPA is not specific. Prolonged fever in neutropenic patients unresponsive to broad spectrum antimicrobials, with clinical and radiological signs of bronchopneumonia are common scenario. Hemoptysis and pleuritic chest pain (due to small pulmonary infarcts) could be present.

Although diagnostic criteria and procedures are well defined, diagnosis of invasive aspergillosis (IA) still remains a challenge. Criteria for proven infection are histological or cytopathological confirmation or positive culture test with clinical and radiological abnormalities. Patients in risk for IA are usually in a serious clinical condition, with low platelet count which makes invasive diagnostic procedures impossible.

Radiological confirmations of lesions in the lung parenchyma are reasonable alternative. However, nodular lesions, halo and crescent signs are neither specific nor sensitive for IPA. This problem is potentiated in pediatric patients in whom no specific radiological presentation exist.

Biomarkers such as galactomanan and beta-d-glucan assays could be helpful in circumstances where invasive diagnostic procedures are not feasible. Galactomanan is a polysaccharide released by *Aspergillus* during growth. It is reported that it could be detected in several days before clinical signs. However, galactomanan test could be false positive since this polysaccharide is found in the food. Concomitant medication with piperacilin/tazobctam could also give a false positive result. One of the major limitations of galactomanan test is that it is not specific for *aspergillus* spp. Infections with *Fusarium* and *Zygomycetes* could also be galactomanan positive.

Beta-d-glucan assay is a nonspecific diagnostic marker that could be found in a wide range of fungal infections, including *Pneumocystis jirovecii*. Concomitant use of meropenem, piperacilin/tazobactam and cefepime could give false positive results.

PCR testing is not recommended as standard diagnostic tool, since there is a great false positivity, and PCR cannot discriminate between colonization and infection. Also, this method is not fully standardized.

Because of plenty of diagnostic difficulties, treatment should be started as soon as clinical circumstances justify it, without waiting for radiological, mycological and antigen detection tests confirmation.

The drug of choice for the treatment of IA is voriconazole. Lipid formulations of amphotericin B could be used (bearing in mind that *A. terreus* and *A. nidulans* are resistant to amphotericin b). Echinokandin derivatives could be effective in IA refractory to standard treatment.

Preventive measures for IA are directed to the high risk patients, the population of bone marrow transplant recipients and patients after the lung transplantation. The measures include isolation of the patient in the room with positive air pressure and filtrated air and prophylactic treatment with antimicrotics given peroraly, intravenously or by inhalations.

Conclusion:

Despite contemporary diagnostics and treatment, invasive infection with *Aspergillus* spp. still carries a great burden of morbidity and mortality. Infection with *Aspergillus* could be proved by culture and/or histology only in a small number of patients, due to a almost universally present contraindications for invasive diagnostic procedures. Since neither radiological findings nor biomarker studies are completely sensitive and specific, early treatment according to a high index of suspicion is usually necessary for successful outcome.

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5. RECURRENT GENITAL CANDIDOSIS OF WOMEN – DIAGNOSTIC AND EPIDEMIOLOGICAL ASPECT

5. REKURETNA GENITALNA KANDIDOZA ŽENA – DIJAGNOSTIČKI I EPIDEMIOLOŠKI ASPEKT

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Abstract

Recurrent GC, the infection that afflicts an extremely large number of women worldwide, is characterized by at least three or more vulvo-vaginal fungal infection episodes per year, in spite a conducted therapy with antimycotics. The cause of primary, recurrent GC is still unknown. In the opinion of clinicians GC (GC) is a syndrome that includes *Candida spp.* colonization of vaginal mucosa and diverse range of genital yeast infections, depending on the symptoms, duration of infection and its recurrence, number of microorganisms and species of the genus *Candida* causing human infection.

Key words: Recurrent GC, diagnosis, prevalence

Introduction

The prevalence of recurrent vaginal candidosis of women has been constantly increasing in recent years. Although this fungal infection is not characterized by severe symptoms, the problem in fact lies in its very high incidence and prevalence. Millions of women suffer from persistent yeast infections, despite many treatment modalities that are presented as effective and efficient. Considering the problem, we have to admit that unfortunately the only certain things are successiveness of these infections and our inability to resolve them. Until today it has not been established whether attenuation of local protective mechanisms in the vaginal mucosa influence the infection or recurrence of GC. There are many new potential risk factors for GC, many false positive or negative diagnoses, there are no rapid diagnostic methods, so the theoretical and practical solution of this considerable health issue is still to be sought for¹.

These infections are not life threatening but affect the self esteem of women, being potentially the generator of intimate, psychological, marital, social problems, and still an uncomfortable topic for discussion, not to mention that they are often wrongly treated by practitioners².

Beside bacterial vaginosis, GC is the most common genital infection of women³. About 30% of women have an isolate of *Candida spp.*, 15-30% with the isolate have symptoms, 20% of women have asymptomatic *Candida*-colonization, and 75% of women in their lifetime and 55% up to the age of 25 at least once have had this fungal infection. And according to the latest data, 10% of women are suffering from recurrent vaginal candidosis^{1,2,4,5}.

The predominant cause of sporadic and recurrent candidosis of the female genital tract is *Candida albicans* (*C. albicans*) (85-90%). *Non- albicans* species such as *C. tropicalis*, *C. krusei*, *C. kefyr*, *C. parapsilosis*, have become more frequent agents in recent years. It is assumed that antifungal single-dose drugs, treatment with low doses of antimycotics and over-the-counter availability of these drugs have significantly influenced the rising prevalence of non-albicans species⁶.

The symptoms of GC in women are often vulval itching or soreness, vaginal discharge, superficial dyspareunia and external dysuria, with clinical signs such as erythema, fissuring, non-offensive discharge, satellite lesions and oedema. Until now, there have been few sporadic cases of abortion caused by *C. albicans*, and fungal infections of the fetal tissues and placenta⁷.

According to the latest classification, GC includes Candida-colonization, sporadic GC and chronic genital yeast infection caused by *Candida species*¹.

Candida spp. is an opportunistic fungi and part of the physiological flora of the vaginal mucosa in a large number of women (about 20%; about 30-40% of pregnant women)⁴. A positive finding of *Candida spp.* can not differentiate the colonizers of pathogenic yeast, so that positive results have to be interpreted in the context of presence/absence of infection symptoms.

Sporadic female GC is characterized by milder symptoms of infection and after treatment it does not recur, nor persists. Chronic GC of woman is a serious, persistent and recurrent genital fungal infection, including serious forms of GK, persistent non-albicans infections and recurrent vaginal candidosis.

The source of *Candida species* in the vaginal mucosa is a colonized perianal region. Local protection and tolerance mechanisms enable the survival and persistence of fungi-colonization in the long run^{1,2}.

The generally accepted dogma is that the change of environment enables multiplication of *Candida spp.* and occurrence of infection. Colonization factors, aspartyl-proteinase, mycotoxin, the ability of the transition to multicellular form and phenotypic variation are among the virulence factors of *Candida spp.* enabling the transformation of saprophytes to pathogenic fungi, or colonization to fungal infection^{1,2,8}.

Non-specific protection mechanisms controlling the colonization are the protective mechanisms of vaginal epithelial cells, mannose-binding lectins, lactoferrin present in the secretion of vaginal mucosa and phagocytosis. However the protective role of the listed factors has not been fully proven^{1,8}.

Examining humoral and cellular immunity protective role, it has been found that women suffering from GC have higher IgA antibody titers⁹, but it is believed that higher titers of IgE antibodies can contribute to the appearance of infection and symptomatic disease².

In terms of systemic cellular immunity, a dysregulation of cellular reactivity has not been proven at the system level. The valid assumption is that Th-1 cytokine profile has a protective role, whereas Th-2 cytokine profile predisposes the multiplication of fungi and infection, and so far there are only experimental studies to demonstrate that the local immunization may be protective¹⁰.

This monomicrobe disease has many risk factors such as immunodeficiency, diabetes mellitus, even refined sugar diet, pregnancy, oral contraceptives, long-term use of antibiotics, behavioral factors such as sexual activity, chemical contacts, atopy, allergy or local hyperreactivity reaction. In terms of the mentioned risk factors, based on contradictory data in the literature, it can be said that these risk factors may predispose to sporadic GC, but are not established as the principal risk factor in the development of recurrent infections^{1,2}.

Recurrent genital candidosis is considered to be a consequence of reinfection or relapse¹¹. Regarding the fact that genital candidosis in women is followed by colonization of the intestinal mucosa with the same strains, the digestive tract after local antifungal therapy can be the reservoir of *Candida spp.*¹². Exogenous reinfection due to absence of partner treatment

is registered in 15-20%¹³ of women with this form of infection. A significant percentage of women with recurrent GK, 30 days after treatment and with negative mycological analyses have manifest infections again. It is thought that important characteristics of the micro-organism responsible for relapse are the resistance to the applied antifungal agent, virulence of the strain, or presence of hyperactivity in the vaginal mucosa^{1, 2}.

Since symptoms and signs of this infection are non-specific, diagnosis of genital candidosis involves microbiological examination.

In the case of a positive microscopic findings blastoconidia and/or hyphae with a neutral pH, cultivation of materials is not required and physicians can prescribe an antifungal therapy. In the case of pH > 4.5 and presence of leukocytes, a mixed infection has to be considered. Unfortunately, half of women with GK and a positive culture do not have positive microscopic findings. In view of that, all the materials of symptomatic women who have microscopically negative findings, pH < 4.5, no Clue cells neither protozoa *Trichomonas vaginalis* presence, should be cultivated^{1, 2}.

Since *Candida spp.* colonizes the vaginal mucosa, positive culture results have to be interpreted in relation to the clinical and microscopic findings, and only then antifungal therapy can be taken into consideration. There are no commercial serological or molecular tests available, and many laboratories are not equipped adequately for microscopic or microbiological diagnosis, so that a large number of women with GC or recurrent GK remain undiagnosed¹.

The treatment of asymptomatic carriers is not recommended. Any antifungal protocol is successful in most cases of sporadic *Candida* genital infections of women.

The management of recurrent GK form involves diagnosis with positive cultivation of yeast, prescription of local or oral antifungals, and follow-up of the patients until the termination of symptoms and negative mycological examination.

As much as 50% of treated patients will have relapses in the following three months. For women found to have recurrent GK, a prolonged administration of antifungal drugs within some of the valid protocols is recommended¹.

In conclusion, we can say that after numerous investigations the cause of primary recurrent GC in women has not been established. The symptoms and clinical findings of infection are not specific and laboratory confirmation is necessary for the diagnosis of GK, while the diagnosis of recurrent form involves careful review of clinical, mycological and earlier findings, with mandatory consideration of other etiologies.

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6. REKURETNA GENITALNA KANDIDOZA ŽENA – MOGUĆNOST FARMAKOTERAPIJE

6. RECURRENT GENITAL CANDIDOSIS OF WOMEN – POSSIBILITY OF PHARMACOTHERAPY

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More than 50 percent of women older than 25 years have one episode of vulvovaginal candidiasis,¹ but fewer than 5 percent of these women experience recurrent infection.² Vulvovaginal candidiasis is considered recurrent when at least four discrete episodes occur in one year or at least three episodes occur in one year and are not related to antibiotic therapy. Recurrent vulvovaginal candidiasis is distinguished from persistent infection by the presence of a symptom-free interval. Although *Candida albicans* (*C. albicans*) is the pathogen identified in most patients with vulvovaginal candidiasis, other possible pathogens include *Candida tropicalis* and *Candida glabrata*. Increasingly, *Candida species* other than *C. albicans* have been found to cause yeast vaginitis. Sobel suggests that some cases of reinfection may actually be cases of relapse, due to either inadequate testing methods, which result in false-negative results after treatment, or to ineffective treatments. Misdiagnosis of the causative organism may also result in ineffective treatment. The most common causal *Candida species* is *C. albicans*. However, other, less easily eradicated species may also be involved. In fact, recurrent infections may be caused by the resistance of non – *C. albicans* species to antifungal agents.

Every effort should be made to eliminate factors that predispose an individual to vulvovaginal candidosis. No correctable causal factors are apparent in most women; moreover, recurrent vulvovaginal candidosis is multi-factorial in terms of cause. A small subgroup of women seem to benefit from restricting dietary intake of refined sugars. Before therapy, mycological culture should be obtained to confirm diagnosis and to identify the specific *Candida spp.* involved. The optimal treatment for recurrent vulvovaginal candidiasis has not yet been defined. Consequently, treatment must be individualized based on a comparison of effectiveness, convenience, potential side effects and cost.

Successful therapy requires an induction course of either oral or topical azole, continued until the patient is asymptomatic and culture negative (7–14 days). In recurrent vulvovaginal candidosis, failure to initiate a maintenance regimen results in clinical relapse in 50% of patients within 3 months. Maintenance-suppressive regimens include ketoconazole (100 mg daily) and once-weekly regimens of either 500 mg clotrimazole suppositories or 150 mg fluconazole orally. All three regimens are effective in preventing breakthrough vaginitis, however, the better safety of fluconazole and clotrimazole means that ketoconazole is rarely used for maintenance suppression. One should note that, no matter what maintenance regimen is chosen, symptomatic relapse is seen in half the women within a short time of cessation of treatment.

There are a number of therapeutic options. The treatment of choice is with a single dose of fluconazole, 150 mg, or other azoles, or intravaginal clotrimazole, 100 mg, daily for 7 days. Oral and topical treatments with azoles for 1 to 14 days are also useful and there are no significant differences between them. The adverse effects of oral therapy that have been

reported include gastrointestinal discomfort, headache, tiredness, and skin rashes, but they are rare and well tolerated. Fluconazole and itraconazole can cause arrhythmias when associated with cisapride or H1-antihistamines such as astemizole. Topical azoles belong to risk category C and since they have not been associated with any increase in the risk of congenital defects they may be used for 7 days during pregnancy. The efficacy of oral and topical treatments is similar, and the decision regarding which to use will depend on the doctor's experience and patient's preferences. Fluconazole, 150 mg (2 doses separated by 3 days), is used in recurrent candidal vulvovaginitis. Maintenance treatment should be continued for 6 to 12 months with clotrimazole pessaries, 500 mg per week; fluconazole, 100-150 mg per week; itraconazole, 400 mg per month; itraconazole, 100 mg per day; or oral ketoconazole, 100 mg per day. The same regimen is used in patients with human immunodeficiency virus infection who develop vulvovaginal candidiasis. There is no evidence that treatment of sexual partners contributes to resolution of the condition. Treatment of the partner is therefore only recommended in symptomatic cases. Although 90% of patients do not suffer recurrences during maintenance treatment, symptoms do recur in 30%-40% of patients after withdrawal of the treatment. The maintenance regimen can be repeated in these cases.

If a woman with an established diagnosis of recurrent vulvovaginal candidiasis does not respond to an imidazole, infection with a resistant non – *C. albicans* species may be present. Terconazole vaginal cream is the agent of choice when infection with a species other than *C. albicans* is suspected. The potent interference of this agent with the cytochrome P450 isoenzymes makes *C. tropicalis* and *C. glabrata* more susceptible to treatment.

Itraconazole may have a greater in vitro activity against non-albicans species than other azoles, like fluconazole. Therefore, itraconazole may be more effective against a broader range of causative organisms. Oral therapy with itraconazole tends to be shorter in duration than topical therapy. Moreover, patients often prefer oral treatment due to the shorter treatment period and to the ease of administration compared to topical treatments, resulting in increased patient compliance. As well, itraconazole used as a prophylactic treatment is a viable option in preventing future recurrence of infection.

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II USMENA PREDAVANJA

II ORAL PRESENTATIONS

1. SYSTEMIC FUNGAL INFECTIONS IN PRETERM INFANTS

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Introduction: Systemic fungal infection is the inflammatory response to the presence of fungi. According to the pathogenesis it is divided into early and late. Incidence of fungal infection is 3 to 4/1,000 in low birth weight newborns (LBW). The most common cause of fungal infections in neonates are *Candida albicans*, *Candida tropicalis*, *Candida parapsilosis* and less frequently *Candida lusitanae* and *Candida glabrata*. In untreated newborns the mortality rate was 80%. Clinical signs of fungal infection are nonspecific. Diagnosis is confirmed by its verification in blood cultures, lumbar aspirate and urine culture.

Objective: Report of a newborn with systemic fungal infection, monitoring of the disease, diagnostic procedures and the effects of treatment.

Results: The newborn in the 30th week of gestation, with a birth weight 1550gr was admitted to our Intensive Care Unit from the Gynecology and Obstetric Clinic with severe signs of perinatal asphyxia and respiratory failure. All clinical, laboratory, bacteriological and antimicrobial analysis were done. Due to necessity of respiratory support, mechanical ventilation was performed for three weeks. Chest X rays showed RDS III-IV degree. Exogenous surfactant (Curosurf) was commenced as well as double antimicrobial therapy along with other symptomatic treatment. After obtaining positive cultures (nasal tube - *Stenotrophomonas maltophilia*, aspirate - *Klebsiella sp.*, *Acinetobacter sp.*, Blood culture - *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Candida parapsilosis*) antibiotic therapy was changed and we started with systemic antifungal treatment in the preventive dose (Fluconazole). After confirmation of *Candida parapsilosis* in blood culture we started therapeutical doses of Fluconazole. Several consecutive blood culture and urine samples confirmed *Candida parapsilosis*. During hospitalization blood derivatives and immunoglobulins were administrated. After several weeks of treatment an improvement in general condition and normalization of inflammatory parameters was achieved. The newborn was discharged with bronchodilatory and long-term corticosteroid therapy due to development of bronchopulmonary dysplasia (BPD).

Conclusion: The risk of invasive fungal infections is high, especially in premature low birth weight newborns. They require mechanical support and are exposed to a wide range of antibiotics. These are all contributing risk factors for development of fungal infection, which require timely diagnosis and treatment.

2. GLJIVIČNE INFEKCIJE KRVI U JEDINICI INTENZIVNE NEGE - OPŠTA BOLNICA SOMBOR

2. FUNGAL BLOOD INFECTIONS IN MEDICAL CARE UNIT -GENERAL HOSPITAL SOMBOR

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Objective: Showing the results of positive hemocultures with isolated *Candida spp.* in period from 2009 until middle of 2013 as well as their sensibility in intensive care unit (ICU) patients.

Materials and methods: Hemocultures are done according to standard operative procedures of microbiological laboratories (Bact/Alert–Biomerieux France). Retrospective 5-years analysis of hemocultures results at Center of Microbiology, Department for Public Health, Sombor. Review of medical documentations of the patients with isolated *Candida spp.* treated in ICU.

Results: Among approximately 1500 isolates per year, *Candida* is isolated: **2009**-*Candida spp.*-4, *Candida albicans*-3; **2010** *Candida spp.*-3; **2011**-*Candida albicans*-2, *Candida spp.*-5, *Candida parapsilosis*-1; **2012**-*Candida spp.*-6; **2013**-*Candida spp.*-3. 10% patients had *urosepsis*, 25% had malignity and 65% had acute surgery disorder. Nine mortal cases were registrated. 27 patients received triple antimicrobial therapy/beta lactams, chinolons and metronidasol/and later antimycotics. Five patients weren't supported by mechanical ventilation.

Conclusion: An increase of *CANDIDA spp.* noticed as well as the need of obligatory identification of the isolate, sensibility tests to antimycotics for focused treatment. It's important to emphasize the clinical value of early empirical use of antifungal agents within the high –risk patients.

Key words: fungal blood infection, *Candida spp.*, Intensive Care Unit, antifungal agents

3. INVAZIVNE MUKORMIKOZE KOD PACIJENATA SA MALIGNITETIMA U SRBIJI - PRIKAZ DVA SLUCAJA

3. INVASIVE MUCORMYCOSIS AT PATIENTS WITH NEOPLASM IN SERBIA – REPORT OF TWO CASES

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Objectives: Invasive mucormycosis (IMM) is the third most frequent fungal infection in patients with malignancies often resulting in fatal outcome.

Case report 1: A 52-year-old male was diagnosed with acute myeloblastic leukemia. Following febrile neutropenia chest computerized tomography (CT) showed soft-tissue consolidation change. Bronchoscopy and histology indicated aspergillosis. Galactomannan (GM) test showed low positivity and voriconazole was included. After two months, the patient developed a fever and the chest multislice CT showed soft-tissue mass. Voriconazole was reintroduced and bronchoscopy was repeated but new histological and mycological examination confirmed pulmonary IMM, fungus *Rhizopus oryzae*. Amphotericin B (AmB) was started and the complete remission was verified.

Case report 2: A 53-year-old male was diagnosed with neoplasm Squamocellulare oesophagi. Following the induction chemotherapy he developed febrile neutropenia. Patient was admitted to the clinic with a hemorrhagic-necrotic lesions of the zygomatic, orbital and frontal regions of the face and with lung infiltrates (CT). Facial necrotic changes were spearheaded expansively and vital parameters were worsened. Mycological examination indicated IMM. AmB therapy was included resulting in favorable outcome.

Conclusions: As a rare and emerging disease IMM is not well understood by the medical community. An improvement of education about prevention, timely diagnosis and proper treatment is necessary.

Key words: Invasive mucormycosis, malignancies, galactomannan test, mycology examination, *Rhizopus oryzae*

4. GENOTIPIZACIJA I OSETLJIVOST NA ANTIMIKOTIKE KLINIČKIH IZOLATA *CRYPTOCOCCUS NEOFORMANS* U SRBIJI

4. *CRYPTOCOCCUS NEOFORMANS*- GENOTYPES AND ANTIFUNGAL SUSCEPTIBILITY PROFILE OF CLINICAL STRAINS IN SERBIA

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Objectives: *Cryptococcus neoformans* is an opportunistic fungal pathogen that may cause life-threatening illness in immunocompromised patients. The aim of study was to determine genotypes and antifungal susceptibility of *C. neoformans* strains collected in Serbia over a 20-year period (from 1989 to 2009).

Materials and methods: We investigated 34 *C. neoformans* clinical isolates, obtained from 25 immunocompromised patients. Using amplified fragment length polymorphism (AFLP) technique, genotypes were determined. Antifungal susceptibility was tested by a broth microdilution method (Micronaut MHK-2 plates, Merlin Diagnostika, Germany).

Results: The majority of isolates was genotype AFLP1 ($n=20$; 58.8%), followed by AFLP2 ($n=10$; 29.4%), AFLP3 ($n=3$; 8.8%) and AFLP1B ($n=1$; 2.9%). Susceptibility testing of isolates showed that minimum inhibitory concentrations (MIC, in $\mu\text{g/ml}$) were: 0.5 for amphotericin B and 5-fluorocytosine, 2 for fluconazole, 0.125 for itraconazole and 0.062 for voriconazole and posaconazole. Resistance was observed for 5-fluorocytosine ($n=2$; 5.8%) and fluconazole ($n=1$, 2.9%).

Conclusion: This is the first epidemiological study of genotypes and antifungal susceptibility of *C. neoformans* clinical strains isolated in Serbia.

Key words: *Cryptococcus neoformans*, epidemiology, genotyping, susceptibility testing, antifungals

III POSTER PREZENTACIJE
III POSTER PRESENTATIONS

1. EPIDEMIOLOŠKE KARAKTERISTIKE PACIJENATA SA CANDIDA-
ONIHOMIKOZOM

1. EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS WITH CANDIDA-
ONYCHOMYCOSIS

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Objectives: To determine the epidemiological characteristics of patients with *Candida* infection of nail was the goal of this study.

Materials and methods: The data for 2012. from the laboratory for mycological analyses, Centre of Microbiology, Public Health Institute Niš were reviewed. For statistical analyses of collected, systematized and encrypted data, statistical calculator within the program Epi Info (Ver.6.04) and statistical package SPSS (16.0 for Windows) were used.

Results: It was found that the prevalence of *Candida* onychomycosis is 23.11%. There were no statistically significant differences between the positive and negative results of fungal infection with regard to sex, age, or in relation to the place of patients' residence. *Candida* onychomycosis of hand nails was found in a large number of patients (39/84,8%). The dominant cause of onychomycosis was *Candida albicans* (*C. albicans*) (39.1%), followed by *C. parapsilosis* (26.1%) and *C. guilliermondi* (15.2%). There was no statistically significant difference in *i*) distribution of isolated species regarding to gender ($\chi^2 = 10.08$, $p = 0.260$), age ($p = 0.350$), and place of residence ($\chi^2 = 12.31$, $p = 0.138$); *ii*) the localization of onychomycosis in relation to patients age ($p=0,797$), sex ($p=0,556$) and place of residence ($p=0,663$) *iii*) the distribution of isolated species of *Candida* in relation to the localization of infection ($\chi^2 = 13.73$, $p = 0.089$).

Conclusion: A significantly higher number of patients with hand *Candida* onychomycosis supposed that risk factors can be in hand exposure to certain physical and chemical effects that cause damage of the nail and maybe predispose this infection.

Key words: *Candida spp.*, onychomycosis, epidemiology

2. IMUNOGLOBULIN-E POSREDOVANA HIPERREAKTIVNOST NA AEROALERGENE GLJIVA

2. IMMUNOGLOBULIN-E-MEDIATED ALLERGY TO FUNGAL AEROALERGENS

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Objectives: Molds can provoke hypersensitivity and may play a role in chronic allergic To determine the prevalence of atopic patients with significant level of specific IgE antibodies to antigens of fungi commonly present in the environment and the air, was the aim of this study.

Materials and methods: The data from the polyclinic Human - Niš were reviewed. In this retrospective study 65 examinees (34 female/31 male) were evaluated for aero-allergies. The specific IgE to antigens of fungi *Aspergillus fumigatus*, *Alternaria tenius*, *Candida albicans*, *Cladosporium herbarum* or *Penicillium notatum* was determined by the Polycheck^R method (Biocheck GmbH, Germany). For statistical analyses of collected, systematized and encrypted data, statistical calculator within the program Epi Info (Ver.6.04) and statistical package SPSS (16.0 for Windows) were used.

Results: Eight patients (12,3%) had positive findings of specific antibodies (AB) to fungi antigens. In only two patients (3,1%) diagnostic significant titre of specific AB was established. In these bouth cases hypereactivity was proved to all used fungi antigens. There was no significant difference in the frequency of positive findings in relation to gender ($p = 0.138$), despite the fact that 75% of those with positive findings of specific AB are male. Diagnostically significant titers of specific AB were proved in children younger than 10 years, but the statistical analysis did not show significant difference regarding the age patients ($p=0,606$). All positive results were recorded in the winter-spring period, but it was not found that the occurrence of positive findings have seasonal character ($p = 0.452$).

Conclusion:. The prevalence of hyper reactivity to fungal aeroantigens is not significantly high due to the fact that fungi grow almost everywhere.

Key words: Moulds, fungi aeroallergen, hypersensitivity

D. SESIJA: MIKROBIOLOGIJA DANAS
D. SESSION: MICROBIOLOGY TODAY

I USMENA PREDAVANJA
I ORAL PRESENTATIONS

1. SEROEPIZOOTIOLOŠKO - EPIDEMIOLOŠKA ISTRAŽIVANJA INFEKCIJE
ZAPADNOG NILA U REPUBLICI SRBIJI U PERIODU 2008-2013.

**1. SEROEPIZOOTIOLOGICAL - EPIDEMIOLOGICAL STUDY OF WEST NILE
VIRUS INFECTION IN THE REPUBLIC OF SERBIA DURING THE 2008-2013
PERIOD**

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Abstract

The disease caused by the West Nile virus (WNV) has been known since 1937 when it was described for the first time in Uganda. After spreading to Europe and the Middle East, the disease has changed its primary location. Today WN infection is a significant health problem in the world. Due to the current epizootiological and epidemiological situation in Europe investigations occurrence of WNV were introduced in Serbia, also. The testing for WNV antibodies have been intensified in the period from 2008 to 2012. During this period a total of 3618 serum samples from 18 localities (2736 animal sera taken from 8 different species and 882 human sera samples) were tested. Applied examination method was gel immunodiffusion test and the representative samples were confirmed by the plaque reduction test (PRNT-90).

The results have confirmed that WNV antibodies are present in 9 out of 18 tested locations in the Republic of Serbia. The percentage of seropositive samples varies from 0.42% in Požarevac (horses and humans) up to 6.45% in Novi Pazar (dogs). Out of the species that were tested, the highest seropositivity was recorded in horses (3.97%), and lowest in poultry (0.31%). The available data show that WNV is present and widespread in the Republic of Serbia, which allowed the mapping of its distribution.

Key words: seroprevalence, Republic of Serbia, West Nile virus

Acknowledgements – The work was carried out by the projects TR 21047 and TR 37015 funded by the Ministry of Education, Science and Technological Development of the Republic of Serbia

2. PRIMENA BACTEC 9120 SISTEMA U PREGLEDU HEMOKULTURA U INSTITUTU ZA JAVNO ZDRAVLJE NIŠ TOKOM 2010 – 2012.

2. APPLICATION OF BACTEC 9120 BLOOD CULTURE SYSTEMS IN THE PUBLIC HEALTH INSTITUTE NIS DURING 2010 – 2012.

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Introduction: Fast identification of pathogens present in the blood of patients is extremely necessary due sepsis is a common cause of morbidity and mortality in hospitalized patients. Applying the standard procedures for processing blood cultures considerably prolongs the time required for diagnosis (1). Utilization of automated and computerized monitoring blood culture system represents a significant contribution to the diagnosis of sepsis. During the previous twenty years several automated systems for monitoring blood culture (Bact-Alert, Extra Sensing Power, Vital etc.) were developed (2, 3). Automated systems procedures for processing involves incubating blood culture material 5-7 days at 35 °C (6), continuous data monitoring, with different method for detection of micro-organisms present in the blood (detection by chemical sensors, CO₂ manometer, fluorescent scanner).

Objectives: Analysis of the results obtained using the automated blood culture system BACTEC 9120 in the laboratory of the Centre of Microbiology, Public Health Institute Nis, during the 2010-12 was the goal of this retrospective survey.

Materials and methods: The study group included 831 patients with symptoms and signs of sepsis, hospitalized in the Clinical Center of Nis. Blood culture procedure was performed using the BACTEC 9120 blood culture system.

The microbiological data from the Centre of Microbiology (the type of isolated organism, the number of sampled blood, the number of positive blood culture and time required for procedure in hours) and data from medical histories of patients (the body temperature, blood pressure, the number of respirations per minute, the number of white blood cells per 3 mm of blood) from Clinical Centre-Niš, were reviewed.

Blood samples (10ml from adults and 3ml for pediatric patients)) were inoculated in commercial media Bactec Plus Aerobic F + media, Becton Dickinson; Bactec Plus Anaerobic media + F, Becton Dickinson for adult patients and Pedes Bactec Plus + F, Becton Dickinson for pediatric patients. Microorganism growth was monitored by Bactec 9120 (Automated Blood Culture Systems Becton Dickinson, Diagnostic Instrument System, Sparks MD, USA) in the standard protocol of 5 days (120 hours) and incubation at 37 °C. Each positive sample subcultivated on solid media (blood, endo, SS and chocolate agar). Identification of isolates was based on standard microbiological methods, API and Vitek 2 COMPACT system (bioMerieux, France). Negative samples were cultured on blood and endo agar.

Bacterial growth is interpreted as finding the pathogen or contaminant according to the criteria MacGregor and Beaty's (4)

The main clinical criteria for identification of sepsis was the presence of one or more parameters: the value of body temperature (≥ 38 °C or <36 °C), hypotension (<90 mmHg), tachypnea > 20 respirations/min, white blood cell count $> 12,000$ or $<4,000$ /mm³ (5).

Coagulase-negative staphylococci or polymicrobe flora of the skin that were isolated from patients blood without clinical signs of sepsis were considered as contaminated blood cultures.

Results: Using automated method during the three-year period we examined 1532 blood culture sampled from 831 patients. Different types of microorganisms were detected in the blood of 187 (22.50%) patients.. However, clinical data showed that in 39.57% (74/187) causes, positive blood culture represented contamination (Table 1).

Table 1: Number of examined patients with sepsis and contaminated blood cultures

Clinical status	Number of patients	Positive blood cultures	The total number of examined blood culture
Sepsis	113	144	153
Contamination	74	90	163
Total	187	234	316

Types of microorganisms isolated from blood cultures are shown in Table 2.

Table 2: Types and frequency of isolated microorganisms

TYPE OF MICROORGANISM	Num.	%	NUMBER OF PATIENTS	
			sepsis N	contaminated blood culture N
<i>Staphylococcus epidermidis</i>	78	33.33	8	61
<i>Staphylococcus aureus</i>	39	16.66	31	/
<i>Staphylococcus sp.</i>	23	9.83	10	7
<i>Streptococcus β hemolyticus gr. A</i>	1	0.43	1	/
<i>Streptococcus agalatae gr. B</i>	2	0.86	1	/
<i>Streptococcus pneumoniae</i>	4	1.71	3	/
<i>Streptococcus viridans spp.</i>	3	1.28	/	2

<i>Streptococcus sanquis</i>	1	0.43	1	/
<i>Streptococcus intrmedius</i>	1	0.43	1	/
<i>Streptococcus anginosus</i>	1	0.43	1	/
<i>Enterococcus faecalis</i>	8	3.41	7	/
<i>Enterococcus faecium</i>	2	0.86	1	/
<i>Enterococcus sp.</i>	3	1.28	/	2
<i>Bacillus spp.</i>	3	1.28	/	2
<i>Difteroies</i>	3	1.28	/	2
<i>Listeria monocitogenes</i>	1	0.43	1	/
<i>Acinetobacter baumannii</i>	8	3.41	6	/
<i>Acinetobacter calcoaceticus</i>	5	2.14	4	/
<i>E.coli</i>	9	3.85	7	/
<i>Serratia spp.</i>	1	0.43	1	/
<i>Klebsiella pneumoniae</i>	7	2.99	3	1
<i>Citrobacter sp.</i>	2	0.86	1	/
<i>Enterobacter sp.</i>	5	2.14	3	/
<i>Proteus mirabilis</i>	4	1.71	2	/
<i>Providencia spp.</i>	1	0.43	1	/
<i>Salmonella enteritidis</i>	1	0.43	1	/
<i>Pseudomonas aeruginosa</i>	9	3.85	7	/
<i>Pseudomonas spp.</i>	1	0.43	/	1
<i>Candida albicans</i>	5	2.14	5	/
<i>Corinebacterium poprinicum</i>	1	0.43	/	1
<i>Corinebacterium bovis</i>	1	0.43	/	1
<i>unidentified microorganisms</i>	1	0.43	/	1
Total	234	100	187	

Based on MacGregor and Beaty's criteria, and the analysis of clinical data, microorganisms are classified into three groups. Isolation of species *Staphylococcus aureus*, *Streptococcus β heamolyticus gr. A*, *Streptococcus pneumoniae*, *E. coli*, *Proteus mirabilis*, *Salmonella enteritidis*, *Pseudomonas aeruginosa* and *Candida albicans* was clinically significant finding, while isolating of difteroids and *Bacillus spp.* was indicator of contamination. It should be noted that the growth of *Enterococcus spp.* and bacteria of Enterobacteriaceae family in most cases confirmed sepsis (in 90% of cases). Isolation of *Pseudomonas aeruginosa* was also confirmed sepsis unlike others species of *Pseudomonas* genus.

The third group of bacteriae are the micro-organisms that with the presence of clinical signs confirm sepsis, however in the absence of clinical signs indicate contamination. For example, only a 11.59% (8) of the patients with isolated coagulase-negative staphylococci from blood had sepsis.

Data on the time period that was necessary for software program to determine the presence of microorganisms in the patients material is present on the table 3.

Table 3: Average time to determine the presence of microorganisms in the patients blood

Type of microorganism	The average time to determine the presence of microorganisms in patients blood	
	Patients with sepsis	contaminated blood cultures
<i>Staph. epidermidis</i>	20.45 ^h	39 ^h
<i>Staph. aureus</i>	20 ^h	/
Family of <i>Enterobacteriaceae</i>	19 ^h	38.5 ^h
<i>Unfermentative bacillus</i>	23.5 ^h	39 ^h
<i>Streptococcus spp.</i>	20 ^h	31 ^h
Difteroides and <i>Bacillus sp.</i>	/	39.58 ^h
<i>Candida albicans</i>	22 ^h	/
Mean	20.82 ^h	37.42 ^h

Discussion: The hemoculture results validity is in direct correlation with the applied methodology. Standard microbiological method has a number of disadvantages as a long incubation period, frequent drilling, the possibility of contamination of the sample and the lack of selective culture media. By introducing of automated hemoculture processing systems many deficiencies of standard methods have been overcome or reduced.

The percentage of positive blood culture (22.50%) is similar to our findings in the previous period and to the percentage that was determined by other authors who have used this system in the processing of hemoculture (7, 8, 9).

Type of microorganism isolated from the blood and the number of samples from which they were isolated are the basic criteria for distinguishing bacterial infection from contamination. However, the results in this study confirm that the final evaluation is possible only with the compliance of microbiological analysis results with clinical data for each patient individually.

Isolation of *Streptococcus β heamolyticus gr. A*, *Streptococcus pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella enteritidis*, *Pseudomonas aeruginosa* and *Candida spp.* confirmed bacteremia. Difteroides and *Bacillus spp.* were contaminants in blood culture.

Staphylococcus epidermidis considering as the most common contaminant can be the cause of bacteremia in patients with intravascular catheters, as well as in patients on hemo or peritoneal dialysis.

The results of Washington et al. (10) research that included 67 medical centers in Europe, Asia and America indicate that *Staphylococcus sp.* is the most common cause of sepsis patients from America, contrary *E. coli* is dominant in patients from Europe and Asia. Coagulase-negative *staphylococci* are the most prevalent cause of sepsis in 7 States and 28 European centers. *Streptococcus viridans* group, normal inhabitants of the oropharynx, when is penetrate to the blood often causes inflammation of endocardium. Ruiz et al. (11) confirmed that *Streptococcus sanquis*, *Streptococcus mitis*, and *Streptococcus anginosus* can cause clinically significant bacteremia. Fungemia represent common complication of hospitalized patients with severe burns and cardiac surgery patients (12). In our study, all five cases of fungemia were caused by *Candida albicans*.

Blood culture contamination is a common problem in microbiology laboratories and it is usually caused by improper sampling of samples. However, some authors believe after their investigation that the contamination is a consequence of irregularly material processing than in the blood sampling (6). Careful treatment of personnel and the environment, influence that the rate of contamination can be reduced to 4%. Also, the reducing of contamination is possible in closed systems where the blood is inoculated in a vacuum-sealed bottles and microorganisms growth follow by the automated systems.

Conclusion: Based on our results it can be concluded that *Streptococcus spp.*, *Staphylococcus spp.*, *Candida spp.* and *Enterobacteriaceae* family are the most frequent causes of sepsis. The multiplication of various microorganisms present in the patients blood can be recorded by the Bactec 9120 system in significantly shorter period of time then in standard protocol, therefore the results of the microbiological analysis can be get faster.

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3. PREŽIVLJAVANJE *CAMPYLOBACTER JEJUNI* I *CAMPYLOBACTER COLI* U PILEČEM MESU

3. SURVIVAL OF *CAMPYLOBACTER JEJUNI* AND *CAMPYLOBACTER COLI* IN CHICKEN MEAT

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Introduction: One of the most important bacterial zoonosis is campylobacteriosis. The genus *Campylobacter* consists 18 species, including *Campylobacter jejuni* (*C. jejuni*), *Campylobacter coli* (*C. coli*) which are the most common causes of bacterial enteritis in the modern world, with about 400 million patients each year. Bacterial reservoir of this genus are domestic and wild animals, and the sources of *Campylobacter* infections are: food (undercooked chicken and raw and pasteurized milk) and unprocessed drink water (from cold mountain streams).

Objectives: To determine the survival of *C. jejuni* and *C. coli* at refrigeration temperature (+4°C) and freezing (-20°C) in chicken meat after different periods of incubation (30 minutes, 1, 2, 4, 8 and 10 weeks), and to evaluate the effect of different types of substrates and the presence of aerobic bacteria on their survival.

Materials and methods: Samples of meat that did not contain wild strains of *Campylobacter* were inoculated with known strains, *C. jejuni* NCTC 11351 and *C. coli* ATCC 33559 and packed in special bags which were stored at +4°C and -20°C. The presence of *Campylobacter* was tested according to ISO 10272-1:2006, on selective and nonselective media.

Results: The mean number of surviving *C. jejuni* was 7.48 log₁₀ CFU/g of meat specimens incubated 30 minutes at ambient temperature. At +4°C until the fourth week this number had reduced to 3.70 log₁₀ CFU/g, and 8 weeks was below the level of detection. The average number of *C. jejuni* on the incubation temperature of -20°C up to four weeks reduced to 3.01 log₁₀ CFU/g and on the 10th week was 2.82 log₁₀ CFU/g. The mean value of the number of surviving *C. coli* in meat specimen incubated 30 minutes at ambient temperature was 7.17 log₁₀ CFU/g. At +4°C this value was reduced on the fourth week to 1.32 log₁₀ CFU/g, and after 8 weeks was below the level of detection. At the incubation temperature of -20°C, the number of survived *C. coli* after four weeks was reduced to 3.08 log₁₀ CFU/g and after 10 weeks it was 2.60 log₁₀ CFU/g. The presence of aerobic bacteria did not affect the survival of *C. jejuni* and *C. coli* in chicken meat.

Conclusions: Saving the chicken on the low and freezing temperatures reduces the number of present *Campylobacter* bacteria, which is an important preventive measure in reducing campylobacteriosis in the human population. However, a number of these bacteria survive at low temperatures, and thus the way of keeping the food products of animal origin may be only one of the preventive measures.

Key words: *Campylobacter jejuni*, *Campylobacter coli*, survival, chicken

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4. NADZOR NAD IZOLATIMA *SERRATIA MARCESCENS* U NEONATALNOJ JEDINICI INTENZIVNE NEGE

4. SURVEILLANCE OF *SERRATIA MARCESCENS* IN A NEONATAL INTENSIVE CARE UNIT

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Objectives: To investigate the colonization patterns and identify potential outbreak sources of *Serratia marcescens* in neonatal intensive care unit of the Institute of Neonatology in Belgrade during the period from January 2010-June 2011, epidemio-

logical investigations, environmental surveillance and typing by pulsed-field gel electrophoresis (PFGE) of the recovered isolates were performed.

Materials and methods: Bacterial isolates were identified using standard phenotypic methods and sensitivity to antibiotics was carried out by Kirby-Bauer disc-diffusion method. PFGE using endonuclease XbaI as a restriction enzyme was performed for genotyping.

Results: One hundred and eighty-eight specimen cultures from colonized or infected neonates were positive for *S. marcescens*. Environmental screening was performed and the majority of samples were negative for *S. marcescens* (only 1 of 96 samples was positive). Eleven *S. marcescens* isolates from neonates and one environmental isolate (from hand washing soap bottle) were further genotyped. The investigation demonstrated a genetically related cluster of *S. marcescens* isolates in 9 neonates and 1 environmental isolate, while two remaining isolates had different genotypes.

Conclusion: PFGE typing is useful in distinguishing strains which appeared to be the same by phenotyping in order to facilitate prompt evaluation of possible outbreak so that effective preventive measures could be instituted.

Keywords: *Serratia marcescens*; neonatal unit, PFGE

5. DETEKCIJA ANTIOKSIDATIVNE AKTIVNOSTI CIJANOBAKTERIJSKIH SOJEVA FRAP METODOM

5. DETECTION ON ANTIOXIDANT ACTIVITY OF CYANOBACTERIAL STRAINS BY FRAP METHOD

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Objectives: Cyanobacteria represent an interesting source of various bioactive compounds with an antioxidant activity. Antioxidants are the compounds, which combat the free radicals by intervening at any of the three major steps of the free radical mediated oxidative process.

Materials and methods: In the present study, the antioxidant capacity of 11 cyanobacterial strains belonging to the *Spirulina*, *Microcystis*, *Anabaena* and *Nostoc* genera have been tested using FRAP assay. The reduction potential of intracellular ethanol extracts has been calculated based on the calibration curve of standard solution of ascorbic acid. The antioxidant activity has been expressed as mg of ascorbic acid (AA) equivalent per gram of dry extract.

Results: Cyanobacterial strains belonging to the *Nostoc* genus (2S₇B, 2S₁, 2S₉B, LC₁B, S₈, 2S₃B) have expressed the highest antioxidant activity compared to the other tested genera, whereby the obtained values ranged between 651,634 and 1.684,402 mg of AA equivalent/gram of dry extract. In the case of two strains, Č₂ and Č₅, belonging to the genus *Anabaena*, the recorded values have been 158,774 and 629,948 mg of AA equivalent/gram of dry extract. A radical scavenging activity has also been observed in the referent strain *Microcystis* PCC 7806 (135,076 mg of AA equivalent/gram of dry extract). The lowest antioxidant activities have been found in two *Spirulina* strains (163,746 and 1,141 mg of AA equivalent/gram of dry extract).

Conclusion: The intracellular extracts of all tested strains have showed a radical scavenging activity whereby each strain has expressed a different antioxidant capacity indicating that antioxidant activity is a strain-specific property. Based on the presented results, the tested cyanobacterial strains, especially the strains of the *Nostoc* genus, can be a concern as a potential natural source of antioxidant compounds.

Keywords: Microbiology, FRAP assay, antioxidant activity, cyanobacteria

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6. PROBIOTSKI SOJ *LACTOBACILLUS RHAMNOSUS* LB-64-PRIKAZ DOSADAŠNJIH
EKSPERIMENTALNIH I KLINIČKIH ISPITIVANJA

**6. PROBIOTIC STRAIN OF *LACTOBACILLUS RHAMNOSUS* LB-64:
PRESENTATION OF PREVIOUS EXPERIMENTAL AND CLINICAL TRIALS**

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Lactobacillus rhamnosus LB-64 is a strain used as the active component of probiotic preparation in the regulation of human gastrointestinal tract (GIT) microflora disorders. Its application started in 1968 and it has been used ever since owing to the strain properties. LB-64 has the characteristics of a probiotic strain, particularly the ability to survive well in and colonize the gastrointestinal tract.

The **aim of this paper** is to present the previous experimental and clinical trials of *Lactobacillus rhamnosus* LB-64 that demonstrated its beneficial effects on human health and safe application in all age groups.

Material and methods: Confirmation of strain identification was carried out in the reference laboratory in Scotland (NCIMB) using PCR and API 50 CHL set. The experiments performed in the Institute Torlak included the following tests: strain viability test by growing on the modified MRS medium, LB-64 propagation test to obtain the specific number of colonies – effective dose, and survival test by lyophilization to preserve probiotic properties for the period of three years; testing antagonistic effect on pathogens *in vitro* using strains from the Institute’s collection; antibiotic susceptibility test by dilution method; safety test on white mice. Randomized clinical studies of beneficial effects on the health of children and adults, as well as safe application of the strain were carried out in in-patient clinics.

Results: *Lactobacillus rhamnosus* LB-64 demonstrated good viability, antagonistic effect on numerous pathogens, resistance to the tested antibiotics, and safety. Beneficial properties have been confirmed by establishing balance in the oral microecology and in the disturbed ecosystem of the entire gastrointestinal tract in case of diarrheas with different etiology, reduction in hypercholesterolemia and hyperammonemia, stabilization of intestinal mucosa and its permeability to allergens. The application of LB-64 to the most susceptible population – prematurely born babies - showed no side effects, thus confirming its safe use.

Conclusion: Beneficial properties and safe application of the strain *Lactobacillus rhamnosus* LB-64, representing the active component of the probiotic product Liobif, justify not only its use as a food supplement, but also the continuation of clinical trials.

Key words: *Lactobacillus rhamnosus*, probiotic, gastrointestinal tract disbalance

II POSTER PREZENTACIJE
II POSTER PRESENTATIONS

1. PRIMARNA DIJAGNOZA INFEKCIJE *HELICOBACTER PYLORI* KOD
DISPEPTIČNIH PACIJENATA DETEKCIJOM ANTIGENA SA MONOKLONSKIM
ANTITELIMA

**1. THE PRIMARY DETECTION OF HELICOBACTER PYLORI INFECTION IN
DYSPEPTIC PATIENTS USING EIA STOOL ANTIGEN TEST WITH
MONOCLONAL ANTIBODIES**

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Backgrounds: The latest Maastricht Consensus Report recommended stool antigen test (SAT) using monoclonal antibodies as an efficient noninvasive test for the diagnosis of *Helicobacter pylori* (*H. pylori*) infection.

Objectives: To report the primary diagnosis of *H. pylori* in Niš area using monoclonal stool antigen test, and to analyze association of upper gastrointestinal symptoms with *H. pylori* infection.

Materials and methods: The specimens were analyzed among 55 hospitalized patients (28 male and 27 female; the mean age 62.59) and 92 outpatients (41 male and 51 female; the mean age 45.98) using Amplified IDEIA HPStAR (Oxoid, England) test.

Results: The overall incidence of *H. pylori* infection was 56.46 % (147/69). We found high rates of *H. pylori* infection in all investigated age groups ranged from 39.47 to 100%. In hospitalized group *H. pylori* was most frequently detected in patients with gastric ulcer (80%), following in patients with duodenal ulcer (50%), and antral gastritis (50%).

Conclusions: This study showed that the *H. pylori* infection among dyspeptic patients is still high in this region. Also, the strong correlation between *H. pylori* and peptic ulcer disease has been reconfirmed.

Key words: *H. pylori*, monoclonal stool antigen test

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2. PRISUSTVO ANTITELA PREMA *CAMPYLOBACTER JEJUNI* I *YERSINIA ENTEROCOLITICA* O:3 KOD SUMNJE NA REAKTIVNI ARTRITIS

2. PRESENCE OF ANTIBODIES TO *CAMPYLOBACTER JEJUNI* AND *YERSINIA ENTEROCOLITICA* O:3 WHEN REACTIVE ARTHRITIS IS SUSPECTED

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Objectives: To determine the presence of serum antibodies against *Yersinia enterocolytica* O:3 and *Campylobacter jejuni* in patients suspected of suffering from reactive arthritis.

Materials and methods: The humoral immune response to *Y. enterocolytica* O:3 and *C. jejuni*, followed by a period of three years with 122 persons who are suspected to be suffering from reactive arthritis. The level of antibody class IgA and IgG was determined by ELISA.

Results: The presence of total serum antibodies to *Y. enterocolytica* O:3 was observed in 39 patients. Positive values of immunoglobulin classes A and G were found in 22 sera (20 patients -16.39%), the presence of only IgA was observed in 16 (13.11%) and in 10 (8.19%) patients recorded the presence of IgG. Positive values of some of the classes of immunoglobulins to *Campylobacter* were found in 14 patients. The presence of serum antibodies of both classes were found in five patients (4.09%), only IgG in three patients (2.46%).

The presence of serum antibodies to *Y. enterocolytica* O:3 and *C. jejuni* were recorded at the same time in two patients.

Conclusion: In suspected ReA finding of serum antibodies is more often to *Y. enterocolytica* O:3 than to *C. jejuni*.

Key words: *Yersinia enterocolytica*, *Campylobacter jejuni*, serum antibody, ELISA

3. SEROLOŠKA POTVRDA RESPIRATORNIH INFEKCIJA IZAZVANIH
CHLAMYDOPHILA-OM PNEUMONIAE I *MYCOPLASMA-OM PNEUMONIAE* U
POPULACIJI JUŽNO BAČKOG OKRUGA

**3. SEROLOGIC CONFIRMATION OF RESPIRATORY INFECTIONS CAUSED
BY *CHLAMYDOPHILA PNEUMONIAE* AND *MYCOPLASMA PNEUMONIAE*
IN THE RESIDENTS OF SOUTH BACKA DISTRICT**

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Objectives: Global incidence of pneumonia caused by *Chlamydomphila pneumoniae* (Cp) is ranging from 5% in Asia to 8% in the North America, while *Mycoplasma pneumoniae* (Mp) is responsible for around 2 million pneumonia cases per year. Objectives is to determine frequency of upper respiratory infections caused by Cp and Mp in population of South Backa District, particularly in children and young adults.

Material and methods: 2262 sera in 5 year period (2008-2013) were tested for the presence of specific IgM and IgG antibodies. The study was done at the Institute for Public Health of Vojvodina, Virology Center. Sera were analyzed by ELISA (Euroimmun, Germany).

Results: Cp (25,4%) was significantly more common causative agent of acute infections compared to Mp (13,5%). School-age children are the most susceptible, being equally vulnerable to either pathogen - Cp (30,3%) and Mp (22,5%). Cp is more frequent in fall and winter months, while Mp predominates in the summer and early fall.

Conclusion: Obtained results suggest that Cp and Mp have an important role in the onset of acute upper respiratory infections in the population of South Backa district, especially in school-age children. To establish accurate etiologic diagnosis, it is recommended to use both serologic and PCR methods.

4. BETA HEMOLITIČKI STREPTOKOK IZOLOVAN KOD INFEKCIJA MEKIH TKIVA 4. BETA HAEMOLYTIC STREPTOCOCCI ISOLATED FROM SOFT TISSUE INFECTION

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Soft tissue infections are common and could be caused by a numerous organisms. An etiologic diagnosis is often necessary for adequate therapy. The objective of the this study is to determine the distribution of groups of beta haemolytic streptococci isolated from soft tissue infections and their susceptibility to antibiotics. A total of 207 isolates of beta haemolytic streptococci were collected from patient specimens between September 2011 and September 2013 at laboratory for pioculture in Institute for public health Niš. The isolates were identified by standard methods. Susceptibility to ampicillin, ceftriaxone, tetracycline, ofloxacin, vancomycin, erythromycin, clindamycin, and azitromycin (Rosco, Denmark) was tested by the Kirby-Bauer disk diffusion method following CLSI guidelines. The most of isolates belongs to group B of beta haemolytic streptococci (56,52%). Isolates of group C beta haemolytic streptococci were present in 25,6%, group A in 11.1%, group D in 1,44%, group F in 5,31%. All isolates were susceptible to ampicillin and ceftriaxone. Susceptibility rate of *Streptococcus beta haemolyticus* gr.A to tetracycline, erythromycin and clindamycin was 65,21%, 69,96%, 73,91%, of isolates respectively. Susceptibility rate of group B and group C beta haemolytic streptococci to erythromycin was 66,66% and 52,8% respectively. We found that erythromycin and clindamycin resistance of isolates of beta haemolytic streptococci was common. Ampicillin remains the treatment of choice.

Acknowledgments: This work was supported by Ministry of Science and Technological Development of the Republic of Serbia, Project No 31079.

5. ZASTUPLJENOST BETA HEMOLITIČKOG STREPTOKOKA GRUPE A U
IZOLATIMA IZ BRISA ŽDRELA U 2012.GODINI
**5. PRESENCE OF GROUP A (BETA HAEMOLYTIC) STREPTOCOCCI IN
ISOLATES TAKEN FROM THROAT SWABS IN 2012**

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Aim: To demonstrate the presence of of group A (beta haemolytic) streptococci in isolates from throat swabs in 2012 and its resistance to erythromycin.

Materials and methods: During 2012, we have processed 69,236 throat swabs in Laboratory for Swabs and Pyocultures. The number represents 53.01% of all the samples processed in the Laboratory.

To isolate and identify strains, we have used standard laboratory methods. We examined sensitivity of the isolated strains group A BHS to erythromycin.

Results: Out of the total number of bacterial isolates (7,663) beta haemolytic streptococci were isolated in 7,593 (99.08%). Out of this number, we have isolated 7,269 (95.73%) of group A BHS. Out of 7, 269 isolated strains of group A BHS, 609 (8.38%) were erythromycin- resistant.

Conclusions: Group A BHS is largely represented in the throat swabs processed in our Laboratory. Expressed in percentages, Group A BHS is most frequently found. In comparison to previous research, our examinations have shown increase in the number of erythromycin-resistant strains.

Key Words: Group A Beta Haemolytic Streptococci- Erythromycin

6. DIJAGNOZA CITOMEGALOVIRUSNE INFEKCIJE U ŽENA GENERATIVNE DOBI U JUŽNO BAČKOM OKRUGU U PERIODU OD 2007. DO 2012.

6. DIAGNOSIS OF CYTOMEGALOVIRUS INFECTION IN WOMEN OF GENERATIVE AGE OF SOUTH BACKA DISTRICT (VOJVODINA, SERBIA) IN THE PERIOD 2007-2012

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Objectives: The objective of the study was to evaluate the frequency of cytomegalovirus (CMV) infections in women of generative age who underwent anti CMV IgG and IgM antibody screening during the period 2007 -2012

Materials and methods: Seven hundred and forty serum samples were collected over a 5 – year period from 740 women, 19 to 45 years of age, from South Backa District. For the detection of anti CMV IgM and IgG antibodies an enzyme – linked immunosorbent assay (ELISA) (Virion/Serion, Würzburg-Germany) was used. Commercial avidity test for IgG antibody (Euroimmun, Luebeck, Germany) was applied to test the samples that were IgM – positive at ELISA..

Results: In 87.8% (650/740) women past CMV exposure was detected (IgM negative, IgG positive), without any significant differences between age classes. In the period 2007-2012 there were 4 cases of suspected primary CMV infection with IgM and IgG ELISA positive. In all IgM positive cases IgG avidity level was high. High IgG avidity level exclude an infection contracted less than three months

Conclusion: The prevalence of anti CMV antibodies in women of generative age of South Backa District in the period 2007-2012 was high. Only 11.6% seronegative women have a risk to acquire primary CMV infection. The presence of specific CMV IgM is not sufficient to establish the diagnoses of primary CMV infection. Avidity IgG test aids in the diagnosis of primary CMV infection.

Key words: Cytomegalovirus, ELISA test, IgM, IgG, avidity test

7. UČESTALOST SALMONELA KOD OSOBA KOJE PODLEŽU REDOVNOM SANITARNOM PREGLEDU

7. THE FREQUENCY OF PRESENCE OF SALMONELLA IN PERSONS UNDERGOING MANDATORY SANITARY EXAMINATION

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Introduction: Laboratory for Stool Cultures and Sanitary Surveillance (Institute of Public Health of Belgrade) has been performing bacteriological analyses of stools (for Salmonella and Shigella spp.). Analyses are performed in accordance with (and based on the provisions of) Law on the Protection of Populations from Communicable Diseases (Official Herald RS, No125/2004) and Rulebook on Mandatory Sanitary Examinations for Defined Categories of Employees, Other Persons and Carriers (Official Herald RS, No20/2006).

Aim: We wanted to show presence of the Salmonella enterica subspecies enterica in the material we have examined between January 2004 and June 2013.

Materials and methods: We analyzed stools of the persons who had undergone mandatory sanitary examination in IPHBelgrade. We used standard methods for isolation and identification of Salmonella.

Results: Laboratory for Stool Cultures within Sanitary Surveillance examines over 120, 000 stool samples annually. From January 2004, to December 2010, we have found Salmonella spp. in about 0.03% of the samples (annual level). However, from January 2011, this number has tripled and reached 0.09% a year.

Conclusions: In relation to previous years, frequency of Salmonella findings in the stool in the persons for whom sanitary examination is mandatory has tripled from January 2011. That is why we need to take special care of the hygiene- in the production and processing of foods and in their further marketing. Our results point to the importance of periodical mandatory sanitary examinations. Prevention of the spread of Salmonella spp. should be the common assignment for specialists in microbiology, epidemiology and doctors of veterinary medicine.

Keywords: Stool, Salmonella, frequency

8. ANTIMIKROBNA AKTIVNOST EKSTRAKATA AROMATIČNIH BILJAKA PROTIV PATOGENIH BAKTERIJA IZOLOVANIH IZ HUMANOG MATERIJALA

8. ANTIMICROBIAL ACTIVITY OF EXTRACTS OF AROMATIC PLANTS AGAINST PATHOGENIC BACTERIA ISOLATED FROM HUMAN MATERIAL

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Aim: To determine the antimicrobial activity of methanol extracts of selected aromatic plants (from the family Lamiaceae, Asteraceae and Apiaceae) against pathogenic bacterial strains isolated from human material;

Material and methods: Aerial parts of *Hyssopus officinalis*, *Achillea grandifolia*, *Achillea crithmifolia*, *Tanacetum parthenium*, *Laser trilobum*, *Angelica sylvestris*, *Angelica pancicii* and *Artemisia absinthium* were collected during the summer 2012th, in the territory of South East Serbia. After drying, the material was milled and extracted with methanol. Antimicrobial activity of obtained extracts were studied, using the micro-dilution method, against 16 multiresistant isolates from human material: *Escherichia coli* (from wound swab, aspirate and throat), *Pseudomonas aeruginosa* (from wound swab and two isolates from sputum), *Klebsiella sp.* (from wound swab and sputum), *Proteus mirabilis* (from wound swab), *Acinetobacter sp.* (from wound swab), *Staphylococcus aureus* (from wound swab and nasal), *Streptococcus pyogenes* (from wound swab and throat), *Streptococcus pneumoniae* (from nasal swab) i *Enterococcus faecalis* (from wound swab)– obtained from the Public Health Institute in Nis. As a reference, antibiotics Ciprofloxacin and Erythromycin were used.

Results: The tested extracts showed similar minimal inhibitory activity in the range of MIC = 6.25 to 100.00 mg/mL, with the best action of extracts of type *T. parthenium*, *A. crithmifolia*, *A. grandifolia*, *L. trilobum* and *A. pancicii*, especially against strains of *Streptococcus pyogenes*. Bactericidal activity (MBC) was recorded at the highest tested concentration of 100 mg/mL or above.

Conclusions: The tested extracts of aromatic plants may be applied as a natural source of antimicrobial agents with potential use in the treatment of infectious diseases.

Keywords: antimicrobial activity, aromatic plants, pathogenic bacterial strains

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9. ANALIZA UZROČNIKA PERITONITISA KOD PACIJENATA NA PERITONEALNOJ DIJALIZI – PETOGODIŠNJE PRAĆENJE

9. ANALYSIS OF PERITONITIS CAUSATIVE AGENTS IN PATIENTS ON PERITONEAL DIALYSIS- FIVE YEAR FOLLOW UP

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Objectives: Peritonitis represents the leading complication in patients on peritoneal dialysis, and greatly affects morbidity and mortality in these patients. The aim of our study was to analyze incidence, causative agents and therapy outcome of peritonitis in patients on peritoneal dialysis, in the period from 2007. to 2011. year.

Material and methods: Peritoneal fluid samples of 213 peritonitis episodes used from 145 patients hospitalized at the Clinic of Nephrology, was examined at the department of Microbiology, Public Health Institute Nis.

Results: During the five year period, incidence was 0.32 peritonitis/per patient per year but statistically significantly lower in 2011.comparing with prevalence in 2007. (0.22 – 0.44, $p < 0.001$). Microbiological finding was positive in 74.18% of all samples. The most common isolate was coagulase-negative staphylococci (26,29%), of which the *Staphylococcus epidermidis* was found in 78.57%. *Staphylococcus aureus* was found in 22,54%, while the Gram-negative bacteria were isolated in 20.66%. The percentage of fungal (2,82%) and peritonitis caused by *Pseudomonas* spp. (1.88%) were low. One episode of peritonitis per year had 72.41% of the patients, 15.86% of them had two, while 11.72% of patients had three or more episodes per year. Positive therapeutic outcome was found in 95.31% of episodes, 4.23% of patients were switched to heamodialysis and 0.47% of episodes finished lethal.

Conclusion: In the five-year follow-up significant prevalence reduction of peritonitis was confirmed. Gram-positive bacteria were the most frequent causative agent. A high percentage of episodes were cured due to effective treatment protocols based on microbiological sensitivity.

E. SESIJA: HIGIJENA
E. SESSION: HYGIENE

TOPIC 1: ENVIRONMENT AND HEALTH

Ia PREDAVANJA PO POZIVU
Ia INVITED LECTURES:

1. ADAPTACIJA NA EKSTREMNE USLOVE SPOLJAŠNJE SREDINE
1. ADAPTATION TO HARSH ENVIRONMENTS

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Abstract

Humans' working ability and performances are under significant influence of environmental conditions. Contemporary demands consider engagement in any possible environment on the Earth (and even out of the Earth!) where harsh conditions may impose extreme physiological exertion. In order to maintain physiological homeostasis, the human organism needs to perform serious adjustments. For example, adaptation to heat considers cardiovascular strain reflecting in increase in heart rate and profuse sweating leading to dehydration. Prolonged exposure to cold environment may involve complex adaptation of endocrine, respiratory, renal and immune system. High altitudes, such as mountains, inevitably lead to oxygen insufficiency, which leads to incapacity to sustain physical exertion. In order to compensate the reduction in ambient oxygen, the increase in ventilation occurs, as well as hemodynamic and hematologic changes. Underwater diving imposes particular strain to almost every organ in human body, because changes in barometric pressure induce extreme adaptation either on descent or ascent. Deficient adaptation, often as consequence of neglecting the procedures, can lead to barotrauma, or decompression sickness. Acceleration (G-force) is the major physical stress associated with combat flying, with loss of consciousness as possible (and probably fatal) result. Adaptation to such efforts requires wearing anti-G suit, together with centrifuge training to ensure that fighter pilot makes optimal use of straining maneuvers and maintain vision and consciousness. Preventive approach to decrease attrition due to harsh environments considers predicting the likelihood of its occurrence and enhancing the awareness of how specific factors (eg. gender, nutritional status) are sometimes important determinants of outcome.

Key words: exertion, human adaptation, preventive medicine

The functioning of human organism is supported by complex mechanisms of homeostasis maintenance. Stress represents unspecific reaction to demands that exceed our comfort zone. The major feature of stress is impairment of homeostatic balance. Stress reaction is always

directed toward reestablishment of homeostasis. Regardless the nature of stress stimuli, it always activates the same defence mechanisms. Stressor may be of family or social nature, professional, and environmental. The most frequent environmental stressors are extreme hot or cold conditions, increased or decreased barometric pressure, hypoxia and fatigue, while increased or decreased humidity, noise and vibrations are less frequent. Besides professional exposure to these environmental factors, we also find them important for athletes, and sometimes even during everyday activities. Physiological reaction to stress is always uniform, regardless of stress factor and is characterized by glicogenolysis, hyperglycaemia, switching to anaerobic metabolism with consequent increase of lactate and ammonia levels, changes of concentration and activity of serum enzymes, and stress hormone response. As part of the stress response, organism initiate chain of reactions called **adaptation**. Considering environmental stress, adaptation is defined as reaction of organism to repetitive exposures to given combination of environmental conditions, with the acquired tolerance as a result. Contrary to stress reaction which is uniform, adaptation mechanisms depend of the stress nature.

HIGH TERRESTRIAL ALTITUDES

On the altitudes higher than 1500 m hypobaric hypoxia occurs. There is a decrease in availability of oxygen necessary for human metabolism, which is manifested as “mountain sickness”. High terrestrial altitudes decrease physical performance, together with cognitive functions, particularly in physically active individuals. Health impairments on high terrestrial altitudes may be the consequences of sheer hypoxia, but also may be the result of interaction of hypoxia with other environmental factors like rough and steep terrain, and rough weather.

Acute mountain sickness may be manifested as insufficient adaptation or maladaptation. Insufficient adaptation considers mobilization of useful adaptive mechanisms, but without enough capacity to compensate increased demands. On the other hand, maladaptation considers responses directed also towards homeostasis maintenance, but lacking to do so; rather they substantially impair some other functions. On high terrestrial altitudes, the total barometric pressure is decreased, with proportional decrease of partial pressure of oxygen. Partial pressure of oxygen at sea level is 159 mmHg, while at Mount Everest is only 53 mmHg. Adaptation on high terrestrial altitudes considers adaptation of ventilation through 4 phases: first, in a few minutes, there is an increase of ventilation in order to increase the oxygen supply. However, after few hours, the ventilation decreased, due to hypocapnia, which induces depression of respiration. Third phase represents complete acclimatization, with changes in systemic oxygen transport, increase of cardiac output and decrease in VO_{2max} . In addition, after several weeks and months, the haemoconcentration occurs, together with the increase in arterial oxygen content. These changes enable gradual adaptation to high altitudes, so in few months the human organism becomes capable of sustain the physical strain as equal as at the sea level.

INCREASED BAROMETRIC PRESSURE

After countless attempts, man succeeded in conquering the ultimate depths. Breath-hold diving is performed usually up to 12 meters, although some divers can descent 10-fold deeper. Autonomic diving systems enable diving on a 100 m below surface. The deepest descent with pressured garment was at 432 m. Bathyscaphe with human crew successfully reached the deepest point on Earth – Marianas trench, at 10740 m.

Aquatic environment is extremely harsh environment. The water is usually cold, visibility is decreased, diver completely depends on his equipment, and changes of barometric pressure require extremely complex adaptation, which challenges the human physiological limits.

Structures in the body contained air like lungs and inner ear are not able to respond adequately to changes of ambient pressure without major and sometimes fatal injuries. Barotrauma is specific type of injury caused by pressure changes. It occurs when pressure in body cavities filled with air failed to equalize with changed ambient pressure. Middle ear barotrauma is the most frequent type, while pulmonary barotrauma of ascent is the most severe, and may occur regardless of diving type and depth. It is caused by overinflation of the lung as the gas expands during ascent, either by breath-holding or by some local pathology that prevents gas from escaping from a portion of the lung. Pulmonary barotrauma may result in local or wide damage to lung tissue, characterized by disruption of the alveolar-capillary membrane and consequent passage of alveolar gas into the mediastinum, causing mediastinal emphysema; or into the pleural space, causing pneumothorax; or into the capillaries, with probable resultant cerebral arterial gas embolism.

Decompression sickness refers to the overt illness that follows a reduction in environmental pressure with the development of endogenous gas bubbles. It occurs in diving, caisson work, rapid ascent to high altitude, and following hyperbaric chamber work. The initiating cause is the formation of bubbles of the inert gases dissolved in the tissues. When an inert gas is breathed at elevated pressure, its partial pressure in lungs initially exceeds that in the tissues. As the time at pressure lengthens, the inert gas is progressively absorbed by the tissues until its partial pressure there equals that in the lungs. Decompression sickness occurs when ambient pressure decreases, i.e. at ascent. Decrease of partial pressure of gas leads to decrease of its solubility in blood with subsequent formation of stable bubbles. These bubbles grow by the inward diffusion of nitrogen as they are carried by the venous blood to the heart and lungs. The lung filter small quantities of bubbles, but if the volume of gas becomes overwhelming, as may occur in accidental ascent from great depth, blood can be displaced from the heart, leading to death by asphyxia. Of course, the symptoms usually are not so dramatic, and sometimes may be subtle or even absent. The common cause of decompression sickness is inadequate decompression due to ignoring the procedure (decompression tables), panic attack, equipment malfunctioning or frequent diving (more than once in 12-24 hours).

FLYING

The physiological consequences of rapid ascent to high altitude are a core problem in the field of aerospace medicine. Today it is considered that staying at altitudes above 12 km without adequate equipment is physiologically impossible. The pilots are exposed to hypobaric hypoxia, with progressive increase in heart rate, increase in cardiac output, increase in systolic arterial pressure, while decrease in peripheral resistance. This is followed by selective vasodilatation in heart and brain, as well as in coronary vessels. Neurological symptoms of acute hypobaric hypoxia include impaired psychomotor functioning and progressive memory loss.

Acceleration (G-force) is one of the major physical stresses associated with combat flying. The most severe consequence might be the unexpected loss of consciousness (G-LOC) while flying acrobatic maneuvers, when the intensity of gravity may exceed 6 or even 12 G, which is possible in new types of aircrafts. For seated pilot, the most common direction of acceleration is +Gz (head-to-toe), for it follows ascents and sharp turns. Acceleration has mechanical effects on soft tissues and compresses the spine. It also affects the cardiovascular and pulmonary systems, creating increased risks for G-LOC and pulmonary atelectasis. Acceleration increases the weight of the blood and so raises the pressure gradient in the hydrostatic column along the axis of acceleration. It decreases arterial pressure in the head; in the absence of compensating mechanisms, perfusion of the brain would approach zero at

+5Gz. This also makes breathing difficult by pulling down the diaphragm and exaggerates the ventilation-perfusion mismatch in the lungs. Compensatory mechanisms involve the effect of baroreceptor stimulation, but this reaction takes few seconds. The successful adaptation is managed by training in simulators. Anti-G suits and positive-pressure breathing are extremely efficient in improving tolerance to acceleration.

EXTREME ENVIRONMENTAL TEMPERATURE

Maintenance of constant core temperature is one of the most important homeostatic demands in all warm-blooded organisms, including humans. Core temperature in humans vary in narrow range from 36,5 to 37,5 °C. When exposed to heat strain, men are driven to safe behaviour (cessation of physical activity, moving into shade and taking off the excessive cloths), but in athletes or in military personnel, this drive is largely suppressed by high motivation to complete task or to achieve desirable sport result. In these situations, one must lean on to physiological thermoregulation, which results in cardiovascular strain. Namely, heart must support increase in blood circulation in the skin, directed toward heat dissipation, and also in the active muscles, in order to maintain the given intensity of physical work. In hot environment, the only efficient way of heat dissipation is evaporation of sweat, but the increased humidity and/or wearing the insulated protective cloth might completely prevent the evaporation. Uncompensated heat stress inevitably leads to some type of heat illness. Mild and moderate forms include heat edema, cramps and synkopa. The most severe and potentially fatal type is heat stroke. Adaptation to heat considers acquired heat adaptation of every cell, with de novo production of heat-shock proteins, and heat acclimatization. Acclimatization is adaptation to repeated exposure to given temperature conditions and may be acquired by staying in the natural environment, or artificially, in climatic chamber. Both procedures in 8-10 days provide substantial improvement in heat tolerance, reflected in increased cardiovascular compliance and more efficient sweating (that occurs earlier, at lower core temperatures, and sparing of sodium in sweat). The subjective experience of thermal comfort is improved also.

On the other hand, staying and working in cold temperatures also imposes great stress. In order to maintain the core temperature, the blood is withdrawn from peripheral compartment i.e. skin, with subsequent increase in blood flow through vital organs. Decreased blood flow in skin leads to local ischemia and possibly cold injuries. Decrease of core temperature below 35 °C results in hypothermia. Adaptation to cold includes increase of metabolic rate, elevation of blood pressure and increase in heart rate. Mild hypothermia is manifested by shivering, speech difficulties, and hyperreflexia. Further exposure to cold leads to cognitive impairments, decrease in heart rate and increased urine output. Severe hypothermia occurs when core temperature falls below 26 °C, with gradual loss of cerebral and heart activity.

CONCLUSION

In spite of the technological progress directed to creation of ideal working environment, some professions are inevitably related to extreme environmental conditions. Adaptation of human organism to given ambient conditions engage complex mechanisms of ecological stress compensation. Risk assessment and prevention might alleviate the consequences of homeostasis impairment and maintain health of persons exposed.

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2. SAVREMENI IZAZOVI U PREVENCIJI BOLNIČKIH INFEKCIJA/ZNAČAJ HIGIJENSKO – SANITARNIH NADZORA

2. MODERN CHALLENGES IN THE PREVENTION OF HOSPITAL INFECTIONS – IMPORTANCE OF HYGIENE AND SANITARY CONTROL

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The basis of prevention of nosocomial infections is a systematic and continuous monitoring of hygienic conditions in all health facilities through regular hygiene and sanitation monitoring and sampling of materials. Prevention of nosocomial infections is a legal obligation of health care institutions that are regulated by the Law on Protection of Population from Communicable Diseases no. 125/04th. The frequency and types of nosocomial infections depend on many factors: the profile of the hospital, the immune status of patients, hospital hygiene, training of personnel, adopted or rejected the doctrine of the use of antibiotics for preventive and curative purposes, and so on. Their appearance complicates the process and outcome of the underlying disease (increased morbidity and mortality), increasing the time of treatment and significantly increased material costs. Published studies of prevalence in our country would indicate that it is moving to the world average (5.5-9.9 % of MMA) or slightly higher (5.2-15 % in the Emergency CCS). Challengers IHI can be almost all microorganisms: bacteria, viruses, fungi and parasites. The most frequent causes BI are: *Escherichia coli*, coagulase- negative staphylococci and *Staphylococcus aureus* (especially methicillin-resistant strains of staphylococci), *Enterococcus* sp., *Pseudomonas auriginosa*, *Acinetobacter* spp., *Pneumoniae Klebsiella*, *Enterobacter* sp., *Proteus mirabilis*, *Serratia* sp., and anaerobic Gram positive bacteria (*Propionibacterium* sp., *Bacteroides* sp.). In recent years, the causes of nosocomial infections and *Legionella* sp., *Clostridium difficile*, *Corynebacterium jejunum* and *Mycoplasma hominis*.

Infections associated with health care are a big problem all over the world, even 5-10 % of all hospitalized patients develop such an infection during treatment. Since the time I.P. Semelweiss known that hands the single most important factor that can reduce the number of these infections. The World Health Organization (WHO) has recognized this problem and made Guidelines for hand hygiene in health care on the basis of which made national guidelines and guides.

Keyword: hospital infections, prevention, health care facilities

3. KVALITET VAZDUHA I REPRODUKTIVNO ZDRAVLJE

3. AIR QUALITY AND REPRODUCTIVE HEALTH IN WOMEN

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By variety of activities man has manage to change the Earth and adjust it to his needs. Some of these activities, in addition to a desirable have also very undesirable effects on health. One of the most significant consequences of environmental pollution is the phenomenon of air pollution in the communal area and rooms.

Direct effects of human exposure to air pollutants occur in the respiratory organs, and after absorption through the blood, they could penetrate to other organs, where they also can damage, which can manifest certain symptoms and diseases.

The first studies on exposure to air pollution and effects on reproduction were published in 1860 in France, where it was noted that women workers in the industry have lead more spontaneous abortions and more difficult to remain pregnant. Now we are working intensively numerous studies dealing with this issue in order to clarify the mechanism of action and identify pollutants that are responsible for reproductive disorders.

In daily life, women around the world are in constant contact with the entire media environment and are sensitive to changes in its condition as compared to the male part of the population. For these reasons, their health is greatly influenced by harmful and toxic substances from the human environment. Since the human body does not possess effective defense mechanisms against harmful substances, especially those that come from the air we breathe, there are very serious health disorders, which are at the start of the fetus.

Environmental pollution dates back to the origin of man. Its activities that enable him better living conditions, prehistoric man has influenced the change in the quality of its environment. First burning fire in his home, he began a steady process of air pollution, which also is the oldest form of environmental pollution.

Sources of air pollution are numerous. Sometimes they included only households; while today include power plants, industrial facilities, traffic and transport. External air pollution (air pollution from municipal areas) caused by the presence of a large number of pollutants, alone or mixed with other pollutants can cause serious health consequences. The most common pollutants present in the air, the external environment are: sulfur dioxide, particulate matter, nitrogen oxides, ozone, exhaust motor vehicle emissions, carbon monoxide, heavy metals, pesticides, etc..

Health consequences that occur when it can be acute or chronic, depending on the amount of pollutant concentration, duration of exposure the person and their current state of health, as well as the meteorological conditions.

Sources of air pollution in the room can be in every home, with a constant or intermittent emission of its pollutants. Emitted pollutants are different from the external air pollutants by the amount of their concentration, which can sometimes be significantly higher. Harmful substances within the space can be created in various ways: by burning fuel, human activities release harmful substances from building construction and insulation materials for apartments, penetration of harmful substances from the environment.

The rooms are usually present sulfur dioxide, various solvents, tobacco smoke, carbon monoxide, radon, nitrogen oxides, formaldehyde, asbestos, etc. In addition to these chemical pollutants in the premises may be present, and biological contaminants, such as dust mites, insects, fungi spores, animal allergens.

Will the concentration of pollutants emitted indoors increase or decrease, depending on the type of pollutant, character and accommodation of its source, the mechanism of spontaneous removal, as well as the frequency of the application process ventilation of the room, which is of particular importance if the pollutant emitted indoors not reactive.

Of the population, which includes children, pregnant women, the elderly and the chronically ill, especially sensitive to high concentrations of air pollutants, as reflected on the state of their health status.

The mechanism by which air pollutants were damaging the reproductive system is not yet fully clear, although recent studies suggest an association between exposure to xenoestrogens and reproductive disorders.

Xenoestrogens are chemical substances that have ability to disrupt the natural hormonal balance. In addition to air, the organism could penetrate through drinking water and food. Most widely known are xenoestrogens organochlorine pesticides, polychlorinated biphenyls, dioxins, heavymetals and others.

Experiments on animals that were exposed to low concentrations of long-term xenoestrogens have indicated the occurrence of reproductive disorders and various sexual abnormalities, ranging from changes in sexual behavior, feminization, demaskulinisation, to the deformation of the embryo and abnormal sexual development. In addition to the direct effects on the reproductive system, and xenoestrogens act indirectly through neural fetal cells in experimental animals. That changed, neurons can subtly change the nerve connections that control the production of reproductive hormones that can affect fertility and sexual behavior.

Hormonal system disorders caused by xenoestrogens may arise in several ways. Some xenoestrogens can accelerate the degradation or elimination of certain hormones, which leads to hormonal destruction or deactivation of the enzyme necessary for the breakdown of the hormone conditions their accumulation in the body.

Since the demonstration of effect hormones must bind to their receptors, blocking hormone receptors xenoestrogens can disable access to hormones and binding to specific receptors exert their harmful effects. In addition, xenoestrogens may arise stimulation of receptor synthesis, which leads to increasing hormonal effect.

A very important feature is the ability of xenoestrogens imitation hormones, xenoestrogens where newly-receptor complex has the ability to send too many messages or a particular gene or texting at the wrong time, which adversely affects the reproductive organs.

Xenoestrogens also affect the function of the cardiovascular system, leading to dilation of blood vessels and reduce blood flow restriction. Tyrosine and mitogen activating protein kinase activin, xenoestrogens release of nitric oxide involved in the regulation of blood pressure.

Exposure to xenoestrogens affects the nervous system.

During fetal development and early postnatal life, the hormones are essential for proper brain development and maturation of the entire central nervous system. A special role in brain development prenatally have some form of thyroid hormone, which under the influence of xenoestrogens can cause loss of intelligence and behavior change. Lower levels of hormones during pregnancy can cause the appearance of hyperactivity in children. At the same time it is

important to determine whether these substances pass the placental barrier and enter the brain of the fetus. Estrogens do not pass this barrier, but these estrogens have different structures and therefore may behave differently.

Protecting the fetus from harmful and toxic substances depends largely on the efficiency of the placental barrier. The efficiency of the placenta as a barrier for the transport of toxic substances and the month of pregnancy in which the pollutant acts are two very significant moments which give rise to the range of health effects on the fetus. The highest risk period is the first 14 to 60 days of gestation, because it is time intensive cell division, differentiation and formation of fetal organs and systems.

Fetoplacental barrier is very sensitive to the effects of air pollution. With exposure to air pollution in the placenta reduces the amount of soft chorion villus sampling, the vascularisation, DNA adduction occurs and there are involutive changes, which affect the outcome of pregnancy.

The embryo is sensitive to exposure to pollutants embryotoxic during the first two weeks of pregnancy, and often results in embryonic death and abortion. Teratogenic and mutagenic pollutants often seem to result from the third to the eighth week of pregnancy, the period of organ development, system and limbs of the fetus. The achievement of covalent bonds with macromolecules cell embryos, these pollutants can lead to disorder in the synthesis of DNA and RNA and cell division, which causes chromosomal aberrations.

During pregnancy, the mother and her body locks much pollutants from the environment, including the pollutants from the air. The effects of pollutants and causing health consequences for the mother and the fetus should be considered in acute and chronic exposure, since many air pollutants have accumulative effect.

Individual response to exposure to air pollutants depend on the characteristics of pregnant women (including the genetic factors), the way her life and behavior. It is also very important and if there is already a disease of the mother, whether it arose before or while wearing the fruit, which may have an adverse effect on the course of pregnancy and childbirth.

According to the World Health Organization, premature birth is the complete pregnancy that lasted less than 260 days (counting from the last menstrual period), or before the age of 37 weeks of gestation, determined by Naegelovoj formula. Most previous research has shown that among pregnant women living in polluted areas and pregnant women living in less polluted areas, there is a difference in the incidence of premature births.

Low birth weight of the child causes a lower tone of skeletal muscles and consequently the weak development of some reflexes. Cortex such myelization of newborn is less than the cortex of children born with normal weight. Research has also found links between exposure to particulate matter and sulfur dioxide, and low birth weight babies (less than 2500g) mothers who lived in areas of polluted air.

The resulting anomalies in the fetus, with which it is born, the result of the effect of the etiologic factors. It is believed that they are formed genetic factors have a smaller share (40%) compared to environmental factors (60%). Studies have found that exposure to a high content of pollutants from the air in industrial areas is a risk factor for the occurrence of stillbirth and intrauterine fetal retardation in terms of creation and orofacial and cardiovascular septal defect.

Reproductive health is a very important part of the overall health of the population in the preservation, enhancement and degradation affects a range of factors from the environment. According to the World Health Organization Reproductive health is a state of physical,

mental and social well-being in relation to the reproductive system of all age groups. The proper functioning of the reproductive system plays an important role in the health of women through all the years of its life, especially during her pregnancy. Optimal health status of women before and during pregnancy, as well as certain lifestyle expectant mothers, is of great importance in facilitating the normal course of pregnancy ending in the birth of a healthy child.

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IIa USMENA PREDAVANJA

IIa ORAL PRESENTATIONS:

1. ODREĐIVANJE TAČNOSTI I PRECIZNOSTI METODE ISO 21528-2:2004.

1. DETERMINATION OF THE ACCURACY AND THE PRECISION OF THE METHOD ISO 21528-2:2004.

Protić Nada,

EKO-LAB ltd for quality management in restructuring

Objectives. For the purpose of supervision of staff in relation to the method of ISO 21528 – 2: 2004. the accuracy and the precision of this method were determined.

Materials and Methods. A naturally contaminated sample of frozen dairy ice cream was used. The tests were performed by two analysts in ten series with three replications. Test samples were prepared by ISO 6887-5: 2010. Statistical analysis was performed according ISO 5725.

Results. According to the calculated values of repeatability and within-laboratory reproducibility of the analysts, there were no value that can be considered alone and extreme. The values of h Mandel - accuracy were within 1% (2, 18) and 5% (1, 89) and k Mandel - precision within 1% (2, 07) and 5% (1, 71). The systematic error of analysts was determined by the t value which was 0,475 lower than the tabulated (2,002).

Conclusion. Based on the results of statistical processing of the data, it can be concluded that both analysts are trained to test method ISO 21528 - 2:2004.

Keywords: accuracy, precision

2. ODREĐIVANJE TRIHALOMETANA U VODAMA ZA PIĆE RAZLIČITOG POREKLA U REPUBLICI MAKEDONIJI

2. DETERMINATION OF TRIHALOMETHANES IN TAP WATER OF DIFFERENT ORIGIN IN REPUBLIC OF MACEDONIA

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Trihalomethanes (THMs) are formed in water the chlorine used in water-treatment plants react with organic matter. THMs are suspected carcinogens.

The goal of this study is determination of the concentration of THMS in potable water after chlorination. The study included 60 samples of potable water from water facilities that draw water from accumulations and 70 samples of potable water from water facilities that draw water from boreholes and springs. Samples were analysed by GC-ECD method with headspace technique. The obtained results for individual THMs in samples of potable water that draw water from accumulations, range from 15 – 55 µg/l for chloroform; 12 – 27 µg/l for dichlorobromomethane; 2-6 µg/l for chlorodibromomethane and 3 – 13 µg/l for bromoform. The obtained results for individual THMs in samples of potable water that draw water from boreholes and springs range from 5 – 15 µg/l for chloroform; 1 - 5 µg/l for dichlorobromomethane; 1- 3 µg/l for chlorodibromomethane and 1-5 µg/l for bromoform. According to the national Regulation for Water Safety (46/08), the content of chloroform in 7 of tested samples of potable water that draw water from accumulations exceeded the MRL value (30 µg/l).

The concentration of THMs in potable water after chlorination that comes from water facilities as wells and springs show significant decreasing trend in comparison with concentration of THMs in potable water that comes from accumulations ($p < 0.05$).

Keywords: THMs, chloroform, dichlorobromomethane chlorodibromomethane, bromoform

IIIa POSTER PREZENTACIJE

IIIa POSTER PRESENTATIONS:

1. KVALITET VODE ZA PIĆE NA JAVNIM ČESMAMA NA TERITORIJI BEOGRADA U PERIODU MART 2011. GODINE- JUN 2013. GODINE

1. QUALITY OF DRINKING WATER ON THE PUBLIC WATER TAPS ON THE TERRITORY OF BELGRADE FOR PERIOD MARCH 2011 - JUNE 2013

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City Centre for Public Health of Belgrade, Serbia

Objective: To evaluate the quality of drinking water from public taps not connected to water supply system.

Materials and Methods: Within The Program by Belgrade City Secretariat for the Environment, GZZJZ conducts sampling and analysis of water at public taps. We summarized results of analysis ("A" and "B" scale), in period March 2011 to June 2013 for a total of 527 drinking water samples from 22 public taps.

Results: We have identified a total of 68(12,9%) samples with solely physico-chemical contamination, 82(15,6%) samples with physicochemical and microbiological contamination, 186(35,3%) samples with only a microbiological contamination and 191(36,2%) samples without evidence of contamination. In 8(36,4%) public taps during this period there was no finding of contamination according to monitored physicochemical parameters. In 2(9,1%), simultaneous presence of positive physicochemical and microbiological indicators was observed in 7,1% and 7,4% samples, respectively, which together with previous results makes total of 10(45,5%) public taps with stable drinking water quality within the analyzed physicochemical parameters.

Conclusions: A stable quality of drinking water in terms of physicochemical parameters has been recorded in nearly half of the monitored public taps. The most commonly observed is microbiological contamination.

Keywords: drinking water, public tap, safety

2. STATISTIČKA ANALIZA KVALITETA PARAMETARA PIJAĆE VODE REFERENTNIH VODNIH OBJEKATA

2. STATISTICAL ANALYSIS OF THE QUALITY PARAMETERS OF DRINKING WATER IN REFERENCE WATER FACILITIES

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Abstract: This paper presents a statistical analysis of the quality of drinking water in reference water facilities, on the basis of physical, chemical and bacteriological examinations of the Center for Preventive medical care „Nis“. The quality of drinking water was determined by the analysis of the impact of samples on general parameters and specific parameters (NO_3^- , NO_2^- , NH_4^+ , KMnO_4 , Cl^-), electrical conductivity and pH. This study was performed retrospectively, covering the period from 2007 until 2011. Statistical analysis and the presentation of the results was performed using the software packages Excel and SPSS 19.0 (Statistical Package for the Social Sciences). Data analysis was performed using the following statistical methods: descriptive statistics (mean and standard deviation, frequency, percentage) for determining the expression of basic variables; t - test, analysis of variance with post hoc LSD test and the χ -square test for determining the significance of differences. The analysis of measured parameters showed a significant difference between the reference water facilities. All the reference facilities showed increased levels of the maximum values of the organic load and ranged from 10.06 to 12.64 mg/dm³, while the minimum value of pH in 2009 was slightly below the MAC. The values of the concentration of NO_3^- , NO_2^- , NH_4^+ and Cl^- were in the range of allowed values.

Keywords: drinking water, reference water facilities, quality.

3. SADRŽAJ ALKALNIH METALA U MINERALNIM VODAMA IZ PROMETA

3. THE CONTENT OF ALKALI METALS IN MINERAL WATERS FROM THE MARKET

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Mineral waters are largely represented in the daily diet of people. There are in the market a large number of different mineral water whose mineral content is significantly different each others. The concentrations of some anions and cations are prominent on the labels.

Mineral waters contain alkali metals in their composition. Alkali metals are included in the many mineral waters and characteristic for volcanic types of mineral waters that are most frequently met in Šumadija, Tular and Vranje Spa.

We analyzed 12 mineral waters. It was found that alkali metals are presented in all of the samples and that some of them could be significant source of alkali metals.

Key words:alkali metals, mineral waters

4. ODREĐIVANJE NEKIH ZDRAVSTVENIH INDIKATORA VODE ZA PIĆE U CILJU PROCENE HEMIJSKE ISPRAVNOSTI VODE ZA PIĆE U MAKEDONJI
4. DETERMINATION OF SOME POTABLE WATER INDICATORS IN EVALUATION OF CHEMICAL SAFETY OF POTABLE WATER IN REPUBLIC OF MACEDONIA

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Physical and chemical drinking water indicators provide baseline information for water quality and help identify trends or changes in water quality over time.

The main goal of this study is determination of some physical and chemical parameters in potable water in the Republic of Macedonia in order to make physical and chemical safety evaluation of potable water which is distributed to the consumers.

The study included a total of 518 samples of potable water from different supply systems for the period from October 2010 to May 2013. Samples were tested on 64 parameters. Assessment was made according to national Regulation for Water Safety (Official number 46/08).

Testing of all water samples was performed on the content of: routine components; major inorganic components; trace metals and pesticides. The obtained results showed that the percentage of the incompliant samples was within the range from 12.09 % for samples from central city water supply systems to 33.33 % for samples from central rural water supply systems. In the majority of incompliant samples the content of iron, manganese; arsenic turbidity, conductivity and PIV oxidisability was above established MRL-s.

The results showed that 19.85 % from 518 tested samples were incompliant and therefore unsafe for human consumption.

Keywords: chemical indicators, routine components, major inorganic components, water supply system

5. BEZBEDNOST BAZENSKIH VODA – PUT KA EU
5. POOL WATERS SAFETY – WAY TO APPROCHING EU

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Objectives: Monitoring of pool water involves constant monitoring of hygienic quality of water by performing the analysis in an approved medical facility. Since in this area (for water specific purposes) at the state level, there are no specific regulations, laboratory testing and evaluation is done on the basis of existing legislation (for pool water use regulations for drinking water).

Materials and methods: This paper presents the results of monitoring of pool in period of year 2004 up to August 2013. A total of 16 indoor and outdoor pools were monitored. A total of 1950 samples of pool water were analyzed.

Results: Out of the total number of samples 6.26% was bacterial and 18.69% chemical incorrect. The main reasons for non-compliance of pool water were findings of the total number of bacteria that was greater than the standardized 10 – in the EU countries the norm is 200, higher levels of residual chlorine (standard is 0.5 in the EU up to 1 is allowed), pH (decreased or increased, and the reason for it is irrational use of chemical treatment of pool water), color (standard is up to 5, and in the EU up to 20), electrical conductivity (greater than 1000, the EU has no standardized parameter). In the EU countries trihalomethanes, Legionella strains, Pseudomonas and Escherichia coli are analyzed, which is not required in Serbia.

Conclusion: Although Serbia has no rulebook, hygienic quality of pool water in the Nisava and Toplica administrative district is satisfactory. Pool water is analyzed in Serbia under very strict norms for drinking water. It is necessary to introduce mandatory testing for Legionella in order to approach EU legislation, as well as consideration of the sanitary-technical characteristics of the pool to the development of protocols on health safety pool water and control the use of many chemicals.

Key words: water, pool, safety, monitoring, rule book

6. BAZENSKE VODE – HEMIJSKI ASPEKT 6. POOL WATER – THE CHEMICAL ASPECT

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Daily usage of the pool in order to recreate and relax is a huge benefit for the welfare and health of the population. Every major tourist destination in the Republic of Serbia, track trends in world tourism and their guests, and locals wanted to provide some recreational opportunities and the purpose for which it is used, and swimming pools. Swimming pools and wellness centers lately have become an imperative and unavoidable part of modern tourism. Besides the recreational aspects of our area pools are used for sanatorium and rehabilitation purpose. Public swimming pool (regardless of size), which is used in hotels, wellness centers, is considered object of public interest.

Anyway it is important to ensure a good and constant quality of the pool water in terms of hygiene, safety and aesthetics, and in this way to exclude any harmful effect on human health, particularly with regard to the causes of the disease. To define water quality in swimming pools and recreation there are Rules for using the provisions of regulation on hygiene of drinking water (Official Gazette of FRY 42/98 and 44/99). Sampling procedure includes the preparation, retrieval, storage, and transport to the laboratory where physical-chemical analysis of the sample are performed.

In the period from January to September 2013, 325 samples of pool water were analyzed, of which 101 sample showed chemical contamination. The most frequent reason was the excessive use of disinfectants, which reflected a high concentration of residual chlorine, followed by inadequate cleaning and restoring the pool water as evidenced by the increased consumption of KMnO_4 , chloride, conductivity and smell.

Keywords: pool, hygienic, chemical parameters

7. BAZENSKE VODE - MIKROBIOLOŠKI ASPEKT

7. SWIMMING POOL WATERS – MICROBIOLOGICAL ASPECT

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Introduction: Swimming pool waters are analyzed for microbiological purity at the Department of Sanitary Microbiology at the Institute of Public Health in Niš. Monitoring of swimming pool waters has been conducted at 32 pools: 16 closed pools (continually, during the whole year) and 16 open pools (seasonally, during summer).

Objectives: A preview of bacteriological purity of swimming pool waters on the territory of the County of Niš (23 pools) and the County of Toplica (9 pools) during the period from 1st January 2013 until 31st August 2013.

Materials and methods: The analysis is done by using standard methods for microbiological examination of drinking water, in accordance with the valid Book of Regulations.

Results: During the specified period, a total of 277 samples of swimming pool waters were analyzed. The dynamics of the analyses followed the dynamics of sampling and it was conducted through monitoring on a weekly basis during the season and monitoring on a twice a month basis during the swimming off-season period. In coordination with the norms was registered in 13 samples (4.69%), and the reasons are these: a finding of aerophilic mesophilic bacteria count above the norm value 11 (3.97%), total coliform bacteria count 1 (0.35%) and fecal streptococci count 1 (0.35%). As the Book of Regulations for waters which are used for recreation does not exist, and these waters are regarded as drinking waters, the norms are quite strict. The examination should be extended by searching Legionella bacteria, at least as a pilot microbiological research.

Conclusion: Continuous monitoring, as a preventive measure of tracking the regularity of swimming pool waters, is necessary in order to conduct counter-epidemic measures at the right time, but it has to be accompanied by an adequate legal regulatory form.

Key words: recreational waters, monitoring, bacteriological purity

8. HEMIJSKI SASTAV ODABRANIH MINERALNIH VODA NIŠKE BANJE

8. CHEMICAL COMPOSITION OF SELECTED MINERAL WATERS OF NIŠKA SPA

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Mineral waters are a special group of groundwater, owing to their physical properties and chemical composition, a favorable effect on the human body, and can be used for prophylaxis and treatment.

Objective: To determine the complete chemical composition of selected mineral waters of Niška spa and make their categorization.

Materials and methods: In this paper are examined the samples of natural mineral waters of Niška spa, at three different locations.

Results: Determination of the type of mineral waters of Niška spa was performed by applying a formula of Kurlov, based on the following results for each sample individually.

$$M_{272} \frac{HCO_3_{33} SO_4_9 Cl_7}{Ca_{24} Mg_{20} (Na+K)_{15}} T_{38.4} pH_{7.5} \quad \text{sample I-1: alkaline calcium- bicarbonate}$$

$$M_{273} \frac{HCO_3_{72} SO_4_{12} Cl_2}{Ca_{22} Mg_{20} (Na+K)_{14}} T_{36.6} pH_{7.2} \quad \text{sample I-2: alkaline calcium- bicarbonate}$$

$$M_{263} \frac{HCO_3_{30} SO_4_{10} Cl_{10}}{Ca_{22} Mg_{22} (Na+K)_{14}} T_{36.3} pH_{7.2} \quad \text{sample I-3: alkaline calcium- bicarbonate}$$

$$M_{280} \frac{HCO_3_{72} SO_4_{12} Cl_2}{Ca_{27} Mg_{25} (Na+K)_{18}} T_{38.6} pH_{7.4} \quad \text{sample I-4: alkaline calcium- bicarbonate}$$

$$M_{296} \frac{HCO_3_{24} SO_4_9 Cl_2}{Ca_{21} Mg_{22} (Na+K)_{16}} T_{37.3} pH_{7.0} \quad \text{sample II: alkaline calcium- bicarbonate}$$

$$M_{396} \frac{HCO_3_{72} Cl_{10} SO_4_9}{Ca_{27} Mg_{18} (Na+K)_{15}} T_{21.7} pH_{7.0} \quad \text{sample III: alkaline calcium- bicarbonate}$$

Conclusion: Based on the test results of selected parameters of mineral waters of Niška spa, by its physico-chemical characteristics of the water individually and collectively in the category of alkaline calcium-hydro oligomineral waters.

Reference: Antic B, Cupic G: A bioclimatic characteristic of climate natural cures. Balneotherapy-climatological Institute of Serbia, Belgrade, in 1963., Dragišić V: General hydrogeology, Jovanovic T, Janjic M, Popovic G, Conic S: Balneoklimatologija, Faculty of Medicine, University of Belgrade, in 1994.

Keywords: mineral water, Niška spa, categorization, chemical composition, formula of Kurlov

9. SPREMNOST JAVNOZDRAVSTVENIH LABORATORIJA U R. MAKEDONIJI ZA PRIMENU STANDARDA KVALITETA

9. FITNESS OF PUBLIC HEALTH LABORATORY IN THE REPUBLIC OF MACEDONIA FOR THE APPLICATION OF STANDARDS FOR QUALITY

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This study examines aspects of quality management in public health laboratories (PHL) in RM through application of the ISO 9001; ISO 17025 and ISO 15189 standards. The main goal was to determine preparedness of PHL concerning the conditions (area, equipment, and staff) and in relation to quality standard application. Data from a survey conducted on employees and management in IPH of RM and the ten Public Health Centres throughout Macedonia. This research was conducted with Questionnaire (adapted from the ISO/IEC 17025:2005) and we used observational-analytical method. Statistic processing was conducted through application of standard descriptive analyses of quality indicators and check of the hypotheses put forward.

The study identified that globally, the preparedness of PHL in RM in relation to conditions (area, equipment and staff), for quality standard application, is seen as PARTIAL and varies and differs significantly between accredited and non-accredited public health laboratories. Testing laboratories in the IPH of RM and few accredited Public Health Centres have adequate and modern equipment, in line with the testing methods. Most laboratories in Public Health Centres have inadequacy of space in relation to its distribution, non-permitted access, cleanliness and monitoring the ambiance conditions.

Professional and competent staffs work in IPH of RM and all Public Health Centres, in particular when it comes to testing activities. Motivation of staffs instigated by management teams is what is missing.

Key words: Accreditation, standards, quality management, ISO 9001; ISO/IEC 17025 and ISO 15189.

10. ULOGA GEOGRAFSKOG INFORMACIONOG SISTEMA U UPRAVLJANJU
KLIMATSKIM PROMENAMA I NADZORU ZDRAVLJA LJUDI
**10. THE ROLE OF GEOGRAPHIC INFORMATION SYSTEMS TO MANAGE
CLIMATE CHANGE AND HUMAN HEALTH SURVEILLANCE**

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Objectives: Climate change is defined as a long-term change in the statistical distribution of weather patterns over a long period. Climate change may be limited to a specific region, or may occur in the one country. In this paper, with the help of geographic information systems (GIS) will be presented a framework for the assessment of climate change on human health.

Materials and Methods: The issue of climate change has a geographic component. Scenarios of climate change, analysis, assessments and forecasts are analyzed using GIS.

Results: Ecological consequences of climate change affect human health directly and indirectly. Lyme and other diseases transmitted primarily infected *Ixodes ricinus*. GIS is a powerful set of tools for Disease Control, which allows the prediction of potential outbreaks and implementation of intervention programs. Based on the medical information we have mapped the location of ticks infected with *Borrelia burgdorferi*.

Conclusion: The advantage of using GIS to geographically referenced data that indicate the exact place and time. After processing the visual information presented in GIS helps us better understand the data and make decisions based on the best information.

Key words: Geographic information system, Climate change, ticks-borne disease

11. ANALIZA IZLOŽENOSTI REKONSTRUKCIONIM PRISTUPOM KOD SATURNIZMA

11. THE ANALYSIS OF EXPOSURE THROUGH THE RECONSTRUCTION APPROACH IN SATURNISM

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Objectives: The evaluation of the exposure is held as one of four primary steps in the evaluation of the health risk, but it can be also used when the exposure had already taken place. There are various methods od approaches to the analysis of exposure: a) Measurements on the point of contact; b) The evaluation of the scenary; c) The reconstruction approach (which enables the evaluation of exposure which happened in the past). The establishment of the possibilities of the reconstruction approach of the evaluation of exposure of the organism to pollution in the past according to the direct personal biomonitoring of the lead in blood.

Materials and methods: The study involved 335 subjects which were arranged in 2 areas with different ecological characteristics. In the area No. 1 there were 233 subjects while in the area No. 2 there were 102 subjects. The defining of biomarkers and the level of pollution of the environment was carried out via verified and accredited methods.

Results: In the area No. 1 the majority of the subjects-28 (16.3%) had BBL of 15.1 20 µg/dl. The highest level of BBL- above 60 µg/dl, in the area No. 2 there were the most of the subjects-51 (15.2%), whereas in the area No. 1 there were significantly less- 14 (8.1%) of the subjects. The level of pollution of the environment caused by lead in the area No. 1 (GVI=95,06) is significantly lower than in the area No. 2 (GVI=567,91).

Conclusion: The analysis of exposure through the reconstruction approach in the case of pollution of the environment caused by lead is useful only with the subjects with markedly high concentration of lead in blood.

Key words: The analysis of exposure; the reconstruction approach; air pollution

12. HEALTH RISKS OF CHILDREN IN THE SCHOOL ENVIRONMENT IN NIŠ 12. RIZICI PO ZDRAVLJE DECE IZ ŠKOLSKE SREDINE U NIŠU

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Introduction: The health of school children depends on both the physical and mental development of children, and to a large extent on the school environment in which children live. The most common factors that affect the health of children present in the school environment are: micro-climatic conditions in the school premises (temperature, humidity, light).

Objective: The aim of this study was to investigate the influence of microclimate conditions on the health of school children.

Method: The study of microclimate parameters was performed in ten elementary schools in the city Nis measuring temperature and relative humidity. Assessment of the quality of daily lighting was done by the geometric method of measuring the quality of light, determining photo coefficient in classrooms and gyms. Analysis of morbidity school children was performed on the data of the report of the Health of Nis diagnosed diseases in the period in 1998 to 2008.

Results: All measurements were performed during the heating season. The average air temperature in the classrooms on the ground floor was 21.15 ° C, in the classrooms upstairs 21,44 ° C and gyms 19.1 ° C. The average relative humidity in classrooms on the ground floor was 44%, in the classroom on the first floor 52% and 56% of gyms. Calculated photo coefficient tested in classrooms ranged from 1: 3 to 1: 3.7. Calculated photo coefficient in the corridors ranged from 1: 2 to 1: 5.7.

Conclusion: The values of relative humidity with the prescribed standards for the microclimate conditions in the school premises while the values of air temperature show slight variations. The quality of natural light measured on the basis photo coefficient meet the hygiene requirements for brightness school premises. The most common diseases of school children are diseases of respiratory organs. By monitoring the microclimate parameters in the school environment can lead to decrease morbidity of children of school age. Since the testing was done in urban schools need to initiate expansion of testing to rural areas.

Key words: Photo coefficient, school children, school environment

13. EXPOSURE TO BIOLOGICAL AGENTS AND CHILDREN HEALTH
13. IZLOŽENOST BIOLOŠKIM AGENSIMA I ZDRAVLJE DECE

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Biological agents in indoor air are known to cause three types of human disease: infections, hypersensitivity diseases, and toxicosis. The objective of this investigation was to estimate the effects of the biological agents on the prevalence of respiratory symptoms and diseases as well as the prevalence of non-specific symptoms on different organs at children. The study sample consisted of 1074 children aged 7 –11 years from three primary schools in Nis. A questionnaire which was based on recommendations of WHO is used. In this investigation it is established that exposure to biological agents has the significant health effects on exposed children.

Key words: biological agents, children health

14. ODREĐIVANJE OLOVA U SREDSTVIMA ZA ULEPŠAVANJE I BOJENJE USANA 14. DETERMINATION OF LEAD IN THE LIPS BEAUTIFICATION AND COLORING ITEMS

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Introduction: Lead is an element that is located in a natural environment and we are all exposed to small amounts of it in food, water and air we breathe on a daily basis. Traces of lead can get into lipsticks during the production process from ingredients such as dyes and pigments.

Objective: Presentation of the results achieved in the international inter-laboratory testing - Determination of total lead in lipstick-INEP-35 during year 2012, as well as further development of the method used.

Results: In the aforementioned interlaboratory study 18 laboratories from 13 countries participated but 17 sent results. The sample was a mixture of commercially available lipsticks. Assigned value is the average result of two laboratories with experience in the analysis of trace metals in different matrixes.

Laboratory results were evaluated with the z-and ζ -scores. Total percentage of satisfactory results of interlaboratory tests was 75% for the z-score and 50% for ζ -score. Sample preparation was performed by microwave digestion and determination of lead using electrothermal atomic spectroscopy.

Results of the Laboratory of the Public Health Institute Nis show good performance and meet the criteria.

Conclusion: The content of heavy metals and metalloids is part of the mandatory health safety parameters that are regularly monitored in cases of general use.

According to local regulations "items for the beautification and lips coloring" should not dismiss more than 20 mg/kg of lead.

However, the differences in our legislation are in proper working methods which involve the determination of toxic metals after a short 15-minute extraction of 0.1 mol/L HCl. That is why legislation should be harmonized with the European legislation, in order to find wider application for this technique in the laboratory.

Key words: lead, lipsticks, beautification and coloring items

TOPIC 2: NUTRITION AND HEALTH

Ib PREDAVANJE PO POZIVU

Ib INVITED LECTURE:

1. PREVENTIVNO-MEDICINSKI ZNAČAJ PROCENE DNEVNOG UNOSA BENZOJEVE I SORBINSKE KISELINE PREHRAMBENIM ADITIVIMA

1. PREVENTIVE AND MEDICAL SIGNIFICANCE OF THE ASSESSMENT OF DAILY INTAKE OF BENZOIC AND SORBIC ACID THROUGH FOOD ADDITIVES

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INTRODUCTION

Benzoic acid and sorbic acid and its salts are the most widely used preservatives in various ranges of foods. The acceptable daily intake of additives is the amount of the additive which can be ingested every day during the life time without appreciable health risk. Acceptable daily intakes (ADI) of 0-5mg/kg body weight for benzoic acid and 0-25mg/kg body weight for sorbic acid have been established (1).

Some studies suggested that in sensitive persons, daily intake of benzoic acid lower than ADI can cause non- immunological contact reactions (2). Few epidemiologic studies reported allergic reactions to benzoic acid and benzoate (urticaria, rinhitis and pruritis) (3-5) and sorbic acid and sorbate (non- immunological contact urticaria) (6).

The aim of this study is estimation of daily intake of benzoic and sorbic acid, and to assess public health risk for population of Niš.

MATERIALS AND METHOD

The study was conducted on a random sample of 1004 citizens of Niš Serbia aged from 15 to 75, drawn from the Central Population Register. Modified self administered food frequency questionnaires (FFQ) based on those by Willet (7) was used to assess subjects' habitual diet (1 year prior to the interview). Body weight was self-reported during this interview.

Several foodstuffs, in which benzoate and sorbate use is allowed, were not taken into account because of an assumed low consumption: low sugar marmalade, ice tea, energy drink, dressing etc.

Estimation of daily intake of benzoic and sorbic acid was calculated using the recommendations of European Union (*Tier 2*) (8) with formula by Lambe et al. (9).

Estimates of the dietary exposure were then divided by the body weight of the respondent to give a dietary exposure in benzoic or sorbic acid mg /kg body weight/ per day. Tier 2 is calculated by multiplying the average per capita daily food intake by the legal maximum use level or additive by national regulations (10)

$$Y_i = \sum (X_{vi} * C_v) / b_{wi}$$

Y_i- estimated daily additive intake; **X_{vi}** - average daily amount (kg) of a food item consumed by subject; **C_v** - the maximum permitted concentration additive in that food item; **b_{wi}** - subject's body weight (kg).

The reliability of high percentiles (*99 percentile*) (to assess population with high additive intake) is related to the number of subjects used to calculate them (1004 subjects), and according to model by Kroes and al.(11) recommended by EFSA (*European Food Safety Authority*).

RESULTS

Table 1 shows the estimated daily intake of benzoic and sorbic acid for study population.

Table 1. Daily intake of benzoic and sorbic acid (mg/kg bw)

	Mean (SD)	P50	P90	P95	P97.5	P99
Benzoic acid	0.49(0.52)	0.33	1.1	1.4	1.9	2.8
Sorbic acid	0.60 (0.65)	0.37	1.45	1.87	2.4	3.1

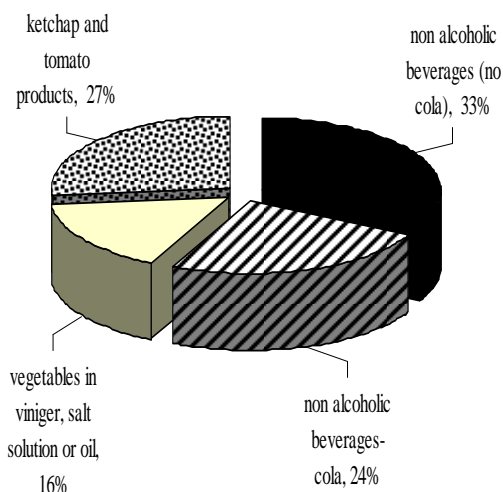
The mean usual intake of benzoic acid was (0.49 mg/kg/bw or 9.8% of ADI) and sorbic acid (0.60 mg/kg/bw or 2.4% of ADI) per day (table 1 and table 2).

Table 2. Percentage of ADI of benzoic acid and sorbic acid

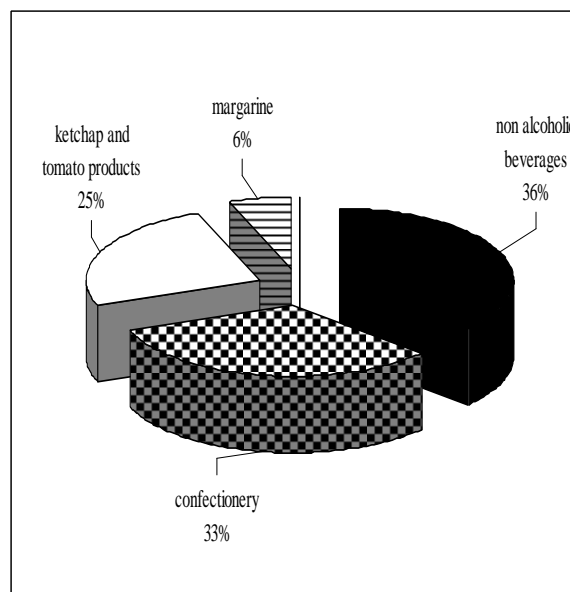
	%ADI					
	Xs	P50	P90	P95	P97.5	P99
Benzoic acid	9.8	6.6	22	28	38	56.4
Sorbic acid	2.4	1.48	5.8	7.48	9.6	12.4

Percentage of daily intake of benzoic acid (56.4%) and sorbic acid (12.4%) did not exceed the ADI at the 99 percentile (table 2)

The greatest contributor to the total estimated benzoic acid intake was the group of non alcoholic beverages (57%). Other important contributors to benzoic acid exposure in consumers were ketchup and tomato products (27%) and domestic pickled vegetables (16%) (graph 1).



Graf. 1. Food groups' contribution (%) to the intake of benzoic acid.



Graf. 2. Food groups' contribution (%) to the intake of sorbic acid

The major intake of sorbic acid for study subjects came from non alcoholic beverages (36%), confectionery (33%) and ketchup and tomato products (25%) (Graph 2).

DISCUSSION

According to the Council of Europe, percentage of ADI for benzoic acid via food additive in adults, in Denmark, Estonia, France, Italy, Netherlands, United Kingdom and Norway, were below the ADI (between 8-64% of ADI) (8). Data from the Fifty-first report of the Joint FAO/WHO Expert Committee on Food Additives also indicate that intake of benzoic and sorbic acid was below ADI. It is evident that the group of non alcoholic beverages, as in our study, was the main source of benzoic and sorbic acid in most of countries, but not in all. The major intake of in China came from soya sauce. In Japan, soya sauce is in second place in benzoic intake by food (11).

Bread is the dominating source for the intake of sorbic acid in Denmark (12). In New Zeland, refrigerated orange juice, pikelets, crumpets and muffins, and margarine were the major contributors to dietary sorbate exposure. (13).

The highest contributors to benzoic and sorbic acid intake in Austria were fish and fish products, including also mayonnaise-containing fish salads. Mean estimated dietary intakes of benzoic acid exceeded the ADI in all population groups (14).

The main contributors to the dietary exposure to benzoic and sorbic acid in our study are not regularly consumed (pickled vegetables are consumed in winter, and consumption of non alcoholic beverages is higher in summer months).

Great differences exist between mean intakes of specific food among study subjects (high standard deviation). Harmonized food consumption data collection among countries and new exposure assessment methodologies (Nusser method, Monte Carlo simulation and etc) are needed in order to make correct assessment of exposure to food additives using probabilistic analysis.

The results of this study indicate that dietary exposure to benzoic acid and its salts as well as to sorbic acid through food preservatives does not represent public health risk for the population of Niš. In order to reduce the intake of benzoic and sorbic acid, it is appropriate to recommend moderate consumption of non alcoholic beverages.

Acknowledgement

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IIb USMENE PREZENTACIJE
IIb ORAL PRESENTATIONS:

1. EVALUACIJA ANTROPOMETRIJSKIH INDIKATORA METABOLIČKOG SINDROMA I NJIHOVA POVEZANOST SA METABOLIČKIM FAKTORIMA RIZIKA KOD ZDRAVIH OSOBA U NOVOM BEOGRADU

2. EVALUATION OF ANTHROPOMETRIC INDICES FOR METABOLIC SYNDROME AND THEIR ASSOCIATION WITH METABOLIC RISK FACTORS AMONG HEALTHY INDIVIDUALS IN NEW BELGRADE

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The aim of the study was to evaluate the anthropometric indices for MetS and determine which of simple anthropometric measurements is most closely associated with metabolic risk factors.

Methods: The research included 264 individuals, of which 132 men and 132 women. Anthropometric indicators were measured using standard protocols. BMI was calculated as weight/height²(kg/m²) ratio, as recommended by the WHO. Blood pressure measurements were obtained with the subject in a seated position by using a mercury sphygmomanometer. The metabolic parameters (HDL, LDL, triglycerides, blood glucose) were analyzed by standard procedures. Analysis of the examinees' medical records was also performed. Metabolic syndrome was diagnosed using the IDF criteria. The analysis of the research results were performed using SPSS version 10.0 for Windows.

Results: The prevalence of the metabolic syndrome was 44.7% in men and 43.2% in women. Normal-weight subjects of both sexes were significantly younger and had significantly lower blood glucose, total cholesterol, LDL and triglycerides than overweight and obese subjects. SBP and DBP values were significantly increased in parallel with increasing of BMI. For the whole sample, both anthropometric indices had significant associations with the other five components of MetS.

Conclusion: Waist circumference is a simple measure of adiposity most strongly associated with metabolic abnormalities. The results obtained in this study indicate that measurement of WC by BMI categories may indicate a person with an increased risk of development of chronic diseases.

Key words: waist circumference, body mass index, metabolic syndrome, health risk appraisal

2. ZDRAVSTVENA ISPRAVNOST PLASTIČNIH MATERIJALA KOJI DOLAZE U KONTAKT SA HRANOM I DEČJE IGRAČKE POVEZANOM SA ISPITIVANJEM MIGRACIJE PRIMARNIH AROMATIČNIH AMINA (PAAS) U INSTITUTU ZA JAVNO ZDRAVLE R.MAKEDONIJE U PERIODU 09.2011 – 06.2013 GOD.

2. HEALTH SAFETY ON PLASTIC MATERIALS THAT COME INTO CONTACT WITH FOOD AND CHILDREN TOYS ABOUT MIGRATION OF PRIMARY AROMATIC AMINES (PAAS) EXAMINATION IN IPH- RM IN PERIOD 09.2011 – 06.2013

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Humans can be exposed to PAAs by the usage synthetic products which come in contact with food. PAAs are suspected to be toxic and carcinogens. PAAs are mainly originated from synthetic azo dyes applied as colorants and from the use of adhesives based on polyurethanes (PU).

The main objective of this work was determination of migration level of PAAs from plastic materials that come in direct contact with food and plastic toys in model solution of 3 % acetic acid. Quantitative determination of sum of PAAs, expressed as aniline was made using spectrophotometric method based on diazotisation of PAAs and subsequent coupling of the obtained diazonium salts with N-(1-naphthyl) ethylenediamine dihydrochloride. Detection (DL) and quantification limit (QL) was 0,000715 mg/l and 0,002165 mg/l, respectively.

The number of tested samples in IPH of RM for a period of 09.2011 – 06.2013 was 1171. From the tested items, 557 were plastic toys, and 614 were plastic containers, utensils and items. Samples were tested using official method ("Amtliche Sammlung von Untersuchungsverfahren nach § 35 LMBG L 00.00-6"). Assessment of obtained data was made according to EU Regulation 10/2011, so 24 samples exceeded DL value (0.01 mg/kg) - 18 were toys and 6 were sets coming in contact with food.

Requires increased sanitary inspection market, amid frequent occurrence of PAAs in plastic kitchen utensils, especially black and children toys made in China.

Keywords: food-packing materials, children toys, primary aromatic amines (PAAs), migration, health safety.

IIIb POSTER PREZENTACIJE
IIIb POSTER PRESENTATIONS:

1. NIVOI GLIKEMIJE KOD STARIH SA DEPRESIVNOŠĆU
1. GLYCAEMIC LEVELS IN ELDERLY PATIENTS SUFFERING FROM DEPRESSION

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³Medicinski fakultet, Kragujevac

Objectives: Diabetes mellitus (DM) leads to a range of complications, which could significantly jeopardize one's health. This is particularly the issue with the DM that has not been recognized and treated, especially among the elderly patients suffering from depression, who often do not use adequately the available medical care. The aim of this paper is to examine the glycaemic levels in elderly patients suffering from depression.

Materials and methods: The study included 135 respondents for whom depression was established through the Geriatric Depression Scale (GDS) questionnaire (score 6 or above). The sample included 99 women and 36 men, with the average age of 80.55 ± 6.49 . The glycaemic level was established in the respondents' homes. The insight into the medical documents of the respondents showed that 31.9% of them were suffering from DM.

Results: Our results showed that the average glycaemic level in the group with DM was 10.02 ± 4.80 mmol/l. The glycaemic level among the patients who had not been previously diagnosed with DM was 6.96 ± 1.67 . However, among 9.72% of them the level of 7 mmol/l was established, 8.69% had the value of 8 mmol/l, 5.43% patients had the level of 9 mmol/l and in as much as 8.69% patients the glycaemic level was over 10 mmol/l.

Conclusion: High level of unregulated and undiagnosed DM among the elderly patients with depression symptoms, combined with the fact that due to the nature of depression there is a poor compliance among these patients, calls for the need for preventive check-ups, monitoring and adjustments in the therapy, as well as for the education of such a population.

Key words: elderly, deression, diabetes mellitus, GDS

2. NAJVAŽNIJI KONTAMINENTI ANTROPOGENOG POREKLA U VODI ZA PIĆE 2. MOST IMPORTANT CONTAMINANT IN DRINKING WATER OF ANTHROPOGENIC ORIGIN

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Introduction: Human population grows and develops expecting safe drinking water, although achieving this is not simple. Aquatic pathogen, synthetic chemicals, toxic metals, pesticides, radio nuclides are diverse risks to human health if they are present in drinking water.

Aim: Unfortunately the list of chemical, biological and physical of risk bearers is expanding so the public is rightly concerned.

Method: Review of the internet literature

Results: One third of the world's population lacks safe water supply. To the year 2025 UN predicts that two-thirds of world's population will live in countries with serious lack of water. According to the data of UNICEF in the countries in which high percentage of population (almost 100%) has access to safe water (USA, Sweden, New Zealand, United Arab Emirates) mortality with children less than 5 years of age has been reduced to 10, calculated at 1000 people. Another group, usually African countries, in which low percentage of population (50%) has the access to safe water, mortality with children under 5 years of age is more than 200 calculated on 1000 people. In the second half of the previous century, man produced more than two million synthetic chemicals out of which 100.000 was produced in very big quantity, and about 2% new products, at the annual rate of 25.000 tons and this is the serious problem because of the possible influence on the environment.

Conclusion: In vivo experiments proved carcinogenic influence of certain synthetic compounds identified from chlorinated drinking water, suspected to cause cancer of genital tract and cancer of colon. Based on studies referring to general exposure in a community as well as studies referring to individual exposure the current position was made, there are not enough proofs of carcinogenic influence of chlorinated drinking water and its consumption in the cases of research of experimental animals.

Key words: drinking water, contaminants of anthropogenic origin

3. ODREĐIVANJE SADRŽAJA BENZOJEVE KISELINE U ENERGETSKIM I
BEZALKOHOLNIM GAZIRANIM OSVEŽAVAJUĆIM NAPICIMA
**3. DETERMINATION OF BENZOIC ACID CONTENT IN ENERGY DRINKS AND
NON-ALCOHOLIC CARBONATED REFRESHMENTS**

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Objectives: Benzoic acid and its salts belong to the A1 list of additives under the label E210 for benzoic acid, and E211 for sodium-benzoate. The acceptable daily intake of benzoic acid is 5mg/kg of body weight. The use of benzoic acid is widely distributed for preserving non-alcoholic refreshing beverages, salted butters, sauces and many other ingredients. The objective of this study was to determine the content of benzoic acid in energy drinks and non-alcoholic carbonated refreshments and monitoring values in relation to the declared value and value of maximum allowed concentration (MAC) specified in legislation.

Materials and Methods: The determination was performed on four different samples: two of them are energy drinks and two are non-alcoholic carbonated refreshing drinks. After sample preparation and extraction, benzoic acid was determined by volumetric analysis.

Results: All results of this analysis are below *the limit* of maximum allowed concentration (MAC), which is prescribed for non-alcoholic beverages (150mg/l). Determined benzoic acid concentrations correspond to the declaration of two products, while the remaining two were inconsistent with the obtained results

Conclusion: It should be taken into consideration is use of carbonated refreshing drinks reasonable or justified, since abundant intake are considered as risk factors for occurrence of obesity, metabolic syndrome and cardiovascular disease.

Key words: benzoic acid, preservative, volumetric methods, energy drinks, non alcoholic carbonated drinks.

Acknowledgements: This research was supported by the Ministry of Education and Science of Republic of Serbia (Grant no. III 46013).

4. PROVERA NUTRITIVNIH I ZDRAVSTVENIH IZJAVA NA PREHRAMBENIM PROIZVODIMA

4. EXAMINING NUTRITION AND HEALTH CLAIMS ON FOOD PRODUCTS

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Objectives: The EU, in the field of marking-labeling of food products, actively applies Regulations 1924/2006 and 432/2012 which harmonize the list of nutrition and approved health claims found on food products. In Serbia there are no health claim rules, and Regulation on labeling and marking of packaged foods ("Sl. list SCG" no. 4/2004, 12/2004 and 48/2004) have clear rules for nutrition claims only. This paper presents research of claims that are found on breakfast cereals and bars.

Materials and methods: The research - filling in forms (list of ingredients, nutrition and health claims, allergenic statements, nutrition charts) for each product taken from shelves of two hypermarkets in June 2013 in Belgrade and statistically analyzing the data.

Results: The majority of examined products up to 75.63% consisted of muesli, corn flakes, rolled oats and other cereals, while 24.37% were bars. With Serbian and EU regulations on product labeling 26.86% complied, with just the EU and not the Serbian 28.57% and with just the Serbian and not the EU 12.61% and even 31.93% were not properly declared regarding any legislation.

On 49.58% of the products there were nutrition claims, and out of these a large 96.61% correctly used the claims. Health claims were found only on 9.24% of the products, and of these, 81.82% were properly used.

Conclusion: It is necessary to educate food producers. Since examining the composition of the products, nutrition claims in this category could have been used on 78.89% of the products and health claims on even 43.73%.

Also, consumer education is necessary so that they would not be misled by improper posting of claims on food products.

Key words: Nutrition claims, health claims, food labels, nutrition, declaration,

5. SO – IZVOR JODA U LJUDSKOJ ISHRANI
5. SALT – SOURCE OF IODINE IN HUMAN NUTRITION

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Mandatory salt iodisation is safe and effective method for preventing negative health consequences of iodine deficiency. The purpose of this paper is to determine the content of iodine in salt in Nisava district markets.

Accredited laboratory of Public Health Nis (ISO 17025), in the period from 2005-2013, using standard method determined iodine in 126 samples of salt (104 samples of rock salt and 22 samples of sea salt). The results were interpreted according to current legal Regulation (Book of Regulation SCG n. 31/2005).

According to the Regulation, the concentration of iodine lower than allowed (<12mg/kg) was present in 9 (7.1%) samples, and concentration higher than allowed (>18mg/kg) was present in a 28 (22.2%) samples of salt. There was no statistically significant difference between the concentration of iodine in stone and sea salt ($z=1.13$; $p> 0,05$). Since 2010, all controlled samples (28) had an iodine value prescribed in the Regulations.

Households in Niš have access to adequate iodized salt, but national surveys should assess iodine status of the population in Serbia to prevent iodine-deficiency disorders.

Key words: iodine, salt, health

6. ANTIOKSIDATIVNA AKTIVNOST ETANOLNIH EKSTRAKATA BILJNE VRSTE
SALVIA VERBENACA L

6. ANTIOXIDANT ACTIVITY OF ETHANOLIC EXTRACTS FROM *SALVIA VERBENACA* L.

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The genus *Salvia* L., family Lamiaceae, is a relevant source of powerful natural antioxidant agents and preservatives used in foodstuff and medical products for centuries. *Salvia verbenaca* L. is an aromatic herb used as a flavoring and spice in foods. The aim of this study was to define the antioxidant capacity of ethanolic extracts prepared from the dried aerial parts of *S. verbenaca* collected at full flowering stage in Niš.

The extracts were prepared by maceration with 96% ethanol (E), in an ultrasonic bath with 96%, 80% and 60% ethanol (EU, E80U and E60U, respectively), and in a boiling bath with 80% and 60% ethanol (E80T and E60T, respectively). Antioxidant capacity was evaluated using two complementary *in vitro* tests, which determined the ability of the extracts to scavenge free radicals in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) system, and the inhibition of lipoperoxidation in the β -caroten/linoleic acid (BL) model.

The results are presented as the concentration of the extract that achieved 50% inhibition of free radicals (IC₅₀). E60T was the most powerful in DPPH (IC₅₀=13.72±1.42 µg/mL) and E80U was superior in the BL system (IC₅₀=16.20±1.95 µg/mL). All ethanolic extracts are effective scavengers of free radicals and inhibitors of lipoperoxidation, and can thus be of importance in stabilizing food against oxidative deterioration.

Keywords: *Salvia verbenaca* L., ethanolic extracts, antioxidant activity

7. *CALLUNA VULGARIS*: SNAŽAN ANTIOKSIDANS I INHIBITOR KSANTIN OKSIDAZE

7. *CALLUNA VULGARIS*: STRONG ANTIOXIDANT AND XANTHINE OXIDASE INHIBITORY AGENT

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Herb of *Calluna vulgaris* (L.) Hull (Ericaceae), is said to be diuretic, antimicrobial, cholagogic, and antirheumatic. Despite the long traditional use, the efficacy is not documented yet. Since one of the claimed indications is gout, the aim of our study was to investigate the xanthine oxidase inhibitory activity alongside antioxidant potential of *C. vulgaris* ethanolic extract.

Material and methods: *In vitro* xanthine oxidase inhibitory activity was assayed spectrophotometrically under aerobic conditions and expressed as the percentage inhibition of enzyme. Three test methods (radical scavenging activity in DPPH test and inhibition of lipid peroxidation in liposomes and in β -carotene/linolic acid system) were employed for preliminary antioxidant screening of *C. vulgaris* ethanolic extract. All assays were done in triplicates.

Results: Tested sample exerted excellent antioxidant activity in all applied test systems (IC₅₀ value in DPPH test was 12 μ g/ml and inhibition of lipid peroxidation up to 90.26%) and good xanthine oxidase inhibitory activity (IC₅₀=319.19 μ g/ml). In conclusion, these data may explain, at least in part, the traditional use of *Calluna vulgaris* as component of herbal teas for the treatment of gout and related symptoms.

Key words: *Calluna vulgaris*, gout, xanthine oxidase inhibitory activity, antioxidant potential

8. PEKARSKI PROIZVODI U PROMETU

8. BAKERY PRODUCTS FROM THE MARKET

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Objectives: Laboratory of the Institute controls food safety. Bakery products, as combination of selected ingredients, rich in composition, make these products important part of a balanced and healthy diet and a wide assortment, ideal bite with all meals or a meal itself.

Materials and methods: A significant part of samples are milling and bakery products, pasta and quickly frozen dough and quick frozen dough products. In analysis are used accredited classic methods.

Results: In the period in 2010. - August 2013. 1797 samples from this category were analyzed, out of which 3.17% were defective. The reason is that the most common samples submitted was insufficient fat content in samples of quick frozen dough products and quick-frozen dough (51% of the number of defective), a higher content of water and salt in pie crusts (42% of the number of defective). Other defectiveness concerns the high content of water and extra ash content in flour, high water content in bread, the presence of impurity ingredients, net weight discrepancy of samples toward the declared weights and inadequate declaration concerning the categorization of the product or composition of the product with the declaration.

Sensory characteristics of all analyzed samples met the minimum requirements at the time of testing.

In production colored, heat-processed ingredients are used instead appropriate amounts of grain mill products that should be used and incorporated into products. Therefore products have lower content of minerals, vitamins, fiber..., for which reason consumers actually choose them.

Conclusion: The reasons for the non-conformities with the requirements are lower cost of production, technological needs, technological error or lack of knowledge or ignorance of the regulations, those manufacturer involved in the production.

Control of bakery products is therefore necessary for further improving, enhancing and providing customers with better quality, and more attractive and more biologically valuable products.

Key words: bakery products, food safety, control

9. NUTRITIVNA ZNANJA I PONAŠANJE REKREATIVNIH SPORTISTA

9. NUTRITIONAL KNOWLEDGE AND BEHAVIOR AMONG RECREATIONAL ATHLETES

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In physically active population, nutrition plays very important role. Even though nutritional knowledge is increasing and dietary practices are on the rise, sports nutrition-associated issues are still a challenge. The aim of this study was to compare nutritional knowledge and behavior among the recreational athletes situated in two different countries.

Material and methods: The anonymous survey was conducted from February 2012 to April 2013 among the recreational athletes aged 18-40 years in 84 subjects. A specially prepared author's two-part questionnaire was used. The questions were categorized into four domains of nutrition: micronutrients, macronutrients, weight management and performance.

Results: The recreational athletes have limited knowledge of the principles of nutrition for sportsmen. The mean nutrition knowledge score was 20 correctly answered questions out of 30 (66.7%) for Italian sample and 19 out of 30 (63%) for Serbian. Also the recreational athletes apply the principles of adequate nutrition in their everyday diet in a limited scale. For example, majority of the subjects do not know the proper percentage of nutrients of a daily balance diet. Although there is a positive attitude toward nutrition, lack of nutritional knowledge and dietary practices were observed in many recreational athletes. Nutritional education among this group of athletes should be planned according to the gaps in nutritional knowledge.

Key words: nutritional education, nutritional knowledge, sportsmen's diet, recreational athletes

10. RAZLIKE U ZNANJU I PRIHVATANJU GENETSKI MODIFIKOVANE HRANE IZMEĐU STUDENATA PRIRODNO-MATEMATIČKOG I FILOZOFSKOG FAKULTETA UNIVERZITETA U NIŠU

10. DIFFERENCES IN KNOWLEDGE AND ACCEPTANCE OF GENETICALLY MODIFIED FOOD BETWEEN STUDENTS OF FACULTY OF SCIENCE AND MATHEMATICS AND FACULTY OF PHILOSOPHY, UNIVERSITY OF NIŠ

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Objectives: This work compare acceptance among biology students and students of social science toward genetic modification. The aim of research was to determine differences among acceptance and their correlation with acquired knowledge.

Materials and methods: Cross-sectional study carried out with university students. The instrument for data collection was the questionnaire. ANOVA test, Kruskal–Wallis one-way analysis of variance by ranks, probit regression, summary and descriptive statistics were used and statistical significance was taken at $p < 0.05$.

Results: The significant difference between two faculties in the acceptance of genetic modification was found only for application in medicine production but not in food production. Both university students group do not accept use of genetic modifications in food production.

Conclusion: Study also demonstrated that knowledge had a partial and specific influence on acceptance of GM. Namely, the main knowledge predictor of rejecting GM was the misconception, whereas real knowledge had no impact. This is important information, primarily for university systems, which points to the need for re-evaluation of curricula and education approaches.

Key words: Biotechnology, GMO, students, acceptance, knowledge.

11. ZNANJA I STAVOVI STUDENATA PRIRODNO-MATEMATIČKOG FAKULTETA
UNIVERZITETA U NIŠU O GENETSKI MODIFIKOVANOJ HRANI
**11. KNOWLEDGE AND ACCEPTANCE OF GENETICALLY MODIFIED FOOD
AMONG STUDENTS OF FACULTY OF SCIENCE AND MATHEMATICS,
UNIVERSITY OF NIŠ**

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Objectives: The aim of this study is to prove that acceptance of students on Faculty of Science and mathematics, especially biology and chemistry students, are supported by their knowledge of biotechnology.

Materials and methods: The survey is conducted by interviewing 10% of students in each department of Faculty of Science and Mathematics, by using stratified sampling method, the number of interviewed students is 165. In data processing, descriptive statistical analysis, ANOVA test and biprobit regression are used.

Results: Knowledge as predictor of acceptance of genetic modification was found only for application in medicine production but not in food production.

Conclusion: It remains unclear which other factors influence the acceptance of GM products in food production and there is a reasonable assumption that further research should take into account the influence of the media.

Key words: Biotechnology, GMO, students, acceptance, knowledge.

F. SESIJA: AKTUELNE PARAZITOZE
F. SESSION: CURRENT PARASITOSSES

I PREDAVANJA PO POZIVU
I INVITED LECTURES

1. NOZOKOMIJALNA TRANSMISIJA: JOŠ JEDAN MOGUÆI PUT PRENOŠENJA
VECTOR-BORNE INFEKCIJA
1. NOSOCOMIAL TRANSMISSION: A SILENT CONTRIBUTION TO THE
VECTOR-BORNE DISEASE SPREAD

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Abstract. Vector-borne diseases (VBD) are parasitoses whose transmission involves haematophagous arthropods. However, their etiological agents, being in the blood, may be accidentally man-to-man transmitted also in absence of natural vectors: vertically, by blood transfusion and by organ transplant. The nosocomial pattern of transmission is assuming an increasing importance in areas where the specific VBD is absent because of the corresponding absence of specific legal requirements to ensure the safety of blood supply and organ transplant, since the sanitary personnel there isn't used to suspect the infection and, more still, because some VBD are totally asymptomatic in the infectious phase. An example of these insidious VBD is the Chagas disease, endemic in Latino-American areas, now identified all around the world. The paper refers the results of a screening pilot-program carried out in Rome, to avoid the nosocomial transmission of *Trypanosoma cruzi* and plasmodia.

Key words: *Trypanosoma cruzi*; Chagas disease; Plasmodia; Transfusion; Organ transplant

Introduction

Vector-borne diseases (VBD) are infectious diseases whose transmission involves haematophagous arthropods. The geographical distribution and incidences of VBD strictly depend on ecological and climatic conditions that make a place suitable or non-suitable for the development of the vector species. In general, tropical and temperate environments are more favourable to the statement of these parasitoses, and colder one may become vulnerable due to global trade and travel, but also to ecological shifts associated with climate change. Other causes, like disruption and movement of human population can expand distribution of pathogens and increase exposure routes (1). In fact, all parasites vector-transmitted have further chances of spreading, as their presence in the blood allows vertical, by transfusion and laboratory accident passage; in addition, their possible collateral location in tissues allows man-to-man infection through organ transplant, like can happen for *Leishmania donovani* and *L. infantum*.

The nosocomial pattern of transmission, well considered and prevented in endemic areas (2), assumes an increasing importance in non-endemic ones because in these countries specific legal requirements to ensure the safety of blood supply and organ transplantation are not established, and not-enough attention is paid to the possible vertical transmission of pathogens that, if identified, could be immediately treated and eliminated in the new-born, without

consequences. Such conditions are, for example, valid for malaria, sickness and Chagas diseases that have, by the vectorial point of view, a geographical distribution well defined. All of them are considered a known public health in their endemic countries whereas, in non-endemic ones, are scarcely considered among the infections that, during pregnancy and before any medical intervention that could be source of transmission must be excluded also through specific and sensitive analyses (3, 4, 5). Moreover, outside endemic areas sanitary personnel is not used to recognize the infection, and the suspecting “exotic” ones in people vertically or by transfusion/transplant/laboratory accident infected is more still difficult, also because some of them are totally asymptomatic in the infectious phase.

This paper reports the results of a systematic screening for *T.cruzi* and plasmodia, approved by the ethical committee, started in 2010 in Rome to evaluate the risk of nosocomial transmission of these VBD.

Study population and Methods

Blood donors screened for *T.cruzi* were volunteer subjects born in Latin American endemic countries or from mother who lived there, and people who there spent more than 1 week for travel or job. Few organ donors, immigrants from endemic countries, were included in the study.

All volunteers were screened using an immunochromatographic assay (ICT) (Chagas Quick Test, Cypress Diagnostics, Belgium) associated to an ELISA based on recombinant antigens (BioELISA Chagas, Biokit S.A., Spain). Blood samples of serologically positive subjects were deeply investigated by microscopy (after triple concentration) and molecular diagnostics (nested PCR for the repetitive area of nuclear DNA using primers TCZ1/TCZ2 and TCZ3/TCZ4, which yield a product of 188 and 149 base pairs, respectively (6), and sequencing).

Blood donors screened for plasmodia were volunteers who referred, during questioning, a history of malaria. They were screened by microscopy (repeated Giemsa stained blood films and thick smears), associated to an ICT (Core Malaria Pan/Pv/Pf, Core Diagnostics, Birmingham, UK) that detects parasite antigens.

Results

A total of 172 subjects have been to date included in the Chagas disease control plan (168 as blood donors, and 4 as organ donors). Most enrolled people (n=141) were immigrants or subjects born from mothers living in Latin American endemic areas, whereas the remaining 31 subjects were Italian travellers.

Organ donors turned out negative, whereas 5/168 (2.98%) blood donors proved positive to at least one serological test. Seropositive individuals were 3 immigrants from Brazil, Bolivia and Colombia, respectively, and 2 were Italian people usually living in Rome. The first Italian donor is a 38-year-old man, backpacker globetrotter who, during 2008-2009, travelled through Mexico and in 2012 run for first blood donation. The other one is a 46-year-old engineer, who worked in Mexico and in impervious internal areas of Brazil, where he stayed till 2011 (six months before his first blood donation that evidenced his positivity to ICT). His blood proved PCR-positive and showed a very light parasitemia. BLAST analysis of the amplicon sequences showed 100% identity to *T. cruzi* strain Y, discrete typing unit (DTU) TcII (7).

All volunteers were informed about the analysis results, and positive ones (all apparently healthy subjects that nobody could imagine as people who need sanitary help) had immediate access to further specific medical checks.

The malaria control plan didn't evidenced plasmodia in the blood of the 4 donors to date examined.

Conclusion

These preliminary results, notwithstanding their methodological limitations (sample size and origin of immigrants, who were mostly coming from countries where Chagas disease has - currently- low prevalence), present a scenario that should be considered worrisome. First at all they suggest that Chagas disease can be an emerging problem also in Italy, new for our sanitary personnel. Infected people are developing a disease that requires further immediate medical checks and appropriate therapy, the more effective the more timely. Indeed, molecular characterization identified in the donor the DTU TcII, the major *T. cruzi* lineage associated with human infections more or less severe(8). Ten, our finding suggest the need of systematic screening plans to control at-risk blood donors, mainly temporary residents in endemic areas, who constitute a possible source of person-to-person *T. cruzi* transmission even more insidious than immigrants.

The application of very sensitive tests and a very accurate pre-donation interview for the proper identification of at-risk donors proved of fundamental importance, also for the risk of plasmodia transmission that is less insidious because asymptomatic cases are rare, and fever is absent only during the first days of infection.

In conclusion, the nosocomial pattern, even if accessory to the transmission of VBD, is assuming an increasing relevance all around the world, non-endemic areas included. Therefore, all countries should paid attention to this insidious pattern of transmission and should activate efficient sanitary plans to prevent and deal with unsuspected nosocomial infections. These are the conclusions of a meeting organized two months ago by the WHO, in which have been stated the initiatives necessary to control, first at all, the transmission of Chagas disease in non-endemic countries (9).

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2. DOSADAŠNJA ZNANJA O VECTOR-BORN ZOONOZNIM INFEKCIJAMA U MAĐARSKOJ

2. UP-TO-DATE KNOWLEDGE ABOUT VECTOR-BORNE ZOONOTIC INFECTIONS IN HUNGARY

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Abstract

It is well known that blood-sucking arthropods can transmit several pathogens (e.g. viruses, bacteria, protozoa and helminths) from wild and/or domestic animals to humans. New insights into the identification of pathogens in vectors, animals and humans have been acquired in recent decade due to molecular biological methods. The knowledge about various vector-borne zoonotic agents has also increased in Hungary recently. The paper summarizes the results related to tick-, mosquito-, flea- and sandfly-borne zoonotic pathogens obtained during the last decade.

Key words: zoonosis, vector-borne, Hungary

Vector-borne emerging and re-emerging zoonotic diseases are increasingly gaining importance all over the world. It is known that the geographic distribution and the activity of blood-sucking poikilothermic arthropods (e.g. ticks, fleas, mosquitoes and sand flies) especially determine the occurrence of these diseases with transmitting different agents such as viruses, bacteria, protozoa and helminths from animals to humans. Besides changing climate a suite of other factors (e.g. political and economical changes, increased global movement of people and animals) alone and in concert, alter the dynamic interactions between arthropod vectors of zoonotic pathogens and their hosts, including humans. Thanks to molecular biology, new insights into the identification of pathogens in vectors, animals and humans have been acquired in recent decade. For this reason increasing knowledge has also been available on the occurrence of various vector-borne zoonotic pathogens in Hungary.

Tick-borne zoonotic pathogens

Like in other Central and Eastern European countries it has also been speculated in Hungary that a number of causes (e.g. change in land cover and use, reduction in the use of pesticides and the increasing abundance of ticks on wildlife reservoir hosts) have resulted in more contacts between people and infected ticks. The most common tick species associated with pathogen transmission of veterinary and medical importance is the castor bean tick, *Ixodes ricinus*. *Anaplasma phagocytophilum* (formerly known as *Ehrlichia phagocytophila*, *E. equi*, or „HGE“ agent) which is the causative agent of human granulocytic ehrlichiosis (anaplasmosis) have been detected in questing and engorged ticks. This bacterium species was the most prevalent pathogen in a recent nationwide serological survey of some vector-borne infections in 1305 randomly selected, apparently healthy pet dogs. Shepherd, hunting and stray dogs should be also considered as synanthropic reservoirs with maintaining *A. phagocytophilum* close to humans. A few hundred cases of human Lyme borreliosis caused by *Borrelia burgdorferi sensu lato* are diagnosed yearly. Checking the occurrence of these pathogens in vectors several *Borrelia* species (e.g. *B. burgdorferi* ss, *B. afzelii*, *B. garinii*, *B. lusitaniae*, *B. valaisiana*) have been identified in questing *I. ricinus*. *Rickettsia helvetica*, a tick-borne member of the spotted fever group Rickettsiae, is a suspected pathogen in humans causing fever, headache and myalgia, has been detected in several studies. Cats may actually

be a reservoir for *R. helvetica*; however its role in animals has been unknown. *R. monacensis* and *R. slovacica* were also detected in pooled samples of *I. ricinus* collected in an urban recreational area of Hungary indicating the risk of human infections caused by these tick-borne pathogens. Investigation of *Dermacentor marginatus* nymphs revealed the presence of a human pathogen, *Rickettsia massiliae* which can cause spotted-fever in humans with which dogs may also become seropositive and/or infected. *Coxiella burnetii* -- the pathogen of an important zoonotic disease, Q fever – its transmission by tick bite to animals has been proposed, but this is not the most important route of infection for livestock, and it is still disputed in humans. Dogs were reported to play a role in the epidemiology of human Q fever; contact with them represents a risk factor for acquiring the infection. Concerning *C. burnetii* infection of dogs in central-eastern Europe Q fever seroprevalence was first reported from Hungary. *Dermacentor reticulatus* is known to be the most frequent carrier of *Francisella tularensis* in Central Europe. *Haemaphysalis concinna* was also infected with *F. tularensis* ssp. holarctica. This tick species may not serve exclusively as an arthropod vector, but it may also harbour bacteria for 3–4 years and it may also play an important role in the long-term persistence of enzootic foci of tularemia. This study supported earlier findings that fleas should be considered of minor importance in the transmission and maintenance of *F. tularensis*. Recently first evidence of 'Candidatus Neohrlichia mikurensis' a Gram-negative, coccoid bacterium in the family Anaplasmataceae has been found in *I. ricinus* collected from dogs in 37 locations of Hungary. The results indicated three endemic regions along the borders of Hungary reflecting transboundary endemic foci. This pathogen has been isolated several times from diseased humans, justifying its zoonotic nature. Among domestic animals the susceptibility of dogs was demonstrated. The zoonotic *Babesia divergens*, *B. microti* and *B. venatorum* (formerly known as *Babesia* EU-1) known to infect wildlife and domestic animals are present in the country but so far no human cases have been diagnosed. A recent study provided serological evidence of **Crimean-Congo haemorrhagic fever virus** (CCHFV) infection in *Lepus europeus*. Of 198 samples, 12 (6%) were positive for immunoglobulin G antibody against CCHFV.

Mosquito-borne zoonotic pathogens

West-Nile Virus (WNV) has been known to be present in Central Europe for a long time. Seroprevalence in humans was reported in several countries, including Hungary. In late summer 2003, an outbreak of encephalitis emerged in a Hungarian goose flock, resulting in a 14% death rate among 6-week-old geese. Chronologically and geographically related to the outbreak in geese, a serologically confirmed WNV outbreak was also observed in humans, which involved 14 cases of mild encephalitis and meningitis. Later WNV infection with nervous symptoms was detected in many wild bird species, sheep and horses. Between 2003 and 2007, a yearly average of six human cases was diagnosed in Hungary.

Dirofilaria immitis and *D. repens* represent the most important filarial species worldwide because of both their pathogenicity in dogs as well as because of their zoonotic potential. Although the first autochthonous *D. repens* infections of dogs were reported in 1998/1999 the recent nationwide survey shown that *D. repens* infection in both dogs and cats is more common than it was considered in Hungary. This study highlights the possible zoonotic risks for humans living in the regions where the positive animals were found. Every year a few human cases are diagnosed and the worms of this species are removed from the tissues around the eyes or other body parts of patients. Up-to-date the geographical distribution and the prevalence of *D. immitis* have been poorly known in Hungary. The first autochthonous canine heartworm infection was reported a few years ago. Since that time the confirmed cases in dogs have been increasing but no human dirofilariosis by *D. immitis* has been diagnosed in the country.

Flea-borne zoonotic pathogens

Five out of 147 (3.4%) DNA samples of 286 cat fleas originated from Budapest and the countryside were found to be positive to *Bartonella henselae*, the pathogen of the cat scratch disease. In another study 759 fleas (the majority *Archaeopsylla erinacei*) collected from 134 hedgehogs were positive for rickettsiae: in two samples *R. helvetica*, and in 10% of the others a novel rickettsia genotype were identified.

Sandfly-borne zoonotic pathogen

Hungary is regarded as free of leishmaniasis caused by *Leishmania infantum*. Only a few imported cases of dogs and humans have been reported and phlebotomine vectors are rare. First record of autochthonous canine leishmaniasis in Hungary was reported recently.

Conclusion

Based on the recent and ongoing studies it can be stated that several vector-borne pathogens have been detected in domestic and wild animals as well as in blood-sucking arthropods in Hungary. Many of these agents have a significant impact on public health due to the geographic distribution and the increasing activity of their vectors. Therefore further epidemiological surveillance are required to map regional risk of these and other vector-borne pathogens which would be useful for veterinarians as well as for public health authorities concerning the disease agents of zoonotic importance.

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3. MALARIJA U MAĐARSKOJ: NEKAD I SAD

3. MALARIA SITUATION IN HUNGARY: PAST AND NOWADAYS

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Abstract

Malaria was an endemic disease in Hungary for many centuries. The major breakthrough came in 1949 by the organized antimalarial campaign applying DDT for mosquito killing. The drastic reduction of the vectors resulted in the rapid decline of malaria cases. Since 1956, there have not been reported any indigenous case in Hungary. During the period of 1963-2011, there were 217 Hungarians and 302 foreigners who imported malaria to Hungary. Majority of cases (272) were caused by *Plasmodium (P.) falciparum*. Further 247 cases were caused by *P. vivax* and other *P.* species. During that period, 8 fatal cases were reported (*P. falciparum*). Diagnostic tools: microscopic examination of Giemsa stained thin and thick blood film, antigen detection and DNA detection by multiplex semi nested PCR. The expansion of migration (both the increase of the number of foreigners travelling into Hungary and of Hungarians travelling to abroad) favours to the appearance of imported cases.

Key words: malaria, imported, *Plasmodium*, Hungary

Malaria Situation in Hungary till 1962

Malaria had been endemic – sometimes epidemic – in Hungary since many centuries. The organized campaign against the disease, however, started only in 1901 by a ministerial decree of the Home Office ordering a survey on the geographical distribution, on the clinical and epidemiological characteristics of malaria and on the pathological role of mosquitoes. The exact clearing of the epidemiological features of malaria, however, had been done after the year of 1927 by the Department of Parasitology of the newly founded Royal State Institute of Hygiene (1). The notification of malaria was made compulsory by a ministerial decree in 1930. The conditions of laboratory diagnostics (including the determination of different *Plasmodium (P.)* species) have been developed. Species of *Anopheles* were also studied. *Anopheles maculipennis*, *Anopheles messeae*, and *Anopheles atroparvus* proved to be the chief vectors (1, 2). These studies also revealed the endemic areas of malaria in Hungary. There were two endemic foci: one in the North-Eastern, the other in the South-Western area of the country (3). These investigations have also established that about 90 % of the infections were caused in Hungary by *P. vivax*, while *P. falciparum* caused approximately 10 % of infections. Part of this program was the introduction of the free of charge examination of the blood smears of persons suffering from malaria or suspected of infection. Also, instructions were given on the proper application of drugs for the therapy of malaria patients. The drugs were free of charge for patients living in poor conditions. Free of charge medical service was also introduced at the malaria stations established in 1937. The major breakthrough in the campaign against malaria took place in 1949 (4, 5). The DDT solution was applied simultaneously in all buildings of a given settlement. The process was repeated in the following three years throughout the country. The campaign was financed by the Hungarian Ministry of Health and the DDT powders as well as the necessary equipment were presented by the UNICEF. The campaign was extended to the surface of fish breeding lakes, ponds, ditches and other wet surfaces which would serve as a breeding place of mosquito larvae.

In addition, a so called „prolonged” cure was introduced for the treatment of malaria, together with the introduction of the so called anti-relapse treatment. In the anti-relapse treatment, all the patients who suffered from malaria in the previous year were treated in March of the coming year.

The favorable effect of DDT spraying and the so called „prolonged” anti-malarial treatment can be judged from the rapidly decreasing number of indigenous malarial cases in the first half of the fifties. No new indigenous malaria infections were discovered since 1956. Relapses also ceased to occur two years later. The end result was that in 1963 Hungary entered on the Official Register of the WHO to the areas where malaria eradication had been achieved (6).

Imported Malaria in Hungary from 1963

Since 1963, only imported cases of malaria have been registered in Hungary. Between 1963 and 2011, altogether 519 malaria cases have been reported. The major half of the cases was discovered in foreigners entering and importing malaria to Hungary. Thus, during the period of 1963-2011, 302 foreigners, and 217 Hungarians were found as having imported malaria. The analysis of the imported malaria cases in Hungary in the period of 1963-2011 shows that two third (65.2 %) of the foreign patients have arrived from Africa. All the other geographical regions are represented by about one third of the malaria cases. The major half of the cases was caused by *P. falciparum* (57.0 %) while one third by *P. vivax* (34.4 %). More than three quarters of the African cases (77.2 %) have been caused by *P. falciparum*, while *P. vivax* was dominant in all Asian regions such as India, the Far-East, and the Middle-East.

The analysis of the malaria cases imported by Hungarian citizens returning from abroad shows that the major half (59.9 %) of the Hungarian patients with imported malaria had been infected in Africa, in the Middle-East (19.8 %) and 20.3 % of the cases were acquired in the Far-East, India, and South-America, respectively. Infection with *P. falciparum* and *P. vivax* was almost equal (46,1%/45,6%) in the Hungarian cases. Most of the infections acquired in Africa (71.9 %) were caused by *P. falciparum* and the cases acquired in other geographical areas are dominated by *P. vivax* infections. *P. knowlesi* was not diagnosed in Hungary. Seven fatal cases of malaria infections have occurred among the Hungarian patients in this period. All these patients returned from Africa and all the infections were caused by *P. falciparum* (7, 8, 9, 10, unpublished data).

The total eradication of indigenous malaria cases in Hungary was not followed by a drastic decrease of imported malaria cases. This can be explained by the rapid increase of travellers. However, if we compare the number of travellers to the number of imported malaria cases in Hungary, we cannot find a direct correlation. General tendency for the constant rise of the number of malaria cases cannot be observed, in contrast to the constant increase of the number of migrations (10).

Prevention of Re-Emerging Malaria in Hungary

The principles of malaria prevention in Hungary are realized through the activity of International Vaccination Stations (National Center for Epidemiology in Budapest and in 13 Regional Institute of State Public Health Service of the counties, and further licensed 20 International Vaccination Stations in capital and throughout the country. Their main task is performing vaccination of those travellers who travel to endemic regions. In addition to that activity, they inform the travellers about the danger of malaria, the importance of malaria prevention, the principles of protection, about the possibilities of antimalarial drug therapy and the proper use of anti-mosquito personal repellents (10).

The fast preliminary laboratory and final clinical diagnosis and treatment of malaria usually do the Szent László Hospital (Budapest, Hungary). Final laboratory investigation and confirmation are performed at the Department of Parasitology, National Center for Epidemiology (Budapest). Methods used: microscopic examination of the Giemsa stained thick and thin blood film, detection of *Plasmodium* antigen in blood (NOW Malaria, Binax, immunochromatographic test), *Plasmodium* species-specific multiplex semi nested PCR. In 2011 from 91 samples of 58 person 130 examinations have been done (microscopic 75, antigen detection 39, PCR 16). Ten malaria cases have been confirmed. All these measures have been ordered and regulated by a decree of the Ministry of Health (18/1998 (VI. 3.) NM). Mosquito eradication is especially important in the most frequented areas of touristic traffic, such as the Lake Balaton and some other touristic frequented regions, as well as at the international airports.

Discussion and conclusion

The last indigenous case of malaria occurred in Hungary in 1955. A considerable number of imported malaria cases has occurred, however, in every year till now. Therefore, the particular attention is required in all imported malaria cases to prevent re-emerging of malaria. Potentially, the parasites are still present in the organism of the patients with imported malaria and there are different species of *Anopheles maculipennis* in Hungary capable to transfer *Plasmodium* to humans. There are very striking instance of some European countries in last decade. However, the total number of reported malaria cases in the European Region decreased from 33 365 in 9 countries in 2000 to just 226 in 5 countries in 2011. Only 69 of the 226 malaria cases were indigenous. In Greece, which has remained malaria-free since 1974, reported 3 locally acquired *P. vivax* cases in 2010 and 40 in 2011, originating primarily from migrant workers from Pakistan. Most of the 40 cases were clustered in the prefecture of Lakonia in the south of mainland Greece, posing a risk of re-establishment of malaria in the country (11).

Countries have to direct particular attention to the risk of malaria spreading among nations in the Region, and between the European and Eastern Mediterranean Regions. The expansion of migration (both the increase of the number of foreigners travelling into Hungary and of Hungarians travelling to abroad) favours to the appearance of imported cases.

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4. LAJŠMANIOZA/HIV KOINFEKCIJA: EPIDEMIOLOŠKE I IMUNESKE KARAKTERISTIKE

4. VISCERAL LEISHMANIOSIS AND HUMAN IMMUNODEFICIENCY VIRUS COINFECTION: EPIDEMIOLOGICAL AND IMMUNE CHARACTERISTICS

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Abstract

The spread and overlap of both leishmaniasis and HIV infections make visceral leishmaniasis (VL) - HIV coinfection a serious worldwide concern. Recently, Serbia was added to the long list of countries with VL/HIV coinfection. In this review discuss the relevance of T helper1/T helper 2 paradigm, adding new data to the acknowledged plasticity in T helper cell function. The most relevant cytokines and host pathogen interactions were also presented as well as complex collaboration between HIV infection and leishmaniasis. Finally immunodiagnostic characteristics and some clinical issues of Leishmania/HIV coinfection were discussed.

Key words: Visceral leishmaniasis, HIV, coinfection, T helper, IL-10

Introduction

Leishmaniasis is one of the most neglected diseases as recognized in the resolution of the 60th World Health Assembly. The HIV/AIDS pandemic has modified the natural history of this opportunistic parasitosis. Visceral leishmaniasis (VL) has emerged as the most common form of parasitosis associated with HIV infection. This was documented by the reports mainly from Europe, where 94% of patients with Leishmania - HIV coinfection suffered from VL, and only 4% had cutaneous leishmaniasis (CL) (WHO 2000). In East Africa and the Indian subcontinent, VL is the commonest form, but exact data are lacking. For this reason the focus of this paper is going to be limited on epidemiological and immunological characteristics of VL/HIV coinfection.

Epidemiology of Visceral Leishmaniasis/HIV

The first report of HIV and VL coinfection appeared in 1985 and since then the number of cases has increased rapidly in southern Europe. Of the first 1700 cases of coinfection reported to the WHO by 1998, 1440 were from southwestern Europe (Guerin et al., 2002). As for the other continents, most coinfections reported in the Americas are from Brazil. In Africa, the number of cases is expected to rise and it is further impaired by social adversities such as mass migration, displacement, civil unrest, and war. In Asia, coinfections are increasingly being reported from India, Bangladesh and Nepal (Sundar, 2001, Sundar et al., 2002).

A recent study (del Giudice et al., 2002) revealed that the incidence of VL in HIV-infected patients decreased from 11.6 + 1.2 per 10 000 persons in the years before 1996 to 6.3 + 0.7 per 10 000 persons after 1996, the year when highly active antiretroviral therapy (HAART) was initiated in France. Similar data have been reported from Spain (de La Rosa et al., 2002). However, at present the benefits of HAART are only available to 5% or less of HIV-infected

patients in the world, so a decrease in this coinfection can be expected only in developing countries (UNAIDS:AIDS Epidemic Update 2002. www.unaids.org).

The first autochthonous cases of VL in Serbia were recorded in 1945 in Niš and the Dobrič district, and this was where the patient was resident (Simić, 1957). Moreover, in the period from 1946 to 1948 in the territory of southern, eastern and western Serbia, more than 350 cases of kala-azar (VL) were recorded (Simić, 1957). The studies performed at that time established that the type of kala-azar was similar to that observed in the Mediterranean basin.

Epidemiologic data show that in the period from 1991 to 2000 there were 39 cases of VL reported in Serbia and Montenegro, with only one case of imported leishmaniasis (Dakić et al., 2009). A recent retrospective epidemiologic and diagnostic study of VL in Serbia for the period 2001-2007 has demonstrated a visit to the Montenegrin coast to be a predominant risk factor in the 22 individuals diagnosed with VL, apart from one case of VL that occurred in southern Serbia and which probably represented a dormant focus of infection (Dakić et al., 2009).

The first case of VL/HIV coinfection in south-eastern Serbia has been recently reported (Marjanović et al., 2012). Based on the patients travel history to Iraq and the type of leishmania, authors suggested that the parasitosis was imported, but autochthonous origin could not be excluded.

As for the reservoirs of infection, the presence of *Leishmania spp.* was proven in dogs (most commonly in asymptomatic infection) in each region where kala-azar was identified in humans. The studies performed in Niš in 1955 showed that over 2% of dogs in the area had an asymptomatic infection (Simić, 1957). Rare autochthonous cases were reported in the Niš municipality in 1968 and 1969 when the presence of vectors, such as *Phlebotomus major* (*P. major*), *P. simici* and *P. perfiliewi*, was also reported (Petrović, 1980).

Immunological perspectives of Leishmaniasis

Neutrophils were identified as the first cells to be infected by the leishmania (Petres NC et al., 2008). The mechanisms by which leishmania promastigotes evade killing by neutrophils may be related to their ability to block the oxidative burst and to enter a nonlytic compartment unable to fuse with lysosomes (Gabriele C et al., 2010). Parasites frequently target apoptotic neutrophils that are normally easily cleared without triggering activation of macrophages, leading to their silent entry into the macrophage and intracellular survival. Macrophages are considered the main reservoir of the metacyclic leishmania promastigotes. Further macrophage inhibition by parasite is established through interfering IL-12 production, down regulation of Major Histocompatibility Complex class II expression, and promotion of immunosuppressive cytokine production such as IL-10 and TGF β . Using the same strategy, leishmania successfully manipulates dendritic cells (DC), leading to avoidance or block of their function (Alexander et al., 2012).

Lack of IL-12 production caused by *Leishmania donovani* (*L. donovani*) is considered the main cause of maturation block of DC in human cells and abortion of immune response in its very beginning.

Excess of IL-10 was associated with delayed healing and disease progression (Nylen et al., 2007). Elevated levels of IL-10 were found in human VL in spleen, bone marrow, lymph nodes and in systemic circulation. Recent study has suggested strong correlation between parasite burdens in post kala-azar dermal Leishmaniasis nodules and IL-10 and the levels of FOXP3⁺ cells (Katara et al., 2011). Therefore, inducible and natural FOXP3⁺ T regulatory cells and adoptive FOXP3⁻ adoptive cells were considered a potential source of IL-10, and

could they could be both found in different experimental models as well as in lesions of humans (Katara et al., 2011).

Immunosuppressive properties of IL-10 on macrophages may be detrimental, rendering them unresponsive to activating cytokines and leading towards limitation of collateral tissue damage. The same cytokine is responsible for impaired DC migration into T cell areas and defective T cell priming (Nylen et al., 2007) (Shmidt et al., 2012).

The relevance of T helper1/T helper2 paradigm

Owing to *L. major* experiments in 1980s, two distinct apparently counter regulatory CD4⁺ T cell populations, T helper 1 (Th1) and T helper 2 (Th2) were identified. Th1 cells were found to control resistance while Th2 mediated susceptibility to leishmania infection. Furthermore, Th1/Th2 paradigm became widely accepted in other disease models and clinical situations.

It is well established that protective immune response against both cutaneous leishmaniosis caused by *L. major*, *L. mexicana* or *L. amazonensis*, as well as visceral leishmaniosis caused by *L. donovani* or *L. infantum* is dependent on Th1 immunity (MacMahon-Prett and Alexander, 2004). Antigen presenting cells produce IL-12, which in turn, drives the proliferation and differentiation of Th1 cells able to produce IFN γ . Macrophages activated by IFN γ produce nitric oxides able to efficiently eliminate parasites (Alexander J et al., 2012).

On the other hand, Th2 cells were originally considered responsible for development of non favorable form of disease. Recent general consensus of opinion is that Th2 response does not contribute adversely to the immunological control of visceral leishmaniosis. Furthermore, it was found that IL-4 and IL-13 generated from Th2 cells need not necessarily counter-regulate type-1 response, but can promote, facilitate or even drive Th1 response (Alexander J et al., 2012).

The more recent characterization of CD4⁺ T cell regulatory populations and further effector CD4⁺ T helper populations, Th17, Th9, and T follicular T(f)h cells as well as the acknowledged plasticity in T helper cell function has further added to the complexity of host pathogen interactions (Alexander J et al., 2012).

The role of Th17 in Leishmaniosis remains unclear and both disease promoting and protective responses have been attributed to their influence. In humans was demonstrated a therapeutic role for Th17 cells as IL-17 and IL-22 have been strongly correlated with protection against visceral leishmaniosis (Pita et al., 2009).

Studies examining the role of Th9 and IL-9 during leishmaniosis are limited and have only involved *L. major*. It seems that Th9 produce both IL-9 and IL-10 and have been associated with unfavorable form of disease (Alexander J et al., 2012).

Follicular T helper cells are specialized for B cell help. Consequently if B cells and or specific antibody production play a significant role in the disease process T(f)h cells would comprise a significant population in determining disease outcome.

B cells and antibodies in Leishmaniasis

The role of B cells (as APCs or regulatory cells) and/or antibody in contributing to susceptibility to leishmania infection appears to depend in large part upon the parasite species examined but also probably to a significant extent upon the host.

B cells and antibodies are generally not considered to be of major importance in protective immunity against leishmania. Antibodies are not effective at killing the parasite as it hides inside the parasitophorous vacuole. High levels of leishmania specific antibodies are observed in patients with VL and other severe forms of leishmanial disease and there is accumulating evidence that B cells and antibodies correlate with pathology. Passive transfer experiments indicated that antibodies, IgM and IgG, induced as a result of parasite induced polyclonal B cell activation promoted parasite growth (Nylen S et al., 2010).

Immunopathological features of leishmaniasis/HIV coinfection

From an immunological perspective the two agents ability to escape and manipulate the immune response seem to a large extent work in synergy. It is thought that the parasitic infection found concurrently with HIV induces chronic immune activation and therefore an increased HIV load and accelerated progression of AIDS (Alvar et al., 2008), whereas immunological disturbances caused by HIV are particularly favorable for the uncontrolled multiplication of the parasite (Alvar et al., 2008).

Experimental studies have demonstrated increased expression of CCR5 chemokine receptor in Leishmania infection. This molecule represents a major coreceptor for HIV entry into target cells (Nigro et al., 2007).

Peripheral blood monocytes infected with HIV-1 virus had decreased production of IL-12 and IFN γ , while IL-10 and IL-4 production was increased, in response to leishmania in patients with VL/HIV. The Th1/Th2 balance was altered, resulting in increased Th2 cytokine responses creating a milieu that supports replication of the Leishmania parasites in patients with VL/HIV coinfection (Wolday D, 2000).

Immuno-diagnostic and clinical implications of VL/HIV coinfection

HIV/AIDS has showed to slow down diagnosis of VL, as antibody based tests may not be indicative of disease in AIDS patients. This makes both serological and delayed type IV hypersensitivity - based tests of limited use in coinfecting patients. Only about 40-50% of HIV/Leishmania coinfecting patients have a positive Leishmania serology (Montalban et al., 1990, Gari-Toussaint et al., 1994). In fact, anti-Leishmania antibodies in AIDS patients are 50 times lower than in those with an intact immune system (Mary et al., 1992). Therefore, using serological methods many false-negative results should be expected in HIV-infected individuals. Ideally, at least two different serological tests should be used for each patient, and the leishmanial antigens employed should be freshly prepared, to increase their sensitivity (Desjeux et al., 2003).

Polymerase chain reaction (PCR) revolutionized the possibility of diagnosing the etiologic agents of infectious diseases. In the past decade, PCR-based techniques have been progressively more applied to diagnosis leishmaniasis, but its use is, to date, limited to tertiary health centers. To avoid invasive procedures, peripheral blood is often used, and the reported sensitivity of PCR on blood ranges from 70% to 96% (Takagi et al., 2009).

Clinical manifestations of leishmaniasis and leishmania - HIV coinfection depend on both the infecting species of leishmania and the cell-mediated immune response of the host. The first episode of VL in HIV infection develops when CD4⁺ cell count falls below 200 cells/ μ l. HIV patients have reduced likelihood of a therapeutic response, and greatly increased probability

of relapse (Lopez - Velez et al., 1998). Several predictive factors of VL relapse were identified: absence of an increase in CD4+ cells at follow-up; b) lack of secondary prophylaxis; and c) previous history of VL relapse. CD4+ counts below 100 cells/mL at the time of primary VL diagnosis (Cotta F G et al., 2011). Relapse rate increase to 60% within 6-9 months posttreatment if a patient does not receive HAART (Lopez-Velez R., 2003).

Conclusion

VL/HIV coinfection has important clinical, diagnostic and epidemiological implications. Its immunopathogenesis is complex, with high degree of plasticity between effector cells and T cell population.

In view of the growing epidemiologic problem of VL spread and especially VL/HIV coinfection, the surveillance of leishmaniasis is imperative, both in human and dog populations in Serbia, paying special attention to the southern regions of the country.

In VL/HIV coinfection, the failure of serological tests is to be expected and, apart from being an easy and non-invasive diagnostic approach, the application of molecular diagnostics to the blood may give a warning about the risk of possible nosocomial infections.

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5. HUMANA BABEZIOZA: EPIDEMIOLOŠKI I DIJAGNOSTIČKI ASPEKT 5. HUMAN BABESIOSIS: EPIDEMIOLOGIC AND DIAGNOSTIC ASPECT

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Abstract

Human babesiosis is a parasitosis caused by protozoas of the *Babesia* genus. Since the first descriptions of the disease in animals and documented human infections in 1957, we may today speak of a cosmopolitan distribution of the parasitosis and endemic areas of the infection, which is nowadays a significant health issue in both human and veterinary medicine. Numerous factors have influenced a changed epidemiologic pattern of tick-borne diseases. The infection is transmitted by numerous tick species and via blood transfusions as well. Most cases of human babesiosis have been encountered in the USA, caused by *Babesia microti* (*B. microti*), while in Europe *B. divergens* is a predominant species. Together with clinical manifestations of the disease, information about a tick bite, and stay in an area endemic for babesiosis, it is necessary to exclude human infection caused by babesia. In addition to conventional diagnostic approaches, molecular methods are today in use as well to diagnose human babesiosis.

Key words: babesiosis, epidemiology, diagnosis

Introduction

Babesiosis is a parasitic infection caused by protozoa of the *Babesia* genus. The first description of intraerythrocytic microorganisms leading to febrile hemoglobinuria in cows was given by Victor Babes as early as 1888, and the family and genus were named after him (1, 2). Not long after that, tick was identified as a carrier of *Babesia bigemina* (*B. bigemina*) (3). In the 1950s, long time after the description of this parasitic disease in animals, the first case of human babesiosis was recorded in a cattle farmer who had his spleen removed (4). After these discoveries, it was thought that it was a sporadic parasitosis in humans, most commonly in immunocompromised individuals. However, new cases of human babesiosis were later identified even in immunocompetent individuals (5).

Nowadays, we may speak of a cosmopolitan distribution of this parasitosis, which is a significant epidemiologic, diagnostic, and therapeutic problem both in human and in veterinary medicine. The infection is transmitted by various types of ticks, but also by blood transfusions. In many parts of the world, the reporting of human babesiosis is mandatory, in view of a growing health risk associated with this parasitosis (6). A significant risk for the transmission of this infection among humans are asymptomatic carriers of human babesiosis. This is especially the case with asymptomatic blood donors in the USA, where babesia is the most common infectious agent transmitted via blood of the infected (7).

Taxonomy and biology of the parasite

Babesias belong to the Apicomplexa phylum, Piroplasma class, Piroplasmida order, containing the families of Babesiidae and Theileriidae, i.e. the genera of *Babesia* and

Theileria (8), termed piroplasms because of the piriform (pear-like) shape in the erythrocytes of vertebrates (9).

Over 100 species of the Babesia genus infect various vertebrate species. Most common causes of human infections are *B. microti*, *B. duncani*, *B. divergens* and *B. venatorum* (10).

Present day methods of molecular biology have made possible for us to discover new babesia species based on their genetic kinship and genome size (2). *Babesia spp.* infecting humans are divided into four groups: the first, *B. microti* complex of small babesias (<3 µm), including all human isolates comprising a subgroup (11, 12); the second, involving also small babesias *B. duncani* and *B. duncani*-type organisms, phylogenetically different from the first group and involving the parasites of dogs and wild game in the western USA (13, 14); the third, involving *B. divergens* (a bovine parasite) and *B. venatorum* (earlier term EU1, infesting roe deer), small babesias phylogenetically closer to large babesias (>3 µm) (15, 16); the fourth group of large babesias, infesting the ungulates, involving the KO1 strain as well (a new babesia agent has been identified in South Korea) (14, 17).

The development of babesia takes place in different species of mammals, as well as in ticks. Within the Ixodidae family, at least six genera are the vectors of babesia, in both natural and experimental conditions. It has been established that there are babesia types with different vectors. A vector can be infested with different babesias, and *B. microti* infests only the ticks the genus of Ixodes (2, 18), and most commonly *Ixodes scapularis* (*I. scapularis*, termed *I. dammini* in the past) (19), which feeds on the host blood in all phases of its life cycle (larva, nymph, adult). In most cases, human infection with *B. microti* is the result of exposure to tick nymphs in the period from late spring and throughout summer (20).

The life cycle of babesia begins in the tick gut (gamagony), continues in the salivary glands (sporogony, asexual multiplication), and then in vertebrate erythrocytes (merogony/schizogony, asexual multiplication) (2). After a bloodmeal on an infected host (a vertebrate), the tick ingests *Babesia spp.* and after several days a zygote/ookinete is formed in the digestive tract, which travels to the salivary glands. From a sporocyst, numerous sporozoites of *Babesia spp.* are produced, which enter the bloodstream of a vertebrate/mammal with a new bloodmeal of the tick (21).

Tick transmission can be transovarial as well, with ookinete reaching various organs (ovaries included) via the tick hemolymph; this provides survival of the tick as a vector through several generations, i.e. enables endemic parasite maintenance (22).

Sporozoites, when present in the vertebrate bloodstream, attack erythrocytes (in some species there is a pre-erythrocytic phase, when lymphocytes are attacked); merozoites are produced, and after a binary division trophozoites appear (in the form of a Maltese cross). The release of merozoites is associated with hemoglobinuria as the result of erythrocyte lysis. Moreover, some trophozoites develop into gametocytes – the infective forms for the vectors (ticks) (2, 21).

Epidemiology of babesioses

A multitude of factors, especially climatic changes, host migration, changes in the distribution of vectors and population, altered practices in cattle farming, have had an impact on the changes of epidemiology of tick-borne diseases, babesiosis included (23).

Since the reporting of the first case of human babesiosis in 1957 (4), and sporadic reports afterwards, we may now speak of endemic areas of this infection (24).

Most cases of human babesiosis have been reported in the USA (Northeast and Upper Midwest), and the causative agent is *B. microti* (24), most commonly transmitted by blood

transfusion (25); next, the Pacific coast, from northern California to the state of Washington, where a small number of cases have been reported, caused by *B. duncani* and *B. duncani*-type organisms (14, 26), while the infection caused by *B. divergens*-type organisms has been sporadically reported in certain parts of the USA (27).

In Europe, *B. divergens* has been predominant, but sporadic cases of human babesiosis caused by *B. venatorum* and *B. microti* have been reported as well (15, 16). A high incidence of bovine babesiosis in Europe caused by *B. divergens* correlates with human babesiosis in individuals who are in everyday contact with cattle, i.e. the infection vectors (21). Sporadic cases have been reported in France, Britain, Ireland, Spain, Sweden, Russia, and former Yugoslavia (10, 18, 21). In Austria, Germany, and Italy there have been reports of infection caused by *B. venatorum* (16, 28), as well as one case of *B. microti* infection in Germany (29).

B. microti-type organisms have caused disease in Japan and Taiwan, while in the south of Korea the KO1 strain has been identified (15, 17). In Africa, Australia, and South America sporadic cases of human babesiosis have been reported too (13, 30, 31).

The range of prevalence of *Babesia spp.* has been different in different types of ticks (18, 32). In Europe, *Ixodes ricinus* is the vector of *B. divergens*, *B. divergens*-type species, *B. microti*, *B. bovis*, and *B. venatorum* (EU1) (33-37); *Dermacentor reticularis* (*D. reticularis*) transmits *B. canis* (38); *Haemophysalis punctata* is the vector of *B. major* and *B. Motasi*; *Rhipicephalus sanguineus* (*R. sanguineus*) carries *B. gibsoni* and *B. canis*, *Hyalomma marginatum marginatum* transmits *B. caballi* (37), and *Ixodes hexagonus* is a suspect vector of *B. microti*-type agent, also known as *Theileria annae* (39).

In the studies based on the polymerase-chain-reaction (PCR) detection of DNA of *Babesia spp.*, different prevalence of babesia has been established in different mammalian hosts. In Slovenia, the Babesia EU1 prevalence of up to 30% in roe deer (*Capreolus capreolus*) suggests that this species is a possible reservoir (40); in Poland, the prevalence of *B. microti* in rodents ranges from 11.90% to 35% (41), while in Greece 15% of analyzed goats and sheep have been infected with *B. ovis* (42).

Based on the clinical, microscopic, and molecular studies in the neighbouring countries, the prevalence of different types of Babesia has been established (38, 43-46). The studies in Slovenia have shown babesial infection in 5.90% of analyzed dogs (43). In Croatia, *B. canis canis*, *B. gibsoni*, *B. canis vogeli*, and *Theileria annae* have been identified in Babesia-positive asymptomatic dogs (44). In Hungary, molecular analysis of blood samples taken from dogs with clinical signs of babesiosis has demonstrated the presence of *Babesia spp.* DNA in 88.60% of cases (45). Similar studies have been carried out in Romania (38) and Albania, where molecular methods have demonstrated *B. canis* DNA positivity in 23% of clinically healthy dogs, with slightly lower prevalence (13%) obtained using the indirect immunofluorescence assay (IFA) (46).

In other parts of Europe, e.g. in Portugal, the presence of *B. canis* has been demonstrated in clinically suspect dogs by bloodsmear microscopy (and confirmed positive by PCR) (47), while in Poland 90.80% of naturally infected dogs have been PCR-positive for *B. canis canis* (48).

In our country, using the methods of conventional microscopy, studies have indicated the presence of *B. canis* in pet dogs and ticks collected from these dogs (32). Babesiae have been detected in *R. sanguineus*, *D. marginatus*, and *D. reticulatus* ticks, with a prevalence of 66.10%, 18.70%, and 46.40%, respectively (49, 50).

Our studies are currently in progress, and the preliminary, unpublished results have shown that by using molecular methods of examination of the blood samples from asymptomatic dogs in two different regions in Serbia, different ranges of prevalence of babesiosis in dogs have been obtained, as well as different *Babesia spp.* genotypes.

Clinical manifestations and treatment

Clinical manifestations of the infection depend on the species of mammals and its resistance, as well as on the virulence of the species. In animals, both domestic and wild, hemoglobinuric fever is the principal element of the clinical picture, occurring due to the damage and decomposition of erythrocytes. Asymptomatic cases of infection have been reported too, detected mostly based on serologic screening analyses to *Babesia spp.* (10).

In human babesiosis, during the incubation period of 1 to 4 weeks (in some individuals even up to a year) general malaise and fatigue is present. The disease occurs abruptly, with hemoglobinuria as one of the first signs. Later on, nonspecific symptoms appear, as well as the disease signs resembling those in malaria: jaundice (due to significant erythrocyte hemolysis), accompanied by irregular high temperature (40-41°C), fever, intense sweating, headache, muscle pain, lumbar and abdominal pain. Diarrhea and vomiting may occur as well. Total hemoglobin values are very low (from 70 g/l to 80 g/l, with reported value of even 40 g/l), haptoglobin is markedly reduced, and all biologic tests of hemolysis are positive. The liver is usually slightly enlarged and tender. In most severe cases the patients have shock-like symptoms, and due to intravascular hemolysis renal insufficiency and lung edema may develop, leading to fatal outcome (2, 3, 28).

The disease usually lasts up to two weeks, but the recovery, accompanied by fatigue, may last for months. Asymptomatic parasitemia may last for months even after therapy, or it may linger for years in absence of any treatment. In immunocompromised patients relapses are possible in spite of appropriate therapy.

A quarter of immunocompetent adults and half of children infected with *B. microti* do not have symptoms, or the infection is mild and with good outcome (51). Severe disease forms occur in immunocompromised patients (those with splenectomy, cancers, HIV infection, hemoglobinopathies, chronic diseases of the heart, lungs, liver) (2, 3, 28). High risk patients are the newborns, those over 50 years of age, patients on immunosuppressive therapy, individuals with organ transplants, as well as those receiving anticytokine therapy. After blood transfusions from asymptomatic blood donors, the blood receiver has reportedly been infected, with an intact spleen and fatal outcome as the consequence of disseminated intravascular coagulopathy (DIC) (52). Complications (acute respiratory distress syndrome, disseminated intravascular coagulopathy, congestive heart failure, coma, liver failure, renal failure, splenic rupture) occur in half of the hospitalized patients with babesiosis, with the mortality rate of 6-9%, reaching even 21% in immunocompromised patients (52, 53, 54). The reported cases of infection with *B. duncani* and *B-duncani*-type organisms have been mostly asymptomatic, but fatal outcomes have been reported as well (13, 26, 55). Severe clinical manifestations of babesiosis have been observed in those infected with *B. divergens*. Aggressive therapeutic approaches (combination of antimicrobial agents and exchange transfusion) can contribute to the reduction of mortality rates (30, 56).

The drug of choice in the treatment of *B. microti* infection is the combination of clindamycin and quinine (57). Most recent studies have shown that minor adverse effects and improved effectiveness are associated with the combination of atovaquone and azithromycin. Such a treatment is recommended for severe cases, but also for those with moderate or mild disease in order to prevent transmission by blood donation and to avoid the development of more serious forms of babesiosis (58, 59).

In most cases, symptoms withdraw after 24h to 48h, and infection itself withdraws in the period of three months after therapy. In severe cases, everyday monitoring of the level of parasitemia (<5%) and clinical status is mandatory. In immunocompromised patients, in addition to standard 7-10 days' therapy, the treatment should be continued in the following six weeks (3).

Chloroquine, probably due to its antiinflammatory action, provides the alleviation of symptoms in most cases of babesiosis; however, it does not affect the level of parasitemia nor its duration.

The combination of pentamidine and trimetoprim-sulfomethoxazole has shown effectiveness in *B. divergens* infected individuals. In those with serious clinical picture and high parasitemia transfusions and dialysis are mandatory (3).

Diagnosis of human babesiosis

In the presence of clinical signs and history of tick bite, differential diagnosis should exclude babesial infection. Nearly 10% of patients with Lyme disease in the southern New England have had accompanying babesial infection in the regions where both infections are present in animals. *Ix. scapularis* is a vector of human babesiosis, and also of *Borrelia burgdorferi*, the causative agent of Lyme disease. In severe cases of Lyme disease or poor therapeutic response of the affected, it is necessary to exclude the infection with *Babesia spp.* In those with inexplicable febrile status, who have travelled or stayed in the regions endemic for babesiosis in the previous two months and/or received blood transfusion in the previous six months, it is also necessary to exclude the infection with *Babesia spp.* (2, 3, 10, 24).

The diagnosis of human infection is made based on the identification of intraerythrocytic parasites in bloodsmears using the Giemsa or Wright staining (21, 30). Trophozoites are most commonly identified in the erythrocytes in the form of little purple rings with light blue cytoplasm, although there are numerous variations in the appearance of the parasite (single or paired rings, most commonly pear-shaped; Maltese cross-shaped tetrads are pathognomonic, but are rarely encountered) (2, 10, 18, 21, 24). Parasitemia is usually low (1-10%), but values exceeding 80% have also been reported (2, 3, 24).

If the parasitemia is low, i.e. microscopy is negative for Babesia, a biological test can be employed. Hamsters are sensitive lab animals in that regard and can be infected by intraperitoneal inoculation with the patient's material. Parasitemia can be established 2-4 weeks of inoculation (60).

Serologic diagnosis of babesiosis is used in chronic infections. A standard test to detect babesial antibodies is the IFA, utilizing the hamster-obtained antigens of *B. microti* (18). In acute phases of the disease, the titer of IgG antibodies usually exceeds 1:1024, with values declining in the following 8-12 months (lit). It is possible that the titer of IgG antibodies is maintained for as long as 6 years in individuals with persistent infection. The presence of IgM antibodies is an indicant of recent infection (61). The results of serologic analyses can be false positive due to cross-reactivity with other protozoal infections and in connective tissue diseases, and in immunocompromised individuals false negative results may also be obtained (21). With *B. divergens* infection the disease appears very quickly, so that antibodies appear rather late (10). In this infection, the results can be false positive due to cross-reactivity with *B. divergens*-like organisms or with *B. venatorum* (10).

An immunoblot assay for detection of *B. microti* is also available. Assays for *B. microti* antibody do not detect *B. duncani*, *B. divergens*, or *B. venatorum* antibodies (3).

Out of the methods of molecular biology, PCR is usually used, as a sensitive and specific method for babesial DNA detection in the blood and for identification of the *Babesia* species (3). PCR is of huge importance in the diagnosis of babesiosis, especially in the presence of a suggestive patient history and clinical manifestations of the disease, and with negative microscopic findings in the blood and negative serology. The use of PCR in the diagnosis of babesiosis requires appropriately trained staff and well equipped laboratories that are able to fulfill the highest standards.

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II USMENE PREZENTACIJE II ORAL PRESENTATIONS

1. KRPELJNI ENCEFALITIS I LAJMSKA BOLEST U MAĐARSKOJ – EPIDEMIOLOŠKA SITUACIJA IZMEĐU 1998 I 2008. GODINE

1. TICK-BORNE ENCEPHALITIS AND LYME DISEASE IN HUNGARY – THE EPIDEMIOLOGICAL SITUATION BETWEEN 1998 AND 2008

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Diagnosed cases of tick-borne encephalitis (TBE) and Lyme disease (LD) have been reportable infectious diseases in Hungary since 1977 and 1998 respectively. Clinically diagnosed cases have been registered in the National Database of Epidemiological Surveillance System (NDESS).

All reported TBE cases are confirmed by laboratory serological and, if necessary, PCR tests, whereas the registered cases of LD are mainly based on the appearance of erythema chronicum migrans in concurrence of possible exposure of tick bite. Our work is the first comparative epidemiological and geographical information analysis of these two diseases together.

The following demographic data from each individual case (703 TBE and 13 606 LD) recorded in NDESS were used: sex, age, the starting date and place of the onset of disease, and a short report from the affected person. The descriptive epidemiological analysis of the incidence was carried out using directly standardized rates and smoothed indirectly standardized incidence ratios calculated by empirical Bayesian methods at municipality level, using RIF.

The average yearly incidence rate of TBE was 0.64 per 100,000 inhabitants (range 0.46 to 0.84) and of LD was 12.37 per 100,000 inhabitants (range 9.9 to 18.1), with the highest incidence rates in 1998 for TBE and 2008 for LD. The most affected age groups were men between 15-59 year of age for TBE, and women between 45-64 year of age for LD.

Seasonality, based on the starting date of the illness, was also characterized.

Extended areas of high-risk were identified in western and northern Hungary, illustrated on high (municipality level) resolution maps.

Based on our analysis it is a possible to associate areas and periods of high-risk with characteristics (sex, age, residence) of groups most affected by tick-borne diseases in Hungary.

Key words: tick-borne encephalitis, Lyme disease, epidemiology, Hungary

2. ULOGA BRZOG ANTIGENSKOG TESTA U DIJAGNOSTICI *PLASMODIUM FALCIPARUM* MALARIJE

2. THE ROLE OF RAPID ANTIGENIC TEST FOR DIAGNOSIS OF *PLASMODIUM FALCIPARUM* MALARIA

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Objectives: Comparison of the findings of the rapid diagnostic test (RDT) and microscopic examination of Giemsa-stained thick and thin smears in diagnosis *Plasmodium falciparum* malaria.

Materials and Methods: A retrospective study was carried out from July 2010 to May 2013 and included 97 returnees from malaria areas who diagnosed in Parasitological Laboratory, Clinical Center of Serbia. For all of them standard microscopic examination of blood smear stained by Giemsa and rapid diagnostic test (RDT) was performed, comparatively. RDT for detection of HRP2 antigen of *P. falciparum* was performed according to the recommendations of the manufacturer (Visitect Malaria Pf-Omega Diagnostics LTD).

Results: Malaria was diagnosed in 45 patients: 42 with microscopic confirmation and 3 without microscopic confirmation who started antimalarial therapy before testing. RDT was positive in 35 patients: 29 with microscopic confirmation of *P. falciparum* malaria, 3 without microscopic confirmation who started therapy and 3 patients treated for *falciparum* malaria shortly before arrival in Serbia. Test was negative in all 12 patients who had another *Plasmodium* species. The sensitivity and negative predictive value of RDT were 100%, specificity 95,4% and positive predictive value 91,4%.

Conclusion: Rapid diagnostic test showed excellent performances for initial diagnosis of *falciparum* malaria.

Key words: malaria, diagnosis, *Plasmodium falciparum*, rapid diagnostic test

3. MOLEKULARNA PROUČAVANJA EHINOKOKOZE I HIDATIDOZE DOMAĆIH I DIVLJIH ŽIVOTINJA

3. MOLECULAR INVESTIGATIONS OF ECHINOCOCCOSIS AND HYDATIDOSIS IN DOMESTIC AND WILD ANIMALS

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Echinococcosis is a zoonotic disease caused by *Echinococcus* spp. tapeworms. The definitive hosts, which include dogs, cats, and other canids carry the adult tapeworms subclinically. Hydatid disease/hydatidosis is caused by metacestode stage of parasites and this is the most important disease in people and many domestic and wild animals. Dogs are particularly important in zoonotic transmission due to their close relationships with humans. Echinococcosis/hydatidosis is a major public health problem in some countries, and very serious economic problem in animal production.

E. granulosus complex has been divided into strains, named G1 to G10. Some of these strains has zoonotic importance (the G1 - sheep strain, G2 - Tasmanian sheep strain, G3 - buffalo strain, G5 - cattle strain, G6 - camel strain, G7 - pig strain, G8 - cervid strains). The G9 strain has reported only from human cases in Poland, and it may be a variant of the pig strain (G7).

The some strains of parasites (G1, G1BC, G2 and G3) grouped together in the species *Echinococcus granulosus sensu stricto*. Other species: *E. equinus* (G4), *E. ortleppi* (G5), *E. canadensis* (G6 - G10) and *E. felids* (reported from Africa) grouped together in the species *E. granulosus sensu lato*.

Echinococcus multilocularis causes a type of echinococcosis known as alveolar echinococcosis or alveolar hydatid disease. *E. shiquicus* has been isolated only from small mammals and Tibetan foxes (*Vulpes ferrilata*), from the Tibetan region of China. *Echinococcus vogeli* and *Echinococcus oligarthus* are known as polycystic echinococcosis and they have been found only in Central and South America,

Different species and strains of *Echinococcus* spp. may differ in their morphology, rate of development, virulence, geographic range and other factors. Virulence and infectivity to human were variable depending on the strain of *E. granulosus*. Knowledge about present strains on some territory has epidemiology significance, and importance in control measures and the means of diagnosis.

Key words: echinococcosis, hydatidosis, genotips, molecular determination

4. ANAFILAKTIČKI ŠOK IZAZVAN PRISUSTVOM NERUPTUIRANE HEPATIČKE HIDATIDNE CISTE KOMPLIKOVAN MULTIPLIM INTRAHOSPITALNIM INFEKCIJAMA

4. ANAPHYLACTIC SHOCK DUE TO UNRUPTURED HEPATIC HYDATID CYST COMPLICATED BY MULTIPLE INTRAHOSPITAL INFECTIONS

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Echinococcosis as a systemic disease can include multiple complications, among which are the rupture of echinococcal cyst and anaphylaxis as an immunological reaction, which is the topic of our study. Anaphylactic shock due to unruptured hydatid cyst is a rare complication of hepatic echinococcosis.

Here we present an unusual case of unruptured hydatid cyst causing anaphylactic shock followed by appendicitis, ileus (which were surgically treated) and complicated by septic condition due to multiple intrahospital infections (*Clostridium difficile*, *Pseudomonas aeruginosa*, methicillin resistant *Staphylococcus aureus*, *Acinetobacter spp.*, *Klebsiella spp.*, *Enterobacter spp.*, *Proteus mirabilis*). In the course of the surgery, an echinococcal cyst was noticed on the right lobe of the liver, but it was not removed. This exploratory intervention revealed no visible cystic lesions in the abdomen. CT scans have shown an intact cyst, with no changes in size, as well as free abdominal fluid, which indicated the microscopic leakage of the cyst contents. The cystic walls were intact, so high intracystic pressure must have been the cause of leakage of cystic fluid into the circulation. The results of the ELISA test for *Echinococcus granulosus* was positive, the indirect hemagglutination assay (IHA) was positive at 1:1024 titer, and the immunofluorescence test (IFT) was positive at 1:160 titer. The therapy by mebendazole, 250 mg/12h per os, was carried through the hospitalization. Already being in an unstable state, our patient's condition was complicated with multiple intrahospital bacteria induced sepsis, so the medical consilium decided to postpone the surgery (cyst removal) after stabilization of his health status, in the course of the antiparasitic therapy. The isolates were treated in accord with the antibiogram, long-term in high dosage, which brought the treatment into a vicious circle, having in mind the appearance of *Clostridium difficile* colitis. However, the patient was discharged after two months of hospitalization to begin outpatient treatment in a good general condition.

Decision of the right moment of the surgical cyst removal and appropriate antimicrobial treatment are key factors for the positive outcome.

Key words: Anaphylactic shock, hepatic hydatid cyst, intrahospital infections

5. PRIMENA MOLEKULARNIH METODA U DIJAGNOSTICI TOKSOPLAZMOZE U VULNERABILNIM KATEGORIJAMA PACIJENATA

5. MOLECULAR METHODS IN THE DIAGNOSIS OF TOXOPLASMOSIS IN VULNERABLE CATEGORIES OF PATIENTS

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Objectives: Timely diagnosis of toxoplasmosis is required particularly in pregnancy and immunosuppression. To obtain precise yet rapid data on *Toxoplasma*-related fetal endangerment during primoinfection in pregnancy, as well as on post-transplantation hazard for *Toxoplasma* reactivation, the diagnosis was based on molecular methods..

Materials and methods: Molecular diagnosis of congenital toxoplasmosis (CT) was conducted prenatally from 42 amniotic fluid (AF) and at delivery from 10 cord blood (CB) samples. Molecular monitoring of *Toxoplasma* reactivation was carried out in 10 patients who underwent bone marrow transplantation (BMT), and included the analysis of 26 peripheral blood samples and one bronchoalveolar lavage fluid (BAL) sample.

The diagnosis was performed by Real-Time (RT) PCR targeting the *Toxoplasma*AF146527 gene (529-bp repetitive element), which was detected with a specific Taqman probe.

Results: Of 52 women diagnosed with primoinfection in pregnancy/periconceptual period in NRLToxo between 2008 and 2012, prenatal diagnosis of CT was established in 13 cases (25%). Of the 10 BMT recipients tested between 2012 and 2013, *Toxoplasma* reactivation was detected in three patients from peripheral blood and, in a case of fulminant pulmonary presentation, from BAL.

Conclusion: PCR-based methods ensure both prompt and precise diagnosis of CT and post-transplantation *Toxoplasma* reactivation, allowing for timely specific treatment.

Key words: *Toxoplasma*, PCR, congenital toxoplasmosis, reactivation, post-transplantation

6. FIRST PROGRAM OF EXTERNAL QUALITY CONTROL OF SEROLOGICAL DIAGNOSIS OF TOXOPLASMOSIS IN SERBIA
6. PRVI PROGRAM EKSTERNE KONTROLE KVALITETA SEROLOŠKE DIJAGNOSTIKE TOKSOPLAZMOZE U SRBIJI

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Objectives: To present the results of the first program of external quality control of serological diagnosis of toxoplasmosis organized in Serbia.

Materials and methods: In the fall of 2012, the National Reference Laboratory for Toxoplasmosis announced, via the Microbiology Section of the Serbian Medical Society, a call for participation in the program. Registered participants received a panel of six identical sera to analyze for *Toxoplasma*-specific both IgG and IgM antibodies using their usual methodology, and were given three weeks to return their results in a provided form.

Results: A total of 12 (7 public, 5 private) laboratories responded. Analysis of the submitted results showed an accuracy of 100% for specific IgG, but of only 50%, 67%, 83% and 100% for specific IgM antibodies by, respectively, 17%, 33%, 42% and 8% laboratories. Participants received individual recommendations for improvement, as well as certificates which could be used for future accreditation.

Conclusion: Serological diagnosis of toxoplasmosis performed in the participating laboratories was of a reasonable quality, but specific issues have been identified. The participant satisfaction rate was 100% and the program will be continued on a yearly basis. It can serve as a model for other reference laboratories for infectious diseases for similar programs, to help selfimprove this important area.

Key words: toxoplasmosis, serological diagnosis, external quality control, reference laboratory

7. TOKSOPLAZMOZA I TRUDNOĆA - KOLIKO SE MOŽE NAUČITI PREKO INTERNETA?

7. TOXOPLASMOSIS AND PREGNANCY – HOW MUCH CAN BE LEARNED FROM THE INTERNET?

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Objectives: To evaluate local internet sites as a source of health education on toxoplasmosis in pregnancy in Serbia.

Materials and methods: Knowledge and sources of information on toxoplasmosis were surveyed by questionnaire in a group of 50 pregnant women examined in our laboratory. The Google database was searched for internet sites in Serbian (and Croatian) using “toksoplazmoza” as the keyword. Twenty three top-ranked sites were checked for comprehensiveness and accuracy of information on the impact of toxoplasmosis on the course of pregnancy, prevention and diagnosis, and scored as offering insufficient, partly relevant and completely relevant information.

Results: Knowledge on toxoplasmosis was reported by 32 (64%) women, of which 34.4% had received information from media (56.2% from physicians, 9.4% from friends). Analysis of interactive internet sites showed that the most frequent questions addressed routes of infection, particularly cat and dog hazard, and diagnosis (whether to be tested, when, where, how to interpret the results). One third of the sites gave partly relevant, but none gave completely relevant information.

Conclusion: The media have proved as an important source of information. Despite numerous internet sites, pregnant women in Serbia still need a Serbian language one completely relevant for toxoplasmosis.

Key words: toxoplasmosis, prevention, source of information, internet

8. TRIHINELOZA U SRBIJI U 21. VEKU 8. TRICHINELLOSIS IN SERBIA IN 21ST CENTURY

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ABSTRACT

In Serbia, infection with *Trichinella* spp. has been recognized as a human health and animal husbandry problem for almost a century.

The objective of this study is to present data obtained from monitoring *Trichinella spiralis* infections in Serbia in 21st century, analyzed by NRLT.

Material and method: Epidemiological data on *Trichinella* infection in animals and humans were collected from 25 districts in Serbia. Information was obtained from annual reports issued upon request from the National Reference Laboratory for Trichinellosis (NRLT) by local/regional veterinary inspectorates (who provided total number of slaughtered i.e., inspected, as well as infected pigs per district) and the Institute of Public Health of Serbia „Milan Jovanovic Batut“.

Results: The rate of swine infection gradually decreased from 0.11% to 0.02% between 2001 and 2012. For the past 5 years, *Trichinella* infection among domestic swine was detected at levels higher than 0.05% in 1 district of Serbia (Branicevo), while prevalence at lower levels exists in almost half of the country today. During this period, there were 2430 cases of human trichinellosis, including 3 deaths. However, a significant decrease in the number of cases was reported during the last 5 years (from 168 in 2008 to 46 in 2012).

Conclusion: The fact that data presented here are similar to those for 1990 indicates that whole period in this century was needed to overcome the re-emergence of *Trichinella* infection in swine and humans that occurred during the last decade of the previous century.

Keywords: *Trichinella*, infection, humans, swine, Serbia

Acknowledgement: Supported by the Ministry of Science and Technological Development of the Republic of Serbia (Project 173047).

9. FAKTORI RIZIKA U PRENOŠENJU TRICHINELL VRSTA UNUTAR DOMAĆEG I DIVLJEG CIKLUSA

9. RISK FACTORS IN TRANSMISSION OF *TRICHINELLA* SPECIES IN DOMESTIC AND WILD CYCLES

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Objectives: In the Balkan region of Europe, *Trichinella* spp. infections are endemic. These zoonotic parasites are a serious problem for the human health and animal husbandry in Serbia. The aims of the present study were to define risk factors in transmission of *Trichinella* spp. in domestic pigs, and synanthropic and wild animals.

Materials and methods: Through the surveillance and monitoring of *Trichinella* spp. in wild boars (*Sus scrofa*), red foxes (*Vulpes vulpes*), golden jackals (*Canis aureus*), wolves (*Canis lupus*), stray dogs (*Canis familiaris*) and domestic pigs (*Sus scrofa domestica*) we investigated presents and possible pathways for transmission of *Trichinella* species. After examination of muscle samples from wild and domestic animals for presents of *Trichinella* larvae, genotyping was performed by multiplex PCR. GIS (Geographical Information System) was used for mapping the spatial distribution of *Trichinella* spp. infected animals and all defined point of interest (pig farms, hunting section, slaughterhouses, dumps).

Results: *Trichinella* spp. infection was detected in domestic and wild animals. *Trichinella spiralis* and *Trichinella britovi* were the only two species identified in the isolates as single or mixed infections. The identification of *Trichinella* spp. positive animals allowed to identify the foci of transmission and to inform the veterinary services, the owners of pig farms and slaughterhouses and hunter's associations about the risk of transmission of these zoonotic agents.

Conclusion: The results point out the circulating of *Trichinella* species by a domestic or a sylvatic cycle, the transmission between these two cycles, and the role of some host species as reservoirs of *T. spiralis* or *T. britovi* or of both species in Serbia.

Key words: *Trichinella* spp., zoonotic, domestic, wild, transmission

10. NOVI ELISA TESTA ZA DETEKCIJU *TRICHINELLA*-SPECIFIČNIH IGE ANTITELA 10. NOVEL ELISA TEST FOR DETECTION OF *TRICHINELLA*-SPECIFIC IGE ANTIBODIES

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Objectives: The major problem for studying IgE response in *Trichinella* infection is lack of commercial test for detection of specific IgE antibody presence. The main problem in development of this kind of test is excessive amount of specific antibodies of the IgG class in sera of patients with trichinellosis. This results in competitive inhibition of IgE binding to antigenic determinants in indirect type of assays giving a false negative result in the test, limiting the sensitivity of the technique. The goal of this study was to develop and validate ELISA test for detection of *Trichinella* specific IgE by which interference of other classes of antibodies would be avoided.

Material and method: Capture enzyme-linked immunosorbent assay based on two types of monoclonal antibodies was developed for detection of *Trichinella* specific IgE. Plates were coated with monoclonal antihuman IgE antibodies. Human sera (28 samples with a confirmed diagnosis of trichinellosis, 10 samples from persons anamnesticly suspected for trichinellosis and 40 samples from blood donors) were added to the wells. For detection of *Trichinella spiralis* (*T. spiralis*) specific IgE bound to the plates the excretory-secretory products (ES Ag) of *T. spiralis* muscle larvae were used. Monoclonal antibody 7C2C5 specific for *T. spiralis* immunodominant epitope, labeled with HRPO, for revealing interaction of specific IgE with ES Ag.

Results: Newly developed *Trichinella* specific IgE ELISA was able to detect specific antibodies in sera from all 28 patients with confirmed trichinellosis, but not in sera of suspected persons or healthy controls. Due to characteristic of this kind of ELISA test to amplify signal and produce wide range of OD values, the capture ELISA enabled clear discrimination between samples from patients with trichinellosis and healthy ones. The level of non-specific IgE either present in sera or added in known concentrations did not influence the sensitivity of reaction. Results of the test are expressed as a percentage of positivity (PP %) of a predefined control serum. According to the ROC curve analyses the best cutoff was 27.5 % PP. This analyze also indicated that specificity and sensitivity of this test were both 100%. Coefficients of variation of PP for intra- and inter-assay variability for 8 different serum samples (6 positive and 2 negative samples) were 3.7 and 5.6, respectively.

Conclusion: Capture ELISA presented in this paper is novel and reliable test. Its application allows us to follow up the dynamic in specific IgE production during the course of disease and to get insight into the immunomodulatory capacities of the parasite.

Key words: *Trichinella spiralis*, specific IgE, capture ELISA.

Acknowledgement: Supported by the Ministry of Science and Technological Development of the Republic of Serbia (Project 173047).

11. HUMANA DIROFILARIOZA - JOŠ JEDAN SLUČAJ NA PODRUČJU JUGOISTOČNE SRBIJE

11. THE HUMAN DIROFILARIOSIS - ONE MORE CASE IN SOUTHEASTERN SERBIA

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We present a case of a middle-aged man who lives in the southeastern part of Serbia with diagnosed of human subcutaneous dirofilariosis.

A 44-year-old man, inhabitant of the territory of city Leskovac, the southeastern part of Serbia (42° 59' North; 21° 56' East), was observed to the Clinic of Maxillofacial Surgery Niš with a subcutaneous nodule in the right infraorbital region. Painless edema of right cheek skin was the first clinical presentation four months ago. Standard laboratory haematological tests did not reveal eosinophilia or any other abnormality in a peripheral blood. After antimicrobial therapy, which was performed five days, edema was withdrawn but subcutaneous nodule persisted. After surgical removal of the subcutaneous nodule which was measured 10 mm in the diameter and partially covered by the skin...., histopathological analysis was performed. Haematoxylin and eosin staining (HE) showed chronic abscess composed of non specific inflammatory infiltrate consisting of lymphocytes, plasma cells, neutrophils and numerous eosinophils localized in the dermis. In the middle of the inflammatory infiltrates we detected transverse and longitudinal sections of a parasite. Applying the software package for image analysis Laboratory Universal Computer Image Analysis System (Lucia M, 1996), Czech Republic on oblique sections of the detected worm-like structures, provided an 8 µm thick cuticle with longitudinal ridges. The number of longitudinal ridges circumference round was 92-102.

Based on facts that Serbia is endemic area for *Dirofilaria* infection in dogs, the region with high seroprevalence of human dirofilariosis (8.4% of in area of Leskovac where patient lives), and microscopic findings permitted us to preliminary identify the worm as a *Dirofilaria repens*-like specimen.

Keywords: Human dirofilarioses, *Dirofilaria spp.*

12. PRVI SLUČAJ HUMANE OKULARNE DIROFILARIOZE NA PODRUČJU GRADA NIŠA

12. THE FIRST CASE OF HUMAN OCULAR DIROFILARIOSIS ON THE TERRITORY OF THE CITY OF NIŠ

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Introduction: The aim of the survey was to present the first case of human ocular dirofilariosis on the territory of the city of Niš, which been known as an area without findings of canine dirofilariosis and the region with the lowest seroprevalence in humans in the Southeastern Serbia.

Material and Methods: Patient S.G. (57 years old) visited an ophthalmologist because of extreme swelling and redness of eyelids of the right eye, scratches and pain in his right eye. For five days he was treated with systemic antibiotics and local antibiotics and corticosteroids. On the sixth day, when the swelling was reduced, on standard examination on biomicroscope, temporally 3mm from the limbus, intrapalpebrally, we observed a mobile parasite in the subconjunctival space. On the same day, under the local anesthesia, complete extraction of living parasites 14cm long was performed, which was in the saline solution delivered to the Department of Microbiology and Parasitology, Public Health Institute Niš. A sample of the nematode was identified as *Dirofilaria* spp. (*Dirofilaria repens* like). After successful extraction, the patient felt no discomfort. History data did not reveal any specifics.

Conclusion: For ocular dirofilariosis, surgical methods and complete extraction of parasite are the only way to achieve complete recovery.

Key words: Human dirofilarioses, *Dirofilaria* spp.

G1. SESIJA: EPIDEMIOLOGIJA MASOVNIH NEZARAZNIH BOLESTI

G1. SESSION: EPIDEMIOLOGY OF NON-INFECTIOUS MASS DISEASES

I UVODNA PREDAVANJA

I INTRODUCTORY LECTURES

1. INCIDENCIJA I MORTALITET OD RAKA GRLIĆA MATERICE U ZLATIBORSKOM OKRUGU

1. INCIDENCE AND MORTALITY OF CERVICAL CANCER IN ZLATIBOR DISTRICT

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Abstract

Introduction/Aim. Cervical cancer is the second most frequent malignant localization in women on a global level. This public health problem is specially emphasized in undeveloped world's countries, whereas in developed countries, thanks to preventive programs it came to a sudden decrease of both incidence and mortality. Serbia is among countries with the most unfavorable situation in Europe. The aim of the paper is to show the incidence and mortality of cervical cancer in Zlatibor District in the period from 1999 to 2008. **Material and Methods.** In this paper was used descriptive-epidemiological method. As a data source of morbidity, were used the data of Cancer Registry of Central Serbia and as mortality data were used the unpublished ones from Statistical Office of the Republic of Serbia. **Results.** The epidemiological situation of this cancer in central Serbia is uneven. In the observed period in Zlatibor District was registered an average incidence rate of 19.3/100.000 and the average mortality of 6.5/100.000. The Zlatibor District is among the areas with medium risk for occurrence of this malignant localization in central Serbia. The highest standardized incidence rate in the period from 1999 to 2008 in Zlatibor District, was recorded in Bajina Basta (41,1/100.000) and the lowest in Sjenica (9,8/100.000). Cervical cancer incidence and mortality have the tendency to decrease.

Conclusion. There is a necessity for introducing the cervical cancer-screening program, in order to rush this trend of decreasing the incidence and mortality of this malignant tumor in women in Zlatibor District.

Key words: cervical cancer, incidence, mortality

INTRODUCTION

Cervical cancer is an important public health problem all over the world. In women in our region, this malignant localization takes the second place by morbidity and the fourth by death. In topographical analyses of the frequency of cervical cancer globally, an uneven distribution of morbidity frequency is registered. There we can clearly see the areas where the incidence rates are lower than 10.0/100.000 (North America, Australia, Italy, Spain, Switzerland, Finland) and the areas with high rates of incidence which go in the range from

33,4 to 87,3/100.000 (some African countries, Latin America, The Caribbean). The highest cervical cancer mortality is in the poorest regions of the world: in Africa (East 25,3/100.000, West 24,0/100.000, South 14,8/100.000), Central and South Asia (14,1/100.000) and in South America (10,8/100.000), and the lowest in the countries of West Europe (2,0/100.000) [1,2].

In Serbia, the diagnosis of cervical cancer is annually set in nearly 1400 women, whereas more than 500 women each year die from this kind of malignant tumor. The standardized rate of cervical cancer incidence in central Serbia of 23, 3/100.000 in 2008 and the standardized mortality rate of 8, 0/100.000, show that Serbia is still among the European countries with unfavorable epidemiological situation, together with Romania and Bulgaria.

In Zlatibor District, every year, are diagnosed approximately 45 newly diseased women with cervical cancer and nearly 20 women cannot win the battle with this disease.

AIM

The aim of this paper is an overview of incidence and mortality of cervical cancer in Zlatibor District in the period from 1999 to 2008.

METHOD

In this paper is used descriptive-epidemiological method. As indicators of morbidity and death are used crude rates, increasingly specific rates and standardized rates of incidence and mortality. Standardization was done with direct method, using the world's population as the standard. [4]. For data source of morbidity and death from cervical cancer were used the data of Cancer Registry of Central Serbia in the period from 1999 to 2008 [5]. The data source about death of cervical cancer was unpublished material of Statistical Office of the Republic of Serbia from 1999 to 2008. The source of data about the population was the Statistical Office of the Republic of Serbia's estimation of the population, done for each year of the observed period.

For the analysis of the morbidity and death trends with cervical cancer were used Poisson regression model and regression program Joinpoint. The trend of standardized rates of incidence and mortality of cervical cancer during the observed period is shown with linear trends. The linear trend represents the linear regression model where independent variable (x) is time. The line of the trend is determined by equation: $y = a + bx$.

RESULTS

In Zlatibor District, cervical cancer is the second most frequent malignant tumor when it comes to morbidity and the fourth when it comes to death from all malignant tumors in women.

In the observed period, the average standardized incidence rate of cervical cancer in Zlatibor District was 19,3/100.000 and the average standardized rate of mortality is 6,5/100.000. The highest standardized rate of incidence is registered in 2002 and 2006 (23,0/100.000), and the lowest in 2004 (12,6/100.000).

The highest standardized mortality rate is registered in 2001 (8,6/100.000) and the lowest in 2006 (5,1/100.000).

In women in central Serbia and Zlatibor District there is a minor decrease of morbidity trend, which is more emphasized in central Serbia ($y=26,39- 0,31x$, $p=0,956$), although there is no statistical significance. During the observed period, cervical cancer is more frequent registered in women in central Serbia compared to women in Zlatibor District.

In women in central Serbia is registered statistically important increase of death trend from cervical cancer ($y=6,91 + 0,07 x$; $p=0,028$). Meanwhile in women in Zlatibor District, as in the case of morbidity, is registered a minor decrease of the death trend from this malignant localization ($y=6,77 - 0,045x$, $p=0,755$), which is not statistically important.

The lowest average increasing specific rate of incidence of cervical cancer with the population of women in Zlatibor District in the period from 1999 to 2008 was recorded in the period from the 20th to the 24th year (0,9/100.0000), and the highest in the period from the 45th to the 49th year (54,9/100.000). At the age of 19, there were no registered diseased women from cervical cancer.

The highest average standardized cervical cancer incidence rate in the period from 1999 to 2008 is recorded on territory of municipality Bajina Basta (41,1/100.000), and the lowest in Sjenica (9,8/100.000).

In the observed period the first and the second stage of cervical cancer in Zlatibor District were mostly present with 56,1%.

In Zlatibor District 90,1% malignant tumors of cervix is developed from exocervical mucosa-plate cells cancer (Ca planocellulare). 9,0% malignant tumors of cervix is developed from glandular epithelium (Adenocarcinoma). The rest of 0,9% are the others histological types (adenoacanthoma, carcinosarcoma, sarcoma).

DISCUSSION

According to the estimates by WHO (World Health Organization) the average annual incidence rate of cervical cancer on the level of world's population is around 15,0/100.000 women, and the average mortality rate around 8,0/100.000 women [2]. An unequal distribution of frequency of morbidity and death is registered. Many countries are conducting national programs for controlling this malignancy. So, the incidence and mortality in the period from 1968 to 1987 were increased both in Finland and Estonia, but in Finland they were higher. In the mid 60s in both countries was introduced the screening program, but it came to a quite decrease of both incidence and mortality in Finland. So, in 1987 the standardized incidence rate in Estonia was 14,0/1000 and in Finland 3,8/100.000. At the same time, the standardized mortality rate in Estonia was 6,0/100.000 and in Finland 1,6/100.000. Main differences can be ascribed to differences in public-health policy, but it can partly be ascribed to social-economical factors [6]. Thanks to this program in Poland, in the period from 2005 to 2010, it came to a decrease of incidence to 5,7%, so the number of newly diseased in 2005 fell down from 3,263 to 3078 in 2010. At the same time it came to the lowering of mortality for 3,4% [7]. According to the data of Cancer Registry of Croatia, standardized cervical cancer rates higher than 20/100.000 in 2010 are registered only in Primorsko-Goransko and Bjelovarsko-Bilogorska area. In the same year in 9 years are registered incidence rates lower than 15/100.000 [8].

According to registered incidence and mortality for the observed period, Serbia is among European countries with most unfavorable situation for this malignant disease. The reason for such a bad situation should be looked for in a small volume of examinations by cytological Papa test, in other words in the differences in public-health policy compared to

countries with favorable epidemiological situation. Organized screening program for cervical cancer started only at the beginning of 2013 in some districts of Serbia, and in other parts of Serbia it is conducted according to valid book of regulations about the volume and content of the services in prime health protection with the range which is not satisfactory.

The differences in standardized incidence and mortality rates can be seen, for the observed period along the districts of Central Serbia. The highest morbidity rate in 2008 is registered in District of Jablanica (41,4/100.000) and the lowest in District of Branicevo (4,8/100.000). Zlatibor District is among districts in which during 2008 the incidence rate was lower than 20/100.000. Besides, Zlatibor District is among districts where in 2008 was registered a fall of incidence compared to 1999. When you look at the fact that in Branicevo District for years has been registered one of the highest incidence rate, in the period from 2004 to 2006, in 8 municipalities of this district was conducted pilot project of cervical cancer screening whose effects are probably registered in 2008. In Zlatibor District this decrease can be assigned to more intense activity of raising the conscience of the importance of regular gynecological examinations in the Institute of Public Health Uzice, Society for Fight against Cancer Uzice and gynecologist from primer and secondary health protection in this area.

Some studies showed that there are differences in the frequency of this malignancy related to ethnical belonging. The incidence rate in women in Zlatibor District corresponds to the rate of Malayan women from the study in Brunei [9]. The average incidence rate in Zlatibor District shows lower values compared to value in Bulgaria in 2006, where it was 21,4/100.000 [10]. The average standardized rate of incidence of cervical cancer in Zlatibor District in the period from 1999 to 2008 was 19,3/100.000 women, which classifies this district among the areas with medium risk for cervical cancer morbidity.

The differences were also noticed in the mortality rates in districts, as in mortality between 1999 and 2008. In most districts of Central Serbia it came, in 2008, to the increase of mortality, whereas Zlatibor District is among districts which had lower mortality rate than the average in central Serbia (8,0/100.000). The differences in incidence in regions of Central Serbia can be partly assigned to the differences in ways of collecting the data. However, regional differences are present when it comes to mortality also, although the data were collected in the same way. It is possible that there are differences in the organization of health protection, informing of women, social-economical situation, and religion and similar, and in order to determine the reasons of these differences along the regions of central Serbia, it would be necessary to conduct additional epidemiological studies. As in the case of morbidity, the women of Zlatibor District are in the medium death risk of cervical cancer, with the average standardized mortality rate of 6,5/100.000.

The incidence and mortality rates are continuously lower in Zlatibor District comparing to central Serbia. Both in central Serbia and in Zlatibor District is registered the fall of incidence and in central Serbia it is more emphasized. However, when it comes to mortality, in central Serbia is registered statistically important increase of mortality rate and in Zlatibor District decrease of mortality. The decrease of mortality in Zlatibor District compared to the increase of mortality in central Serbia points to a more favorable epidemiological situation of cervical cancer in Zlatibor District.

The differences in incidence are present along the municipalities of Zlatibor District, where the highest average standardized incidence rate in the observed period was registered in Bajina Basta, and the lowest in Sjenica. The differences in incidence partly occur because of the differences in collecting the data. Beside the passive way of collecting the data, the Institute of Public Health Uzice collects them actively, too. In that way, for example, one part of the data is collected by analyzing the data about hospitalization from General Hospital

Uzice, which is regional Hospital for Zlatibor District. Meanwhile, a number of patients from Sjenica are being treated in Novi Pazar, which is in the region of Raska, so the data about the hospitalization are delivered in the Institute of Public Health Kraljevo. In that way the data about the hospitalization are insufficient source for collecting the data about cancer in Sjenica area. But, four times bigger incidence rate in Bajina Basta compared to Sjenica shows that there are other causes too, that indicate the necessity of conducting additional studies.

The data about increasingly specific rates in Zlatibor District in 2008 show that the highest increasingly specific incidence rate in Zlatibor District is registered at the age of 45-49, which is the same in women in Brunei[9]. The data about increasingly specific mortality rate in Zlatibor District are consistent when it comes to increasing the rates with the age in other countries and regions [11].

Women with cervical cancer in Zlatibor District, in period from 2000 to 2008 were registered in biggest percent (56,1%) in first two clinical stages, which is better result than in Lithuania [12], where 49,2% women with this cancer is registered in first two stages, so researches of our study show better results. However, in Lithuania was observed the period from 1999 to 2008. In North Carolina, later stages of cervical cancer are registered in older women and women without private insurance [11]. Some authors were dealing with examination of trends of some clinical stages of this malignancy. In the study of linear analysis of the trend of patients with cervical cancer for the period from 2001-2007, which Nincic and his collaborators conducted in the Institute for Oncology Vojvodina, it was noticed that the linear trend of the cases in stage I-IIA, didn't show significant changes [3]. In our study there weren't significant differences in the trend in first two clinical stages of this malignancy.

CONCLUSION

In the period from 1999 to 2008 in Zlatibor District was registered incidence of 19,3/100.000, with the decreasing trend, but with no statistical significance. The average standardized mortality rate in Zlatibor District was 6,5/100.000 with the mild trend of decreasing without statistical significance. In the area of Zlatibor District almost 60% women with this malignancy is registered in the stage in situ and the stage of localized cervical cancer tumor. The data about standardized incidence rates, mortality rates and frequency of registration of cervical cancer in clinical stages, point to the necessity of emergent conducting the cervical cancer screening in Zlatibor District.

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2. OBESITY AND THE RISK FOR BREAST CANCER

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Objectives: To summarise recent literature evidence on the association of obesity with the risk for breast cancer in women, concentrating on the results from human epidemiological studies.

Materials and methods: We provide an overview of obesity's relationship with breast cancer development in women.

Results: The risk of breast cancer associated with increased body size is not uniform across a woman's lifetime. Associations have been shown to vary greatly across population groups according to menopausal status, menopausal hormone therapy use, and tumor receptor status. Epidemiological studies indicate that obesity, usually reflected by body mass index, is a risk factor for the development of postmenopausal breast cancer. It is uncertain whether this relationship is due to non-adipose mass, adipose mass, or the distribution of adipose mass such as central adiposity. Although obesity has been inversely associated with a premenopausal breast cancer, this may be not for women with a family history of the disease.

Conclusion: Obesity is an important and potentially modifiable risk factor for postmenopausal breast cancer, particularly the development of hormone-responsive tumors. Prevention of adult-onset obesity and maintaining ideal body weight after menopause should be a major public health goal to delay or prevent some kinds of breast cancer.

Key words: obesity, Body Mass Index, breast cancer risk, postmenopause, premenopause

The risk of breast cancer associated with increased body size is not uniform across a woman's lifetime. Epidemiological studies indicate that overweight and/or obesity, usually reflected by body mass index (BMI) is a risk factor for the development of postmenopausal breast cancer (1). Although obesity in premenopausal women has been associated with a decreased breast cancer risk, this may be unique to industrialized societies (2) and may be applicable only to younger obese women (3). A prospective study conducted in Norway confirmed the protective effect of overweight and obesity for premenopausal breast cancer, but not for women with a family history of the disease (4).

Weight gain in adulthood also has been implicated as an important determinant of breast cancer risk (5). In fact a publication assessing breast cancer risk factors listed BMI and weight gain between the ages of 20 and 50 yr as second only to Gail Model parameters (quantitative breast density, free estradiol, parity (yes/no), and age of menopause) in importance (6). It has been suggested that body fat may be a better predictor of postmenopausal breast cancer risk than either body weight or BMI (7), and body fat distribution may also impact breast cancer risk (8). However, when conducting large-scale studies, measurements of body fat and body fat distribution are not as easily obtained as height and weight, which can then be used for calculating BMI.

The possible reasons behind the observation that women with a high BMI have a decreased risk of premenopausal breast cancer are complex. One hypothesis is that this may be

attributed to an increased frequency of anovulatory cycles and decreased levels of sex hormone-binding globulin, which results in lower levels of estradiol due to its increased clearance (9). Production of estrogen from adipose tissue is relatively low for premenopausal women, and therefore, the increased production of estrogen from the abundant adipose tissue associated with increased body size is not strong enough to offset the reduction of estrogen due to an increased frequency of anovulatory cycles. It is also unclear whether this protective effect is consistent throughout the years before menopause or is confined to teenage years only (10).

The situation changes after menopause because the ovarian production of estrogen is greatly diminished. The main source of estrogen then is from aromatase converting the androgen precursor androstenedione to estrone in the adipose tissue (11). The change in the relationship between body size and breast cancer risk is not linear during the postmenopausal years and that it does not manifest until ~15 years postmenopause (12). A few studies have found that risk associated with increased BMI is higher in older age (13-15), whereas others have reported no difference (16), or reported a stronger effect for younger postmenopausal women (17).

Some studies have shown that excess central adiposity, usually measured by waist-to-hips ratio (WHR), is related to an increased risk of breast cancer (18). This has led to the hypothesis that hyperinsulinemia may be a direct risk factor for breast cancer (19). Waist circumference may be a better indicator of central adiposity than WHR (12). A study using computed tomography found that, for women, waist circumference was the best overall predictor of abdominal visceral obesity (or deep abdominal obesity) when compared with WHR, percent body fat and BMI (20). In particular, WHR was a poor indicator of abdominal visceral fat. It is reasonable to assume that the increased risk of breast cancer due to an increased waist circumference may be due to visceral fat as waist circumference correlates better with visceral than with abdominal subcutaneous fat (trunk-abdominal obesity) (21).

There is evidence that the body size and breast cancer relationship may be stronger for never users of hormone replacement therapy (HRT) (12,13,16,17). The rationale for this effect modification is that current HRT users have elevated estrogen levels, regardless of their body weight, which greatly reduces the impact on total circulating estrogen of the aromatization of androgens to estrogens in adipose tissue (17).

Several studies have reported on breast cancer risk stratified by the tumor's ER and PR status (22,23). ER+ tumors and PR+ tumors are likely to be sensitive to exposure to estrogen and progesterone, respectively, whereas ER- and PR- tumors may involve mechanisms independent of hormonal exposure (22). The hazard ratios for ER+/PR+ tumors due to increased waist circumference, fat mass, and BMI were moderately positive, whereas the risk of ER- /PR- tumors had modest negative point estimates (12).

Obesity also is associated with greater tumor burden in women diagnosed with breast cancer (15,16) and with higher grade tumors (16). For both premenopausal and postmenopausal women, overweight/obesity is associated with poorer prognosis and/or increased mortality (16).

Because many breast tumors in postmenopausal women are dependent on estrogen for growth, it seems likely that weight loss through either caloric restriction or gastric bypass surgery and the concomitant reduction in estrogen levels should lead to a reduction in breast tumor growth.

CONCLUSION

It is now well established that overweight and/or obesity and/or weight gain are a risk factors for the development of postmenopausal breast cancer, particularly the development of hormone-responsive tumors. Elevated circulating estrogen levels as well as local production of this hormone have been implicated as a primary growth factor in this relationship. With the incidence of overweight and obesity increasing throughout the world, the number of women at risk for developing breast cancer will also increase. Prevention of adult-onset obesity should be a major public health goal to delay or prevent some kinds of breast cancer.

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3. THE EFFECT OF PHYSICAL ACTIVITY ON BONE MINERAL DENSITY AND OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN: META-ANALYSIS

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Objective: The aim of this study was to assess the effect of different types of exercises on bone mineral density (BMD) of lumbar spine in postmenopausal women.

Methods: A systematic review and meta-analysis were undertaken to evaluate the effects of physical activity analyzed in nonrandomized and randomized controlled trials on BMD of lumbar spine. Structured electronic searching of MEDLINE database and hand-searching of reference lists were undertaken to locate relevant studies published from January 1990 to July 2010. Study treatment effect was defined as the weighted mean difference between percentage change in bone loss in the training group and in the control group.

Results: The findings of the study demonstrate that physical activity had an effect at lumbar spine BMD (1.148, $p < 0.001$). Resistance training and weight-bearing training showed positive effect on BMD of lumbar spine ($p = 0.001$, $p = 0.007$, respectively). The effect of exercise was higher in women with osteopenia or osteoporosis (2.855, $p < 0.001$) than in healthy postmenopausal women (0.823, $p = 0.001$).

Conclusion: Physical activity has a significant effect on preservation of BMD at lumbar spine. Furthermore, the effect of physical exercise is higher in women with osteopenia and osteoporosis suggesting nonpharmacological contribution to osteoporosis treatment, but more investigations are needed to confirm these findings.

Key words: osteoporosis, bone mineral density, physical activity, meta-analysis

4. UČESTALOST, FAKTORI RIZIKA I KOMPLIKACIJE ŠEĆERNE BOLESTI 4. FREQUENCY, RISK FACTORS AND COMPLICATIONS OF DIABETES MELLITUS

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Abstract

Introduction. Diabetes Mellitus is a group of metabolic disorders characterized by hyperglycemia as a result of defects in the insulin secretion, insulin activity or in both of these functions. The aims of this study were to analyze the frequency of diabetes type 1 and type 2 in the population of Serbia, to identify potential risk factors for the development of type 2 diabetes, to determine factors that can prevent the development of type 2 diabetes and to estimate the frequency of micro and macrovascular complications at the time of diagnosis of type 2 diabetes, and after four more years.

Method. The incidence of type 1 diabetes in Belgrade population for the period 1982-2005, and the incidence of diabetes type 1 and type 2 in the population of Serbia for the period 2006-2008 year were analyzed in the first descriptive part of the study. In the second part of the study, in order to identify factors associated with the occurrence of type 2 diabetes, a case-control study was used. The study comprised 179 newly diagnosed cases of type 2 diabetes and 358 controls. Patients and controls were matched with regard to sex, age (\pm 2 years) and residence (Belgrade).

In the third part, which was a prospective cohort study, the incidence of micro and macrovascular complications of diabetes type 2 was analyzed both at the time of diagnosis and four years later.

In the analysis of the collected data were used nonstandardized and standardized incidence rates, linear regression analysis and univariate and multivariate conditional logistic regression analysis.

Results. The incidence of type 1 diabetes in Belgrade population 0-14 years old, was 10.4 per 100,000 for the period 1982 - 2005. years (10.7 for boys and 9.8 for girls). Average age-specific incidence rate of type 1 diabetes (per 100,000) increased with age and was 5.5 at age 0-4 years, 11.9 at age 5-9 years and 15.4 at age 10-14. In Serbia, in the period 2006 - 2008, the average incidence rate of type 1 diabetes in the age group 0-29 years was 11.8 in 100,000. In the same period, the incidence rate of type 2 diabetes in the total population (all ages) was 131.0 in 100,000. According to multivariate logistic regression analysis 16 variables were significantly independently associated with occurrence of type 2 diabetes Good socio-economic status ($p < 0.001$), consumption of fatty food ($p = 0.012$), overweight and obesity ($p = 0.001$), obesity in adolescents ($p < 0.001$), sedentary type of occupation ($p = 0.011$), death of a close family member ($p = 0.032$), financial difficulties ($p = 0.026$), rarely getting help from relatives/friends to resolve problems ($p = 0.002$), rarely receiving financial assistance for solving problems ($p = 0.014$), poor coping with monthly income ($p < 0.001$), personal history of hypertension ($p = 0.004$) and family history of diabetes ($p = 0.007$) were all positively associated with type 2 diabetes.

At the time of diagnosis one out of three patients with diabetes type 2, and after 4 years one out of two patients had a complication of diabetes. The prevalence of diabetes complications among people with type 2 diabetes four years after the diagnosis was 45.5% for hypertension, 0.06% for angina pectoris, 0.01% for acute myocardial infarction, 0.01% for chronic heart failure, 0.04% for retinopathy, 0.07% for nephropathy and 0.04% for neuropathy.

Conclusion. Belgrade population, in the same way as in the majority of European countries, belongs to populations with medium high incidence of type 1 diabetes. The incidence rate of type 2 diabetes in Serbia is very low compared to other countries, which indicates inadequate reporting of new cases. According to the present study, in addition to genetic factors, obesity, physical inactivity, stress and poor emotional support are most important in the development of type 2 diabetes. Change of habits could, by keeping normal body weight and increased physical activity, contribute to the prevention of type 2 diabetes.

Key words: incidence, diabetes, risk factors

5. PROCENA KVALITETA ŽIVOTA OBOLELIH OD ATOPIJSKOG DERMATITISA

5. QUALITY OF LIFE IN PATIENTS WITH ATOPIC DERMATITIS

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Quality of life

-The perception of an individual about his position in life within the culture and value systems in which they live and in relation to their own objectives, expectations, standards and concerns

-Broad concept that operate physical health, psychological state, level of independence, social relationships and the most important phenomena in the environment

Source : WHOQOL Group, 1993

Related quality of life with health

-Component of overall quality of life, is primarily determined by a person's health and can be affected by a variety of clinical interventions

-Functional effects of a disease, and consequently the therapy to the patient, as seen, perceived by the patient

Source : Shipper et al, 1990

Measuring quality of life

-General questionnaires

-Specific questionnaires

Atopic dermatitis - definition

-Chronic inflammatory, relapsing, pruritic skin disease

-Wide spectrum of clinical manifestations

-Eczematous changes, itching and dry skin

-Lichenification, papules, vesicles, exudation, excoriation and crusts

-Minor form, major form

periods of remission and exacerbation Classification AD

II USMENE PREZENTACIJE II ORAL PRESENTATIONS

1. SKRINING KOLOREKTALNOG KARCINOMA U SRBIJI 2. COLORECTAL CANCER SCREENING IN SERBIA

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With approximately 4200 patients and 2600 deceased persons, Serbia is in a group of European countries with average rates of morbidity and high mortality rates from colorectal cancer. In developed countries, where screening programs are successfully used for several decades, there has been decline in mortality from these malignant localization.

Objective: Evaluation of the effectiveness of implementation of screening for colorectal cancer in Serbia.

Method: Selected Indicators of the screening process were analyzed with izveštajih forms from 19 municipalities in Serbia, in personnel and equipment to fulfill the necessary conditions for the implementation of screening for colorectal cancer in the first half of the 2013th year. The target population consists of men and women aged 50 to 74 years of age. Screening test was used stool for the presence of occult blood in the stool (FOBT).

Results: Of the 19 277 people invited, screening for colorectal cancer responded to 14,658 participants (76.0 %). With FOBT positive finding was 446 (4.3%), of whom colonoscopy accepted 285 (63.9 %) of the insured. The colonoscopic findings were most

polyps and other diseases (82.8 %), while a one in six colorectal carcinoma (17.2%). Response to screening ranged from 100.0 % in Doljevac to 12.0 % in Nis.

Conclusion: Detection of disease in precancerous stages and stage of benign polyps, allows complete recovery and detection of localized stage disease to cure over 90 % of patients.

Keywords : screening, colorectal cancer, Serbia

2. THE ROLE OF SOME ENDOGENOUS FACTORS IN DEVELOPING LARYNGEAL CANCER

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The **objective** of this study was to perceive the eventual causative associations between some endogenous risk factors and development and distribution of laryngeal cancer (LarC). **Materials and Methods:** This was a case-control study. It comprised 185 patients with LarC and matched controls with no malignant disease (control group-CG). By calculating the odds-ratios, the risk factors that play a role in the disease onset have been estimated. Statistical significance of the examined variables as risk factors has been defined with confidence intervals (CI). **Results:** Malignant disease has been registered in 68 (36.8%) family members diseased with LarC. Their number was slightly smaller in the CG (53 or 28.6%). Data on two family members diseased with malignoma was received by 16.2% of the investigated and 9.4% of the CG. Subjects with a positive family history of malignant diseases were at a 27-fold increased risk of developing LarC in smokers as compared to non-smokers (95% CI, 3.3-220.2). Stress situations were equally present in both groups (LarC-26.3%; CG-25.4%). In LarC patients the mean duration of acute stress was longer than in CG subjects (LarC-4.45±1.37 months; CG-3.73±1.27 months). **Conclusion:** Endogenous factors are a risk factor in developing LarC. Data on malignant disease in the family was given by each third LarC patient. Each fourth patient with LarC was exposed to stress.

Key words: laryngeal cancer, congenital factor, stress.

BALKAN ENDEMIC NEPHROPATHY IN ENDEMIC FOCI OF BOSNIA AND HERZEGOVINA (BIH) - AN EPIDEMIOLOGICAL STUDY

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Balkan endemic nephropathy is a chronic tubulointerstitial disease with a slow progression to chronic renal failure. In endemic foci of the Federation of Bosnia and Herzegovina (in the northeastern part of Bosnia and Herzegovina), since 1989. was not done methodologically sound studies, and recent epidemiological parameters related to the disease of endemic nephropathy in the area of this part of Bosnia and Herzegovina, no. The aim of this study was to examine the prevalence of endemic nephropathy among residents of endemic areas in the Federation BiH, using the criteria for the diagnosis of diseases Danilovic.

In 2012. 2013. year, a cross-sectional epidemiological study, which included eight historically known inhabitants of endemic areas. Respondents who voluntarily responded to the action is submitted to a physical examination, urine test for the presence of albuminuria and set the value of creatinine in urine and collected epidemiological data related to the disease in this study using a specially designed questionnaire. Respondents who, according to the criteria for the diagnosis of endemic nephropathy by Danilovic, belong to the group with intermittent proteinuria were referred for clinical assessment, for further diagnosis and classification.

This paper presents the results of the overall prevalence of endemic nephropathy among surveyed respondents - residents of endemic village in northern Bosnia in the Federation, as well as the prevalence in individual categories (sick, suspicious, with intermittent proteinuria, healthy), using Danilovic's criteria for the diagnosis of disease. It also provides an overview of the corresponding mean values measured (laboratory) parameters : blood pressure, ratio albumin/creatinine in urine, the number of red blood cells, hemoglobin, blood urea nitrogen and creatinine in blood by BEN groups of respondents.

Balkan endemic nephropathy, according to the results of this study continue to be a major cause of chronic renal failure in endemic foci of FBiH, because the prevalence indicates that patients are still endemic, and that process is still ongoing.

Keywords : Balkan endemic nephropathy, the Federation of Bosnia and Herzegovina, epidemiological studies

III POSTER PREZENTACIJE
III POSTER PRESENTATIONS

1. SKRINING KARCINOMA DOJKE U SRBIJI
1. BREAST CANCER SCREENING IN SERBIA

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Serbia is in the group of European countries with high rates of death from breast cancer. Breast cancer is a disease that can not be prevented, but can be successfully treated if caught in time. In developed countries, where screening programs are successfully used for several decades, there has been decline in mortality from this malignancy.

Objective: Evaluation of the effectiveness of implementation of breast cancer screening in Serbia.

Method: Selected Indicators of the screening process were analyzed with izveštajih forms from eight municipalities in Serbia, in personnel and equipment to fulfill the necessary conditions for the implementation of breast cancer screening in the first half 2013th year. The target population consists of women aged 50 to 69 years of age. Screening test was used mammography.

Results: Of the 30,438 women invited, 15,635 (51.4 %) agreed to participate in skriingu, and from them to the screening mammogram responded to 9183 (58.7 %) women. Response to screening ranged from 93.7 % in Senta to 51.4 % in Nis. With BIRADS 4a and 4b finding was 395, with a BIRADS 5 findings were 40 women.

Conclusion: The screening is cost-effective only with coverage of at least 70 % of women. The number of women in whom the tumor was detected by mammography when still clinically nepalpabilan is small (5 %).

Keywords : screening, breast cancer, Serbia

2. SKRINING KARCINOMA GRLIĆA MATERICE U SRBIJI

2. CERVICAL CANCER SCREENING IN SERBIA

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Organized screening program for cervical cancer, the health education of young people and promote a healthy lifestyle, making a significant contribution to the overall reproductive health of women and make great savings the health care system.

Objective: Evaluation of the effectiveness of implementation of cervical cancer screening in Serbia.

Methods: Studies were selected process indicators of implementation of screening in seven municipalities in Serbia, cervical cancer in the first half of the 2013th year. The target population consists of women between 25 and 64 years of age. Screening test was used for cytological smear Papanikolaua.

Results: Of a total of 35 410 invited women, cervical cancer screening, responded to 15,548 (76.0 %). Turnout was 93.3 % in Trsteniku to 11.0 % in Nis. With the group I was 836 (13.9 %), group II - 4376 (73.2 %), IIIa group - 568 (9.5%), group IIIb -119 (2.0%) and group IV - 22 (0.4 %). In 108 patients a biopsy was performed.

Conclusion: The implementation of screening cervical cancer in Serbia is facing a great challenge to the conditions of limited financial means to eliminate the existing shortcomings oportunog screening.

Keywords : screening, cervical cancer, Serbia

3. TREND INCIDENCIJE RAKA GRLIĆA MATERICE NA TERITORIJI NIŠAVSKOG OKRUGA

3. INCIDENCE TREND OF CERVICAL CANCER IN THE NISHAVA DISTRICT

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Cervical cancer is third most common cancer in women in the Nishava District. The aim of the paper was to present the most important epidemiological characteristics of cervical cancer incidence and to analyze trend in the period 1999-2012. Materials and Methods: The data source were the official figures of population cancer registry that is the Nishava District leads the Public Health Institute in Nis. The descriptive epidemiological method. Incidence standardized rates calculate per 100 000 women (Census 2011). A linear trend. Results: The fourteen-year period, a total of 939 new cases was registered in women with cervical cancer. The mean age of female patients was 53.2 years. Average annual non-standardized incidence rate was 35.1 and 24.1. Annual standardized rates ranged from 19.3 (2005) to 30.6 (2003). The incidence trend of cervical cancer in the Nishava District slightly decreased ($y = -0.1127x + 24.81$; $R^2 = 0.0229$). The highest average annual incidence rate was recorded in the municipality Svrlijig (26.08) and the lowest in the municipality Merošina (17,14). According to the place of residence of all municipalities Nišava districts greater number of new women's lives in the country, except in the city of Niš, where a significantly higher share of female patients from urban areas. Conclusion: Cervical cancer is a significant social and medical problem in women. More efficient use of measures of primary and secondary prevention may lead to a decline trend in the incidence of this malignancy.

Key words: cancer, cervix, incidence, trend

4. POVEZANOST OPAŽENIH PROMENA NA SAMOPREGLEDU DOJKI I POZITIVNOSTI MAMOGRAFSKOG NALAZA

4. THE RELATIONSHIP OF THE CHANGES DISCOVERED DURING BREAST SELF-EXAMINATION AND POSITIVE MAMMOGRAM RESULTS

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Introduction: In recent years number of patients with malignant breast tumors is increased. Patients, mostly due to lack of information, neglect changes in breast tissue and visit their general practitioners too late. The only way to reduce the number of patients with malignant breast tumors is timely diagnosis and removal of suspicious changes in breast tissue before these are transformed into a tumor.

Objective: To explore the relationship of the changes discovered during breast self-examination and positive mammogram results.

Methods: This was a cross sectional study. The sample consisted of 763 women who have undergone mammography in the Health center Pancevo, in 2012. Data on sociodemographic characteristics and preventive behavior of women were gathered through a questionnaire consisting of 17 questions.

Results: The mean age of respondents in this research was 55.6 ± 8.6 years. Out of all respondents 42 (5.5%) were subjected to infertility treatment, 713 (93.4%) gave birth, 640 (86%) breastfed, 61 (8.0%) received hormone therapy. Breast self-examination was performed by 525 (68.8%) patients. Out of 763 examined patients 141 (18.5%) had abnormal mammogram results. Incidence of changes in breast tissue discovered during breast self-examination in patients with positive mammogram results was 28.4% (40 of 141), and 16.6% (103 of 621) in patients with negative mammogram results. This difference was statistically significant ($p=0.001$).

Conclusion: Breast self-examination is an important preventive procedure in the early detection of malignant changes in breast tissue. Positive finding during breast self-examination leads to use of mammography as a diagnostic procedure.

Key words: breast self-examination, breast cancer, mammography.

5. PRIMENA GEOGRAFSKIH INFORMACIONIH SISTEMA U SKRININGU RAKA 5. APPLICATION OF GEOGRAPHIC INFORMATION SYSTEMS IN CANCER SCREENING

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Objectives: Geographic Information System (GIS) offers a new way of considering and analyzing data. By linking data from the actual physical locations and mapping, GIS can assist in the detection of relationships, patterns and trends in different geographic areas. GIS was used in the research, identification and mapping of the geographical distribution of health facilities and the response of the citizens who participated in cancer screening

Materials and methods: Geographic information system and mapping tools are used to visually show the health facilities and the response of the citizens who participated in cancer screening, to determine why the different screening coverage in certain geographic regions.

Results: We compared the response to screening cancer with average earnings. The results obtained confirm that the average wage does not affect the response.

Conclusion: GIS software allows users to store, manipulate and display geographic health data. Future research should focus on measuring the accessibility of health care facilities in which cancer screening is conducted taking into account the (non)use of public transport.

Key words: cancer screening, geographic information system, mapping, access facilities for cancer screening

6. VODEĆE LOKALIZACIJE MALIGNIH TUMORA NA RASINSKOM OKRUGU 2006-2010

6. THE MOST FREQUENT LOCALIZATIONS OF MALIGNANT NEOPLASMS IN RASINA DISTRICT 2006-2010

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Aim: The aim of the paper was to observe cancer incidence and mortality rate trends in the period 2000.-2010. as well as to observe frequency of various localizations of malignant neoplasms (incidence and mortality, 2006-2010).

Method: Descriptive epidemiological method. Source of information for cancer incidence and mortality data was Cancer Registry of Central Serbia for the period 2000-2010.

Results: In the period 2006-2010, 5577 men and women in Rasina district were diagnosed with cancer and 4809 men and women that had suffered from cancer, died. Average standardized incidence was 283/100000 in males and 248/100000 in females, and average standardized mortality was 166/100000 in males and 96/100000 in females. In the ten year period (2000-2010) standardized cancer mortality rates increased ($y = 3,15 + 136,51 x$ in males and females $y = 0,0373 x + 97,25$), as well as standardized cancer incidence rate in males $y = 1,83x + 227,2$ (while standardized cancer incidence rate in females decreased $y = -2,2x + 227,3$). The most frequent localizations of malignant neoplasms in males were lung (23,3%), prostate (11,2%) and colorectum (11%), while the most frequent localizations of malignant neoplasms in females were breast (23,5%), colorectum (8,9%) and lung (8,7%). From lung cancer males suffered about four times more than females. Colorectal cancer was more frequent in males than in females, almost every breast cancers affected women (97%).

Conclusion: Rasina district is the district of Central Serbia with a middle risk of cancer incidence and mortality. Increasing trends of incidence and mortality of the most frequent localizations of malignant neoplasms are good reasons for starting organized cancer screening programs in Rasina district.

Key words: incidence, mortality, cancer, epidemiological, Rasina

G2. SESIJA: EPIDEMIOLOGIJA MASOVNIH NEZARAZNIH BOLESTI, NASTAVAK
G2. SESSION: EPIDEMIOLOGY OF NON-INFECTIOUS MASS DISEASES,
CONTINUED

I PREDAVANJA PO POZIVU
I INVITED LECTURES

1. PREVENCIJA KARDIOVASKULARNIH BOLESTI: ŠTA, ZAŠTO, KAKO, KO?
1. PREVENTION OF CARDIOVASCULAR DISEASES: WHAT, WHY, HOW, WHO?

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Abstract

Atherosclerotic cardiovascular disease (CVD), especially coronary disease (CD) is nowadays the leading cause of early non-violent death worldwide. It is believed that a CVD is caused partly by a „bad“ genetic code, while in a larger part it is caused by particular lifestyles, especially by tobacco use, unhealthy diet, physical inactivity, and psychosocial stress. Based on that, current CVD prevention measures are focused on lifestyle changes and possible impact on controllable risk factors. Any decision on the initiation of preventive measures and treatment should be guided by risk assessment for any vascular event. Numerous mathematical models are available today for CV risk assessment, but the model by the European Society of Cardiology is the one mostly used in Europe (Systematic Coronary Risk Estimation, SCORE). The cut-off of high risk based on fatal CV events is defined at $\geq 5\%$. CVD prevention is primarily based on a healthy lifestyle and non-pharmacological impact on risk factors. Individuals who want to be and stay healthy should abide by the measures expressed in the form of a phone number (035140530), meaning: 0 – no smoking; 3 – one 3 km walk a day, or 30 minutes of moderate physical activity; 5 – fruit and vegetable meals eaten five times a day, as raw as possible; 140 – maximum systolic BP; 5 – maximum total cholesterol; 3 – maximum LDL cholesterol; 0 – no diabetes mellitus. These values refer to primary prevention; secondary prevention differs only in lower cholesterol values (LDL cholesterol < 2.5 mmol/l) and glycated hemoglobin < 7 mmol/l.

Introduction

Atherosclerotic cardiovascular disease (CVD) is a chronic, insidious disease, usually detected upon the manifestation of first symptoms, but which is usually in its terminal stage then.

The appearance of fatty streaks – the very beginning of atherosclerosis – has been reported by pathologists even in small children, which indicates early onset and further chronic, dormant nature of the changes. CVD prevention measures should therefore be initiated as early as possible, targeting in fact the mother of the future child and focusing on her bad habits and harmful lifestyle choices. However, even before this issue is opened, it is necessary to get an answer to the question what is CVD prevention? CVD prevention is a set of coordinated actions both at the level of an individual and population as a whole, aimed at eradication, elimination, or reduction of CVD. The basis of CVD prevention is cardiovascular epidemiology and evidence-based medicine.

Why CVD prevention is necessary today? Atherosclerotic cardiovascular disease (CVD), and especially coronary disease (CD), is today the leading cause of early non-violent death worldwide. CVDs affect both genders; 38% of men and 42% of women in Europe die of CVDs before the age of 75 (1).

The tendency of CVD mortality reduction is nowadays reserved for well developed western countries, while in the developing countries CVDs are still the leading cause of mortality, demonstrating even a trend of growth. More than 80% of overall CVD mortality is reported in the developing countries (2). The latest data from Czech Republic and Poland have shown that in the period 1985-2007 there was a significant reduction of both total and CVD mortality by 40-48%. Such a favorable trend was the result of a successful impact on controllable risk factors (68%) and improved treatment of CV events (40%). Most beneficial in that regard were natural, dietary reduction of cholesterol (41%) and blood pressure control (15%) (3). This was a conclusive validation of lifestyle changes via the correction of controllable risk factors.

How should we implement CVD prevention? It is thought that a CVD is partly caused by “bad” genetic code, while in a larger part it is caused by particular lifestyles, especially by tobacco use, unhealthy diet, physical inactivity, and psychosocial stress. Based on that, current CVD prevention measures are focused on lifestyle changes and possible impact on controllable risk factors. There is a simple phone number to be used as a reminder, describing the status of a healthy person – 035140530 – meaning:

0 – no smoking

3 – 3 km daily walks, or 30 minutes of moderate physical activity

5 – 5 portions of fruit and vegetables a day (as raw as possible)

140 – maximum value of systolic blood pressure

5 – maximum value of total blood cholesterol

3 – maximum value of LDL cholesterol

0 – avoidance of diabetes mellitus

Overweight should be avoided as well (especially central obesity), and body mass index should be kept below 25 kg/m^2 , with avoidance of stress too, as much as we possibly can. Regretfully, nowadays, that psychosocial factor is not easy to keep in check.

The results of a number of recent studies have shown that with combination of these recommended measures we should be able to stop the process of atherosclerosis – reduce further plaque growth, or even reduce their volume changing their content. In these studies, nuclear magnetic resonance was used to assess atherosclerotic plaques. Cessation of smoking is a very important factor in arresting plaque progression in the coronary blood vessels, as well as the mediterranean diet with olive oil in combination with nuts, hazelnuts, and almonds. Regular physical activity was shown to be beneficial in CVD prevention in all of the studies (5, 6).

What is the target population for CV prevention measures? Ideally, the expecting mothers should be taught of prevention measures, and they should adhere to them during their pregnancy. From the earliest ages, children should be taught of healthy lifestyles in kindergartens and schools. Healthy and regular nutrition, recreational sports or regular physical exercise are some among the many necessary measures. In some countries, such as the United Kingdom, fast food restaurants have been moved far away from schools, with far greater parent engagement that children get healthy, home-made food. A high incidence of

diabetes and obesity in the USA has led to the initiative against soft drinks, highly refined, and fast foods. Poverty is still one of the major causes of inadequate nutrition – regrettably, healthy foods are very expensive today. In some regions of the world, soft drinks are cheaper than water. The governments and their ministries should make efforts to confront such situation with adequate measures.

In addition to the above, the European Society of Cardiology and almost all other similar organizations worldwide caring for human health, have presented recommendations concerning the creation of precise and as simple as possible estimations of overall cardiovascular risk of contracting and dying of CVDs, creation of action plans, and assessment of intensity of individual CVD prevention measures. Any decision on the initiation of preventive measures and treatment should be guided by risk assessment for any vascular event. Numerous mathematical models are available today for CV risk assessment, but the American (Framingham) model and the one created by the European Society of Cardiology (Systematic Coronary Risk Estimation, SCORE) are today the ones mostly used. The SCORE risk has been obtained from the large data base of European prospective studies, predicting fatal CV events in the period of 10 years. High risk cut-off based on fatal CV events has been set at $\geq 5\%$ (7).

The SCORE system involves the following elements: gender, age, smoking status, systolic blood pressure, total cholesterol, or the ratio Chol/HDL-chol. and HDL – Chol. There are tables for low risk countries (Andorra, Austria, Belgium, Cyprus, Danmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Israel, Luxembourg, Malta, Monaco, Netherlands, Portugal, San Marino, Slovenia, Spain, Sweden, Swiss, Switzerland, United Kingdom) and for high risk countries (all other European countries, including our own). There are countries with very high risk, including Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, FYR of Macedonia, Moldova, Russia, Ukraine, and Uzbekistan. Figure 1 presents the tables for high risk countries.

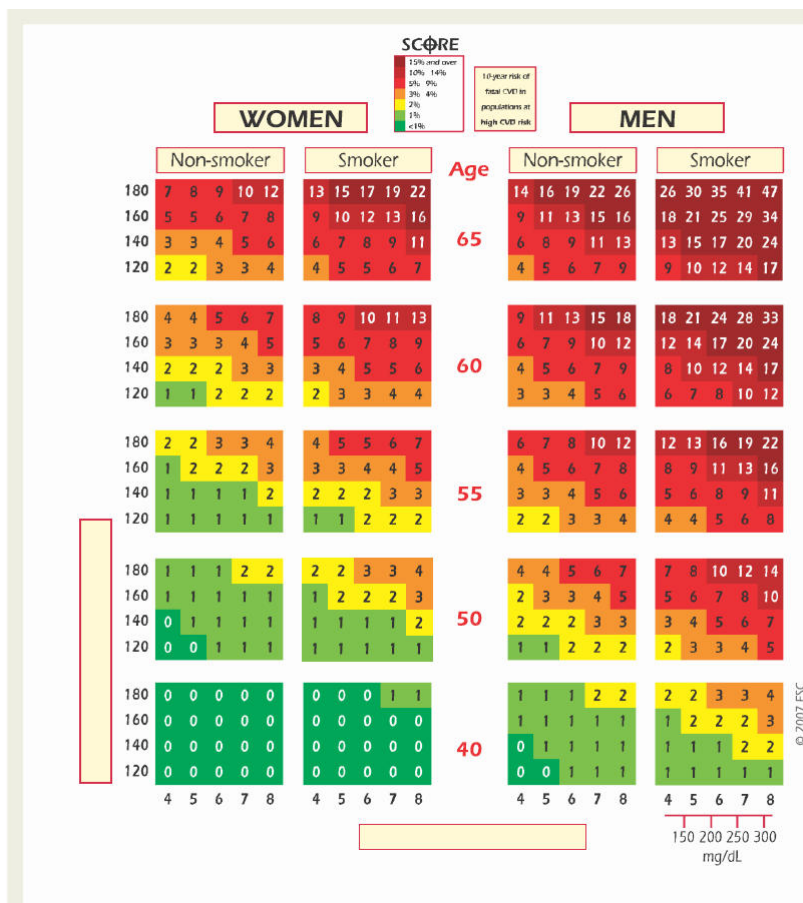


Figure 1. SCORE table: 10-year risk for fatal cardiovascular diseases (CVD) in the countries with high risk for CVD, based on the following risk factors: age, gender, smoking, systolic blood pressure, and cholesterol.

In order to assess the 10-year risk for CV death of a person, the fields with his gender, smoking, and age should be found first. The cell with the closest values of blood pressure and total cholesterol or cholesterol/HDL ratio is then found. Risk assessment is adjusted accordingly (upwards) if the person is close to the next (higher) age category.

Low risk individuals should be advised on how to maintain one’s low risk status. Although there are no universally applicable thresholds, the intensity of advice should increase with increasing risk. In principle, individuals with $\geq 5\%$ risk for CV death should be intensely advised, and they may benefit from medicamentous treatment too. At the risk level of 10%, medicamentous treatment is more often necessary (1).

Years of age constitute a kind of „problem“ in these tables, since they may underestimate the risk in younger individuals. That is why the relative risk table (the same table without years) may be of use in identification and counselling of the young, even in the presence of a low absolute risk level.

The risk may also be higher that estimated in the table in:

Patients with sedentary lifestyle and those with central obesity; increased obesity-associated risk is even higher in younger than in older individuals;

Socioeconomically endangered persons, and in ethnic minorities;

In individuals with diabetes; the SCORE tables should be used only in patients with type 1 diabetes, without target-organ damage; the risk rises with rising blood sugar concentrations before the diagnosis of diabetes;

In individuals with low HDL cholesterol, increased triglycerides, fibrinogen, apolipoprotein B (apoB) and lipoprotein (a) [Lp(a)], especially in combination with familial hypercholesterolemia and increased highly sensitive CRP (hs-CRP). A low HDL level will suggest elevated risk in both genders, in all age groups, and at all risk levels (8).

In asymptomatic individuals with preclinical evidence of atherosclerosis, e.g., carotid artery plaque, seen on ultrasound.

In patients with moderate to severe chronic renal disease [glomerular filtration rate (GFR), 60 mL/min/1.73 m²].

In the presence of positive family history of early CVD.

Who are nowadays the high priority individuals for prevention measures?

The higher the risk, the larger the benefit from prevention efforts, with accordingly set priorities:

1. Individuals with very high risk:

CVD documented using invasive or non-invasive tests (such as coronary angiography, nuclear imaging, stress echocardiography, ultrasound-visualized plaque), survived myocardial infarction, acute coronary syndrome (ACS), coronary revascularization (PCI, CABG) and other procedures of arterial revascularization, ischemic brain stroke, peripheral arterial disease (PAD).

Diabetes mellitus (type 1 or 2), with one or more CV risks and/or target organ damage (such as microalbuminuria 30-300 mg/24 hours).

Severe chronic kidney disease (CKD) (GFR, 30 mL/min/1.73 m²).

Calculated SCORE \geq 10%.

2. High risk individuals with any of the following:

Conspicuous increase of a single risk factor, such as familial dyslipidemia and severe hypertension.

Diabetes mellitus (type 1 or 2), without CV risks and target organ damage.

Moderate chronic kidney disease (GFR, 30-59 mL/min/1.73 m²).

Calculated SCORE of \geq 5%, and $>$ 10% for 10-year risk for fatal CVD.

3. Moderate risk

It is considered that moderate risk individuals have the SCORE of \geq 1 and \leq 5% for 10-year risk for fatal CVD. Many middle aged individuals belong to this category. The risk is additionally modulated using the above criteria.

4. Low risk

The low risk category involves the individuals with SCORE result of 1% in absence of qualifications that would place them in the moderate risk category (1).

How should we today implement CVD prevention using the risk level categories?

As said above, CVD prevention is based primarily on healthy lifestyles and non-pharmacological impact on risk factors. However, medicamentous therapy is warranted already in those with moderate, and especially those with high or very high risk, and those with present CVD or target organ damage. This primarily involves medicamentous control of blood pressure, lipids, and diabetes mellitus.

Blood pressure

The current state-of-the-art is that blood pressure should be lower than 140/90 mmHg in all hypertensive patients. In individuals with I and II degree of hypertension and moderate risk, pharmacological intervention can be postponed several weeks or months in order to assess and validate the effect of lifestyle changes. It is necessary to introduce pharmacological therapy as soon as possible in patients with III degree of hypertension, or those with I and II degree of hypertension if the overall risk estimate is high. Appropriate choice of therapy is of utmost significance, as well as strict patient compliance in the first 6 months of therapy.

Various groups of antihypertensive drugs do not differ much in their effect of blood pressure reduction, so they should be introduced and maintained in the pharmacological treatment. Beta blockers and thiazide diuretics are not recommended in those with multiple metabolic risk factors due to increased risk for diabetes. In diabetics on the other hand, ACE inhibitors or angiotensin receptor antagonists are usually recommended.

All patients with high risk for development of CVD or diabetes, or with 10-year risk for CV death of over 5% (based on SCORE tables) should have statins included in their therapy. Antithrombotic therapy is recommended in all hypertensive patients with any CV event (1, 9).

Diabetes mellitus

The target value of HbA1c for CVD prevention is <7.0% (<53 mmol/mol). Statins are recommended in all cases due to significant reduction of CV risk. Target blood pressure value in these patients is <140/80 mmHg. In patients with complex disease, hypoglycemia and overweight should be avoided. Therapy should be individualized. The first line therapy should be metformin, if not contraindicated and if well tolerated (1).

Lipids

The recommendation for the total cholesterol level is <5 mmol/L (less than ~190 mg/dL) and <3 mmol/L (less than ~115 mg/dL) for LDL cholesterol for individuals with low and moderate risk. In those with high CV risk, target LDL is <2.5 mmol/L (less than ~100 mg/dl). LDL cholesterol <1.8 mmol/L (less than od ~70 mg/dL) or $\geq 50\%$ of the initial value of LDL cholesterol is the target in those with high CV risk. All patients with genetic dyslipidemia have to be recognized and adequately treated with hypolipemic agents. In those with ACS, high dose statins should be introduced while they are still in hospital (1).

Conclusion

Atherosclerotic cardiovascular disease (CVD), especially coronary disease (CD), is today the leading cause of early non-violent death worldwide;

The tendency of reduction of mortality of CVD is today reserved for developed western countries, while in the developing countries it is still the principal cause of mortality, demonstrating even a tendency of growth;

Such a positive trend has been achieved thanks mostly to the favorable impact on controllable risk factors (68%) and improved treatment of CV events (40%);

Any decision on the institution of prevention measures and treatment should be led by the assessment of risk for any vascular event;

People who want to stay healthy should keep the phone number 035140530 as a reminder, meaning: 0 – no smoking; 3 – one 3 km walk a day, or 30 minutes of moderate physical activity; 5 – fruit and vegetable meals eaten five times a day, as raw as possible; 140 – maximum systolic BP; 5 – maximum total blood cholesterol; 3 – maximum LDL cholesterol; 0 – no diabetes mellitus.

These values refer to primary prevention; secondary prevention differs only in the use of medicaments – antihypertensive agents, hypolipemics, antidiabetics – and lower cholesterol values (LDL cholesterol <2.5 mmol/l) and glycated hemoglobin <7 mmol/l.

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2. EPIDEMIOLOGICAL CHARACTERISTIC OF ISCHAEMIC HEART DISEASE AND ACUTE MYOCARDIAL INFARCTION

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Ischaemic heart disease is the leading cause of mortality and morbidity in men as well as in women. Women have their first cardiac event 6 to 10 years later than men do. The aim of the paper was to determine epidemiological characteristics as well as incidence trend and mortality trend of acute myocardial infarction in the city of Niš. Observed period was 2003 to 2012. The data about all the patients aged 30 to 64 were retrospectively analyzed and the analyses was based on the official data from Population-Based Register for acute myocardial infarction of Serbia. The incidence rate, mortality rate, and linear trend were calculated. The method of direct standardization was used and the standardization of rates was done according to the World standard population. Results. The average annual age-standardized incidence rate in men was 147,5 and in women it was 73,8. Age-standardized incidence rate was higher in men than in women for 2 times in average. Age-standardized incidence rate in men younger than 65 ranged from 78,4 (2010) to 188,8 (2007) and in women, age-standardized incidence rate ranged from 20,1 (2010) to 91,2 (2007). The value of incidence trend in men was: $y = -11,74x + 23705$, $R^2 = 0,740$. In women linear trend was: $y = -7,017x + 14141$, $R^2 = 0,679$. The men were 61,8 years old and the women were 65,0 years on the average. In 49,8% men who were younger than 65 and in 41,1% women who were younger than 65, acute myocardial infarction was registered. There were 16,4% fatal acute myocardial infarction (14,4% in men and 25,4% in women). The standardized mortality rate was higher in men than in women for 1,5 times in average. The trend of age-standardized mortality rate in men was: $y = -0,959x + 1955$, $R^2 = 0,271$. The trend of age-standardized mortality rate in women was: $y = -2,086x + 4203$, $R^2 = 0,449$. The average annual age-standardized mortality rate in men was 21,7 and in women 14,8. The average 28 days case-fatality in men was 44,3% and in women 48,5%. Women younger than 45 had greater risk of a fatal acute myocardial infarction and men had greater risk of a fatal acute myocardial infarction at the age from 55 to 64. Conclusions. The increase in both in age-standardized incidence and mortality rate of acute myocardial infarction may be attributed to the increase of the risk factors for acute myocardial infarction both in men and in women.

Key words: acute myocardial infarction, incidence, mortality

3. ULOGA PSIHOSOCIJALNIH FAKTORA RIZIKA U NASTANKU KARDIOVASKULARNIH BOLESTI

3. THE ROLE OF PSYCHO SOCIAL RISK FACTORS IN CORONARY HEART DISEASE

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Abstract

The Etiology of coronary heart disease includes psychosocial factors which are the basis for expression of biological ones. The prevalence of depression is about 20% in the first year after myocardial infarction, higher in women than in men, and associated with increased mortality. Depression tends to take chronic and recurrent course and comorbid anxiety disorders are common. Symptoms of panic disorder overlap symptoms of acute myocardial infarction. Some personality traits like hostility and anger are important in onset and prognosis of coronary heart disease. In type A persons, aggressiveness is consciously well controlled in accordance with good social adaptation. Their emotional tensions remain undischarged and can lead to neurohormonal response that promote atherosclerosis. Social disadvantages: job loss, bereavement and lack of social support are precipitated factors which maintain chronic distress. Changes in behavioral style, treatment of depression and chronic anxiety, therapy for stress reduction and anger control, relaxation therapy are important part of management coronary heart disease.

Key words: Psychosocial risk factors, coronary heart disease

Introduction

Psychosomatic approach to coronary heart disease deals with emotional and behavioral experiences in certain personality type, as crucial causal issues (1). Complex etiology of coronary disease includes psycho-social factors which are the basis for expression of biological ones. Different psychological factors might promote coronary heart disease.

Cardiologists have first recognized close temporal relation between acute coronary syndromes and psychopathological reactions such as: anxiety, depression and hyperactive life style. American Heart Association recommends routine screening for depression in all coronary patients. The prevalence of depression is about 20% in the first year after myocardial infarction, higher in women than in men, and associated with increased mortality (2). This secondary depression is not homogenous diagnostic category but comprise different subtypes, other than endogenous depression in psychiatric patients. Somatic symptoms that are the most prominent, might even reflect the severity of cardiac disease. These patients describe their distressed emotions in physical terms and it is difficult to distinguish them from worsening of coronary heart disease (3). Depression tends to take chronic and recurrent course and comorbid anxiety disorders are common. Depression and anxiety increase symptom severity and functional impairment in cardiac patients. They have often more severe angina and fatigue.

Anxiety is common present in cardiovascular patients and increases the risk of cardiac event if untreated (4). Symptoms of panic disorder overlap symptoms of acute myocardial infarction: sweating, tremor, palpitations. Hyperventilation in panic attack can precipitate coronary spasm in presence of atheroma and increases the risk for development coronary heart disease. In some patients, angina is a cause of panic attacks, and it could be missed

diagnosed as panic disorder (5). Acute anxiety or rage precede acute coronary syndromes and could have trigger role in myocardial infarction. There are still questions if emotional reactions cause cardiovascular dysfunction and influence the survival rate after coronary events (6). Elevated anxiety in the first week after cardiac event is often transient distress reaction to serious life threat.

Prospective studies of health population indicate that alexythymic personality type is prone to coronary disease. The mechanism of suppressing negative feelings without recognition, could influence atherosclerosis by neuroendocrine mechanisms. Some personality traits like hostility and anger are important in onset and prognosis of coronary heart disease. This is person's habitual tendency to experience anger either on minimal provocation or when criticized. It could be expressed as aggression towards other people and objects, inhibited when the feelings are subconsciously suppressed, or voluntarily controlled in an effort to avoid interpersonal confrontation (7, 8). In type A persons, aggressiveness is consciously well controlled in accordance with good social adaptation. High moral standards make them too rigid and scrupulous in interpersonal relations. Their emotional tensions remain undischarged and can lead to neurohormonal response: sympathetic irritation, catecholamine excess.

Psychological factors might cluster together within individuals, they are not uniform across all patients. A disposition to experience psychological distress, in interpersonal and broad social relations, is associated with poor outcome of coronary syndromes. Increased level of stress hormone-cortisol indicates high stress reactivity. Individuals who report a large number of undesirable life events, have blunted cardiovascular reactivity to acute mental stress (9). Psychological factors have indirect impact to outcome via behavior changes. Risk health behavior such as smoking, alcohol consumption, lack of physical activity, are part of passive lifestyle or psychological symptoms.

The outcome of coronary heart disease is influenced not only by cardiac parameters, but by psychological and social as well. Home-coming depression after hospitalization is often enhanced by dysfunctional family relations, poor finances and loss of social position due to chronic disease. The loss of a close person, bereavement and lack of social support enhances distress and cardiovascular disease progression. Moderation of psychological and social factors could improve coronary heart disease prognosis.

Conclusion:

A major challenge is to develop more effective treatments for cardiac patients at risk of poor prognosis and quality of life due to their psychological profile. Therapeutic interventions should be focused to various emotional and social difficulties that patients face. Changes in behavioral style, treatment of depression and chronic anxiety, therapy for stress reduction and anger control, relaxation therapy are important part of management coronary heart disease.

Comprehensive cardiac rehabilitation offers opportunity of psychiatric and psychological treatment when needed.

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4. STRES I KARDIOVASKULARNE BOLESTI

4. STRESS AND CARDIOVASCULAR DISEASES

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Cardiovascular diseases (CVD) are a major cause of morbidity and mortality worldwide. Results from epidemiologic studies show that psychosocial factors such as social environment, personality characteristics, and negative affect increase the risk of incident CVD and affect prognosis of cardiac patients.

There is an enormous amount of literature which suggest that stress has a great impact on health and disease. There are two types of stress: emotional stress and physical stress. Emotional stress is related to our feelings and it is linked to our experience with others, while physical stress is related to physical exertion and can be healthy. Both emotional and physical stress can affect heart and cause increase in heart rate, elevation of blood pressure and release of stress hormones.

Stress can cause a number of consequences on the heart such as heart attack, sudden cardiac death, heart failure, abnormal heart rhythm directly and indirectly. Direct effect of stress is related to acute and chronic stress. Acute stress activates the sympathetic nervous system and cause increase in heart rate and blood pressure, coronary vasoconstriction, and decrease in myocardial electrical stability. Acute stress is related to disasters such as earthquakes. International data demonstrate increased cardiovascular risk after earthquakes, but underlying mechanism for this risk is unclear. Also is noticed that World soccer cup can be trigger for cardiovascular events. One of example of acute emotional stress on the heart is tako-tsubo cardiomyopathy or the "broken heart syndrome" which is a reversible cardiomyopathy, that predominantly occurs in post-menopausal women commonly due to emotional or physical stress.

Chronic stressors activate the hypothalamic-pituitary-adrenal axis producing hypercortisolemia which promotes central obesity and insulin resistance. Chronic stressors also activate the sympathetic nervous system and cause increase in heart rate and blood pressure. People who have had major life changes, such as loss of a spouse or close relative, loss of a job, or movement to a new location, causes an increase in cardiovascular diseases. Psychosocial factors which are connected to atherosclerosis and adverse cardiac events can be divided into two categories: emotional factors and chronic stressors. Emotional factors are related to personality and negative affect. Personality patterns include anger proneness, hostility, type D personality, neuroticism and overcommitment to work. Negative affect include depression and anxiety disorders, and exhaustion, hopelessness and bereavement. Chronic stressors are related to social environment and include low social support, low socioeconomic status, work stress, family stress, and caregiver strain. Emotional factors and chronic stressors often cluster. Individuals who have difficulties at job have higher rates of depression in comparison to those who did not report it. According to INTERHEART case-control study conducted in 52 countries one third of the population attributable risk of myocardial infarction can be assigned to psychosocial factors, including major life events, lack of control over life, depression, stress at work, stress in the family, and with financial issues.

Indirect effect of stress is connected to behavioral causes (individuals under stress are more likely to smoke, drink, over eat, be physical inactive etc).

The effect of positive psychosocial factors are less investigated, but is noticed that some factors such as joy, happiness, optimism, enthusiasm, are connected with lower heart rate and longevity. In healthy populations, positive affects are associated with a reduction in mortality from all causes and from cardiovascular diseases.

The characterization of psychosocial risk factors as “major” cardiovascular risk factors has been debated, but epidemiologic studies showed that psychosocial risk factors and traditional cardiovascular risk factors seem to equally strong predict cardiac risk.

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5. LIPIDI I KARDIOVASKULARNE BOLESTI

5. LIPIDS AND CARDIOVASCULAR DISEASES

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Cardiovascular diseases (CVD) which are the result of atherosclerosis and thrombosis are the leading causes of premature death and disability in the most productive years of life in Europe. In the European Union, its main clinical entities are coronary heart disease (CHD), cerebrovascular accident, and peripheral arterial disease (PAD). Every year 7.2 million people die from coronary heart disease (CHD) around the world, more than from cancer and infectious diseases together.¹ In the United States, 640,000 deaths per year can be attributed to CHD.² The causes of CVD are multifactorial. Among the risk factors that can be modified, in addition to lifestyle and smoking, including high blood pressure, type 2 diabetes mellitus and dyslipidemia. Dyslipidemia is a major risk factor for CVD and its treatment is an essential and integral part of CVD prevention. In recent years, the focus is on the regulation of cholesterol primarily through lifestyle changes, and then applying the medication. HMG - CoA (3 - hydroxy - 3 - methylglutaryl - coenzyme A) reductase inhibitors, or „statins“ are still the basis of the regulation of dyslipidemia.³

Pathophysiology

Cholesterol is a lipid that is primarily used as a precursor of steroid hormones and bile acids, as well as the major component of cell membranes. Cholesterol necessary to perform normal life functions produced by the body, but is derived from exogenous sources, ie. from food. Cholesterol levels in the blood reflects about 40% to 60% of endogenous cholesterol, the rest comes from food. Triglycerides, which consist of non esterified fatty acids and glycerol are used as energy substrate and are obtained from fats in the diet and the conversion of carbohydrates into fat.¹ Cholesterol, triglycerides and other lipids in the body is transported through the bloodstream into spherical particles called lipoproteins. Lipoproteins can be divided into five main categories depending on their composition: the largest and least dense to the smallest and most dense, compose chylomicrons (VLDL), intermediate - (IDL), low density lipoprotein (LDL) and high density lipoproteins (HDL) (Table 1).¹ More mobile particles have a core rich in triglycerides, while smaller particles have a higher density core of LDL cholesterol LDL esters,⁴ approximately 60% to 70% of total serum cholesterol, HDL is around 20% to 30% of total serum cholesterol as VLDL makes up about 10% to 15%.^{5,6} Cholesterol comes from two sources: exogenous source - from the systemic circulation via the intracellular and endogenous synthesis.^{7,8} Exogenous way lipoprotein metabolism is responsible for the synthesis, transport and catabolism of lipoproteins.⁷ Saturated, monounsaturated and polyunsaturated fats and cholesterol esters are digested and absorbed in the proximal small intestine and then restructure and packed in Chylomicron particles in the cells of the intestinal endothelium.⁴ Thus, chylomicrons are primarily composed of fatty acids and cholesterol that come from diet and apolipoproteins. These chylomicrons are then delivered to the lymphatic system and travel throughout the body while the enzyme lipoprotein lipase does not dissolve in the capillary beds of the Chylomicron remnants, which are smaller, contain fewer fatty acids, but kept apolipoproteins B - 48 and E. These residues are then removed from the circulation by LDL - receptor that is found in the liver.⁷ In addition to renewing their supplies from exogenous sources of cholesterol, cells can synthesize its cholesterol through endogenous way. Intracellular cholesterol synthesis involves a series of

biochemical reactions that start from acetyl - CoA (Fig. 1). The enzyme HMG - CoA synthase catalyzes the conversion of acetyl - CoA to HMG - CoA, and HMG - CoA reductase catalyzes the conversion of HMG - CoA liver in mevalonic acid which is used further in the biosynthesis of cholesterol. Statins or HMG - CoA reductase inhibitors competitively inhibit this enzyme and reduce the ability of cells to synthesize cholesterol.⁹ Fatty acids and cholesterol produced by the body pass through the so-called. time endogenous lipoprotein metabolism.⁷ The three main lipoprotein involved in this way: VLDL, LDL, and HDL.⁷ Triglycerides can not be synthesized in the liver, especially in the presence of excess carbohydrates, and then secreted into the bloodstream as VLDL. These VLDL particles contain about five times more triglyceride than cholesterol, and contain apolipoproteins B - 100, E, and C - II. B and E proteins are the link with BE or LDL receptors on the cell surface, and apolipoproteins C - II functions as a cofactor for the enzyme lipoprotein lipase. When secreted into the bloodstream, the molecules to hydrolyze triglycerides in VLDL particles by lipoprotein lipase, which is located in the capillary beds. According to the release, and free fatty acids are used for energy production, particularly for heart and skeletal muscle and is stored in fat cells.⁴ However, the process of lipolysis lowers triglycerides and VLDL particle size, preparing them for one of their two known metabolic fate: cleansing the liver via receptor or further release of triglycerides leading to the formation of IDL particles.

IDL particles in addition to triglycerides containing almost all of the original VLDL cholesterol particles. Lipolysis continues through the action of lipoprotein lipase and liver lipase, and caused much less cholesterol - rich LDL particles. By this time, apolipoproteins E and C are removed, leaving only apolipoproteins B -100 in LDL particles. IDL particles are, therefore, an intermediate product between VLDL and LDL particles and therefore have a short life span. Their cholesterol and triglyceride content does not significantly affect the measurement of cholesterol.⁷ Except in rare dyslipidemia, less than 5% of cholesterol circulating in the IDL particles.⁴ Half of the IDL particles are removed from the circulation by the LDL receptor, and the other half is converted to LDL particles. LDL is the primary atherogenic lipoprotein, and the smaller the size of LDL particles that easily penetrate the subendothelial tissue, which contributes to the development of atherosclerosis.⁷ Excessive circulating LDL cholesterol causes the deposition of cholesterol out of cells and the formation of atherogenic plaques in the vascular endothelium, which can lead to coronary artery disease (BKA).^{5, 6} Two types of LDL particles are associated with a high risk of coronary atherosclerotic disease. First, lipoprotein (a) [Lp (a)] particles, very small LDL particles surrounded by a protein similar to plasminogen. Another subclass of small, dense LDL particles is called atherogenic lipoprotein phenotype B. This subclass can be found in about 30% of the population and is associated with a high risk for BKA. The third major lipoprotein involved in an endogenous way the HDL. Similarly, LDL, HDL particles are rich in cholesterol and very small. However, HDL particles appear to be involved in the reverse transport of cholesterol, leading to anti atherogenic effect. In particular, HDL can prevent or remove deposits of cholesterol in the arterial wall. Another possible explanation for the role of beneficial HDL cholesterol levels are as follows: (1) prevents the oxidation of LDL by acting as an antioxidant, (2) reduces platelet aggregation by increasing the production of prostacyclin (3) stabilizes prostaglandin levels and promotes fibrinolysis, (4) competitive prevent download of LDL endothelial cells, (5) prevents LDL collection and entry into macrophages, (6) reduces cholesterol and the formation of foam cells, and (7) inhibits platelet activation by LDL - TV fosfatidilinozitol time. An important function of HDL is that it may serve as a marker for abnormal metabolism of chylomicrons and VLDL particles. When you increase the concentration of triglycerides, reduced HDL and.

The two key enzymes involved in the transport of cholesterol from the periphery to the liver, where it can be eliminated by using the HDL particle. Lecithin-cholesterol acyltransferase is responsible for the conversion of cholesterol from HDL particles insoluble esters, causing divisions in the core of these lipoproteins. Another enzyme, cholesterol ester transfer protein involved in the transfer of cholesterol esters from HDL particles to triglyceride-rich particles in exchange for triglycerides molecules. Once in VLDL and IDL particles, cholesterol is transported to the liver for elimination (Figure 1).

All three lipoproteins are very actively involved in the transport of triglycerides and cholesterol from the liver to the periphery where they can be used by the cells from the periphery to the liver where it can be eliminated. If the amount of cholesterol is insufficient to meet the demands of any cell, the cell will regulate its synthesis of LDL receptors. The newly formed LDL receptors will migrate to the surface area of the cell called coated pits. Once in coated pits, cells capable of recognizing circling lipoproteins containing apolipoproteins B and E (VLDL, IDL, and LDL particles). And VLDL and IDL particles contain B and E proteins and therefore may have a higher binding affinity for the LDL receptor than LDL. Once binding occurs, lipoproteins are internalized into cells, liposomes are taken up and break down the natural substances used cells. LDL receptor protein back to the cell surface where it can bind to other circulating lipoproteins, repeating process.⁷

Cholesterol and coronary heart disease

The processes through which lipids and lipoproteins participate in the creation of the atherosclerotic plaque of coronary heart disease are still the subject of investigation and controversy. One of the initial event is the formation of atherosclerotic plaques entry lipoproteins LDL and Lp (a) in the subendothelial space with their modified products, the process of oxidation by free radicals arising from the smooth muscle cells, activated macrophages and endothelial cells. These oxidatively modified lipoproteins enter the macrophage via receptors, scavenger, forming a lipid-rich cell bubbly. Monocytes from the circulation are also attracted by the smooth muscle cells and endothelial cells. Scavenging receptors on macrophages continuing to take oxidatively modified lipoproteins, continuing formation, foam cells, and progression to the next level of atherogenesis, formation of fat streaks. At the same time, smooth muscle cells migrate into the subendothelial space and begin proliferation within the intima, contributing to overall atherogenic process. If the process continues, the lesions grow at the expense of smooth muscle cell proliferation and collagen synthesis. Necrosis foamy cells and formation of extracellular lipid core lasts as long as the levels of LDL cholesterol increased. The final step occurs involving autoimmune inflammatory response that causes the infiltration of T lymphocytes in the adventitia (end process covering the vessel connective tissue). Inflammation complete the process of forming plaques underlying coronary artery disease.⁷

Dyslipidemia

Classification of dyslipidemia

Dyslipidemia may be due to genetic predisposition, secondary causes or combinations thereof.¹ Cholesterol and triglycerides can lead to the emergence of three forms of dyslipidemia: hypercholesterolemia, hypertriglyceridemia, or a combination thereof. However, dyslipidaemia is the result of increasing the number or composition changes and increased specific lipoprotein molecule which is important in choosing the right treatment.⁴ Dyslipidemia may be due to other diseases (secondary dyslipidemia) or may be an interaction between genetic predisposition and environmental factors. Increased levels of total cholesterol (UH) and low-density cholesterol (LDL-C) is given most importance, primarily because their levels can be modified by changing lifestyles and using certain medications. In addition to

high levels of carbohydrates and LDL-C, several other types of dyslipidemia may predispose premature CVD. The most common association of elevated levels of certain types of lipids that leads to cardiovascular disease is the so-called atherogenic triad, which implies the existence of high levels of very low density lipoproteins (VLDL), moderately elevated triglycerides (TG), high LDL-C and decreased levels of high-density cholesterol (HDL -H). Evidence of clinical studies are limited in efficacy and safety of drugs that act on the regulation of cholesterol levels of these particles with the aim of primary and secondary prevention of CVD. Dyslipidemia may be compared with a genetic predisposition and/or comorbidities.

GUIDELINES FOR THE TREATMENT AND DIAGNOSIS

Guidelines for the diagnosis and treatment of patients with high blood cholesterol levels are created by the review panel for the treatment of adult American National Programme for Education of cholesterol (NCEP ATP II). These guidelines provide the framework for most treatment decisions based on the design of therapeutic regimes.

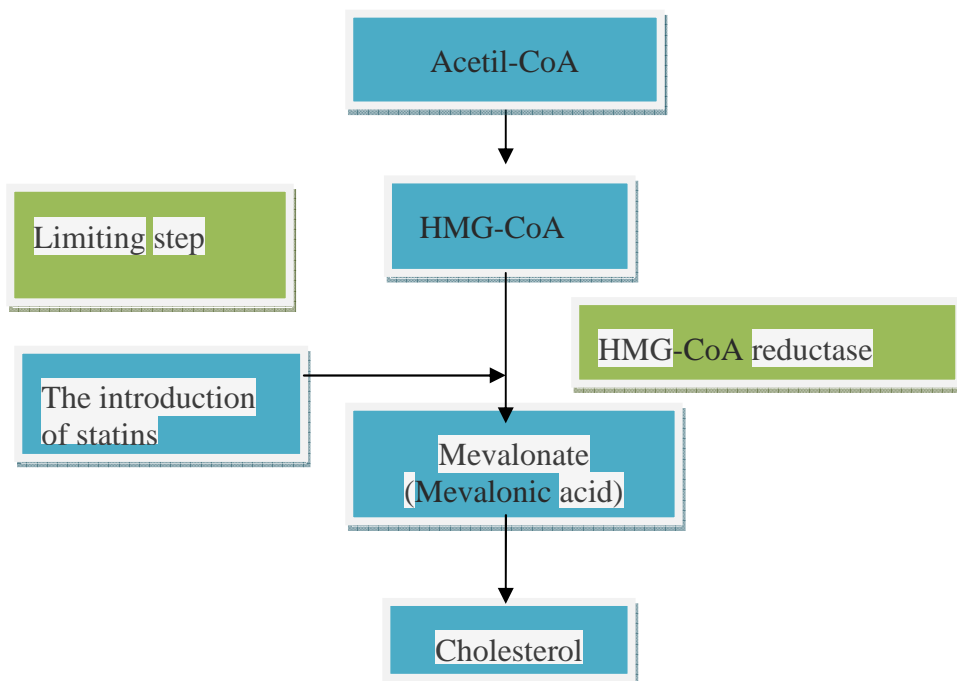


Figure 1. Biosynthesis of cholesterol. „Limiting step“ of the enzyme HMG-CoA at levels that statins reduce

Primary prevention

Primary prevention aims to prevent the onset of cardiovascular disease in people who have no clinical manifestations of the disease. For this group of patients is desirable total cholesterol level of 200mg/dl or below 200-239 mg/dL is the value for the high, and 240 mg/dL high cholesterol level. It is important to measure the level of HDL cholesterol because it is possible that the concentration of any other faction cholesterol HDL - C are reduced (<35 mg/dL). It is well known that low HDL - C increase the risk for CVD. NCEP recommendations is that patients older than 19 years to once every 5 years to determine the levels of total cholesterol and HDL - C. In addition to achieving the target total cholesterol and HDL - C, a change of lifestyle in order to prevent the development of CVD. LDL - C determined using the formula: $LDL\ H = (H\ total - HDL\ H) - (TG/5)$.

The equation loses accuracy when triglycerides are above 200 mg/dL, and the values of more than 400 mg/dL equation will show falsely low LDL - C. Although expensive, the direct measurement of LDL - C may be useful in the initial treatment of CV patients whose TG specific glucose above 400 mg/dL in patients with diabetes, people with vascular disease whose TG above 250 to 300 mg dL. People with cholesterol at the upper limit (200 to 239 mg/dL), HDL - C in the reference values, and less skilled than two risk factors should be advised of the change in lifestyle and the value of total and HDL - C re- designate of 1 to 2 years. Patients with LDL cholesterol between the upper limit value and high-value, low HDL cholesterol, or two or more cardiovascular risk factors should undergo fasting lipoprotein analysis. Those with total cholesterol of 240 mg/dL or higher were classified as having a high risk for future coronary events and need for them to do fasting lipoprotein analysis, regardless of the level of HDL - C. Patients can be further divided into groups according to LDL - C. People with LDL - C in the reference frames (< 130 mg/dL) do not require further investigation. Education and counseling on lifestyle changes designed for the general population could be applied here, as the re-determination of LDL - C proposes after 5 years. People with LDL - C between the upper limit and high (130 to 159 mg/dL) and less than 2 other skilled risk factors should be educated on changing habits and determine the level of LDL - C for 1 year. People at high risk with values ≥ 160 mg/dL and 2 or more risk factors KV should be subject to further investigation and diet to reduce cholesterol levels.

All patients should be categorized on the basis of the average values of 2 measurements of LDL - C. You should also check the existence of secondary causes of hypercholesterolemia, including hypothyroidism, nephrotic syndrome, diabetes, and various forms of hereditary dyslipidemia. An overview of these patients should include a search for evidence of the existence of atherosclerosis and laboratory assessment of renal, hepatic and thyroid function, the presence of *diabetes mellitus*, as well as urine analysis in order to identify potential proteinuria.

As noted above, patients with no known cardiovascular disease or other atherosclerotic disease, with LDL -C ≥ 160 mg /dL and less than 2 KV risk factors or LDL - C ≥ 130 mg/dL and 2 or more risk factors KV should start with lifestyle changes to LDL - C was below the reference value. If, after compliance with recommended measures to change the lifestyle and after 6 months of LDL - C is 190 mg/dL or higher in those with less than 2 KV risk factors, or 160 mg/dL or greater in patients with 2 or more factors KV risk, consider the use of medications. In adult men younger than 35 years and premenopausal women, the critical value for initiation of drug therapy are ≥ 220 mg/dL. Treatment of dyslipidemia is an integral part of the reduction in total cardiovascular risk. The European Society of Cardiology latest version of the European guidelines for CVD prevention published 2007a. year, in 2012. The latest modifications were made. These guides are important not only to doctors and specialists, and cardiologists, but also specialists in biochemistry dealing with the problem of dyslipidemia that is difficult to classify and treat.

Who should control lipid levels in the blood

Screening for risk factors, including lipid profile and in adult males over the age of 40 and women over 50 years of age or postmenopausal women, mainly if they have additional risk factors. In patients with evidence of atherosclerosis in any vascular bed, or type 2 diabetes, regardless of the year there is a high risk for CVD, and it is necessary to determine the lipid profile. People with family history of premature KB also deserve early screening of lipid profile. Several clinical syndrome is associated with early KB: arterial hypertension, central obesity (waist circumference in European of ≥ 94 cm for men, ≥ 80 cm for women).

Autoimmune chronic inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, and psoriasis are associated with an increased risk for CVD. Patients with chronic kidney disease (GFR <60 mL/min/1.73 m²) are also at increased risk for coronary events and to do screening for dyslipidemia. To seek clinical manifestations of genetic dyslipidemia, including ksantomatoze, xanthelasma and premature arcus created cornealis as they may indicate the presence of serious damage to lipoproteins, especially familial hyperlipidemia, the most common monogenetic disorder associated with premature KB. Antiretroviral therapy may be associated with atherosclerosis akceleriranom. The indication for a screening of dyslipidemia in patients with peripheral arterial disease (PAB) or in the presence of thickened carotid artery intima or plaque on them. Finally, it is indicated screening offspring of patients with severe dyslipidemia (FH, familial combined dyslipidemia (FCD) or chylomicronemia) and their monitoring in specialized clinics if any of these lipid abnormalities.

Also, for those who have experienced premature KB, to look for significant lipoprotein disorders in family members (Table 1). Assessment of basal lipid includes UH, TG, HDL - C, LDL - C. It can also determine the relationship apo B and apo B/apo A1, which is a good marker of risk than traditional lipid parameters.¹⁰ Analyses are performed after fasting or not? If possible, a blood sample analyzed after 12 hours of fasting, and for the determination of fasting TG previously required. A large number of clinical studies that have included high - risk patients, have shown that lowering TG and/or LDL - C is associated with a statistically and clinically significant reduction in cardiovascular mortality. Therefore, the level TG and LDL - C remains the primary objective of treatment in clinical practice and guides. Total cholesterol In screening programs, it is recommended to use the values of total cholesterol (UH) for the assessment of total cardiovascular risk SCORE system. In individual cases, the value of carbohydrates can lead physicians astral, especially in women who often have elevated levels of HDL - C in persons with diabetes or metabolic syndrome (MetS), which often have low HDL - C. For adequate risk analysis is necessary to determine the minimum value of HDL - C and LDL - C. The assessment of the overall risk does not mean patients with familial hypercholesterolemia or those with UH ≥ 8.0 mmol/l. These patients are still at increased risk and deserve special attention.

Drugs for the treatment of hypercholesterolemia

The level of cholesterol in the blood is determined of multiple genetic factors and environmental factors, especially eating habits. Hypercholesterolemia may be a secondary phenomenon in other conditions the existence of which should be considered before treatment.

Statins

The mechanism of action

Statins reduce cholesterol synthesis in the liver of a competitive inhibitor of HMG - CoA reductase. The reduction of the intracellular concentration of cholesterol causes the expression of receptors for LDL cholesterol on the surface of hepatocytes, which results in increased extraction of LDL - C from the blood and reducing the concentration of circulating LDL - C and other apo - B lipoproteins including TG - rich particles. Effectiveness in clinical trials Statins are the most studied drugs in the prevention of KV. Numerous clinical studies have shown that statins substantially reduce skilled morbidity and mortality in primary and secondary prevention.^{11,12} It was shown that statins slow the progression or even may lead to regression of coronary atherosclerosis.¹³⁻²¹ Large meta-analysis of 170 000 patients in 26 randomized trials of statins showed 10% reduction in all-cause mortality and 20%

proportional reduction in deaths from coronary heart disease for each decrease in LDL - C of 1.0 mmol/L.²² The risk of major coronary events was reduced by 23% and the risk of stroke was reduced by 17% for each decrease in LDL - C of 1 mmol/L. The proportional reduction in major CV event rates for each mmol/L LDL - C was very similar in all groups. Benefit was significant during the first year, but was higher in the coming years. There was no increased risk for any specific non- skilled cause of death, including malignancy in patients who were taking a statin. Increased risk of rhabdomyolysis with statins was small and insignificant. Compared to the cost - benefit ratio and quality of life, caution is needed in prescribing statins for primary prevention to persons with low total KVrisk.²³

The maximum recommended dose depends on the type of statins and their capacity for lowering LDL - C. Study data suggest that the clinical benefit depends not so much on the type of statin as the degree of reduction of LDL - C, but also the type of statin affects the degree of lowering LDL - C in selected patients.²⁴ Statins may have a direct vasoprotective impact. Numerous pre- clinical studies suggest that statins may affect the vasculature through a mechanism mediated with or without LDL. These mechanisms are often called „pleiotropic effects“ and include suppression of chronic inflammation and improving endothelial dysfunction. A potential molecular mechanism of pleiotropic effects related to the change izoprenilacije protein.²⁵ The primate model that included animals with atherosclerosis pravastatin is administered or applied to reduce dietary lipid titration to the same level of cholesterol during the 2 years. Coronary arteries of animals (monkeys) who were given pravastatin showed higher dilatatornu Func „stable“ plaques (composition).²⁶ There is evidence of the rapid action of statins such results ARMYDA (Atorvastatin for Reduction of Myocardial Damage During Angioplasty) study, which also shows the vascular protective mechanisms. Quantitative clinical significance of these effects in humans remains a subject of debate because they occur parallel to lower the levels of LDL and it is difficult to separate. With the help of alternativnih drugs that lower LDL levels - CETP inhibitors and PCSK9 antibodies - can get additional information on the use of biomarkers of inflammation and endothelial dysfunction tests in humans. In the popular press and to some extent in the medical literature, statins have gained (not all) so undeserved reputation as the „magic bullet“ for the prevention of CVD. However, they do not treat the clinical benefit derived from the prevention of myocardial infarction, but in circumstances where myocardial infarction does not contribute significantly to most causes of death or morbidity, as is the case for example with terminal heart failure, lowering LDL less likely contributes to survival.²⁷ One of the recent paradigm was to lower LDL levels prevent the growth of plaque and reduce local inflammation, and decrease HDL - C can induce lesions in cholesterol reduction and encourage their regression. This mechanistic understanding is undermined by the results from the Dal-OUTCOMES, AIM-HIGH and HPS2-THRIVE (NCT00461630) study, in addition to early results from FIELD and ACCORD study. Expected is a clear benefit in particular from Dal-OUTCOMES (HDL - C increased by 30%) and HPS2-THRIVE (HDL - C increased by 14%) studies, but even in subgroups with large increases in HDL - C, low LDL - C and low or triglycerides in patients with a large increase in HDL - C, dalcetrapib and ER niacin/laropiprant did not lead to a reduction in cardiovascular risk. It could be argued that a well - controlled LDL levels (mean of 63 mg/dL) seen at the beginning of HPS2-THRIVE, is required significantly greater increase in HDL - C was shown to benefit overall, but these data have led to a reconsideration of the role HDL in atherosclerosis, especially considering the effects of elevated HDL - C when the person receives the optimal dose of statins.

There is a clear need for a deeper understanding of the function and its HDL particles in the prevention of CVD. The answers will give a detailed study of lipoproteins in studies such as HPS3-REVEAL (NCT01252953) with anacetrapibom and accelerate (NCT01687998) with

evacetrapibom. A further reduction of low density lipoprotein by using high doses of statins. There is no general consensus on niouou LDL - C as a therapeutic target, but many of the recommendations used this as a basis for aggressive treatment in patients (including asymptomatic with CVD). In the era of the development of generic statins advocated the approach that the lower the LDL - C is better in primary and secondary prevention. However, the clinical and economic evidence such claims may only be designed specifically for the study and goals.²⁸ If the focus in the near future, more aggressive lowering of LDL, you should still consider this approach in theory and practice. Doctors are concerned about the possible side effects of treating most patients with low or moderate to high doses of statins in practice, but are now facing the challenge to start high and continue up to a maximum dose – tolerance where the step of side effects such as muscle bol.²⁹ increase doses (up - titration) is usually achieved by doubling the standard dose of statins, which are on average only 6% further reduce LDL - C, probably due to counterregulatory mechanisms, such as increased intestinal absorption of cholesterol and secretion of PCSK9. Considerations should focus on increasing the susceptibility to develop type 2 diabetes on statin therapy, adverse events, which appears to be dose - dependent, and can be a problem for those with pre-existing risk factors for diabetes. The effects of statins may increase additional diabetogenic properties of other agents as seen in HPS2-THRIVE where there is a worrying increase in the incidence of de novo diabetes (1.8 % higher incidence than placebo), and complications of diabetes (3.7% absolute increase) when the niacin/laropiprant was added to optimized statin therapy.

The use of small doses of statins leads to lower LDL - C 100 mg/dL and the incidence of cardiovascular disease by 15 % (25% relative risk reduction). If the LDL - C decreased to 94 mg/dl, after further doubling doses of statins, it is transferred to a further reduction in risk of 3.4% and an absolute risk reduction of only 0.5%. Therefore, while doubling the statin dose is recommended in the guidelines, it should be recognized that this leads to a moderate additional risk reduction compared with the effect of the initial dose. The use of statins a lesser dose or medium dose range may be a better alternative. What does the future hold? Given the recent research results, we have more questions than answers, eg. what to do next in the prevention of cardiovascular disease? Certainl, the most important short-term goal is to discover the so-called „residual cardiovascular risk“ in patients on optimal statin therapy, to modify it and show the main targets for intervention. A retrospective analysis of studies on lipid lowering identify subgroups that may benefit from the use of fibrates that additional regulation of lipid using other drugs. For example, a post hoc analysis of patients with diabetes and those with low HDL - C (0.9 mmol/l) and high levels of triglycerides (TG over 2.3 mmol/L) showed a potential benefit from the use of fibrata.³⁰ However, it should be considered in light of the negative results of HPS2-THRIVE in the entire study population and TG/HDL subgroups. It is clear that the extensive knowledge needed to understand the epidemiology of cardiovascular disease in patients on statins, as well as to do the risk assessment so as to obtain optimal treatment strategies. Mora et al. in the analysis of new targets in the treatment of TNTs study (Treating to New Targets) found that patients on therapy, serum lipids, including apolipoproteins B and A1 are more predictive, and relatively greater importance have increased non - lipid markers (eg age, sex and smoking).³¹ Other reports suggest that risk in studies with statins significantly lower than in prospective observational studie.^{32,33} A meta-analysis Boekholdt et al. showed predictive significance HDL - C and thus left it as a therapeutic target in intervention.³³ New lipid-lowering drugs will be tested in the light of optimized statin therapy, which, as noted above, provides limited insight into the effectiveness in terms of short-term reduction in the absolute risk. However, when proven to be effective, new drugs can be applied to other groups of patients, such as those who are intolerant to statins or those whose statin therapy can not be adequately dosed due to dose-dependent adverse effects. PCSK9 inhibitors is applied in the form of

weekly/monthly injections have the potential not only as an effective treatment to lower LDL - C but also in addressing compliance issues. Approximately one-third of medicines for chronic diseases such as hypertension, diabetes, coronary heart disease and hyperlipidemia are not taken regularly and adherence to treatment with statins is directly related to the outcome of the primary and secondary prevention.^{34, 35} Other strategies to increase the compliance and reduce clinical inertia are needed to create optimal prevention programs. Additional features to look for in testing agents that reduce lipid levels in patients not on statin pr. for real intolerance to statins or in the initial primary prevention. Studies, however, difficult to implement due to the required large sample size (leading to problems in recruiting patients) and long periods of follow-up patients (follow-up). Further strategic initiatives for statins and new, effective agents need to adopt a more layered approach to medicine where information from genomic analysis and biomarker provides a pathophysiological basis for interventions customized and personalized with a predictable outcome.

Such an approach would increase the clinical benefit and cost-effectiveness. Finally, in collaboration with health economists, epidemiologists, to adopt the methodology of life-long need for regulation of lipid levels. Moving the focus of the „first coronary event“, the terms „illness trajectory“, „lifetime benefit“ and „year acquired health“ is a necessity. This will undoubtedly reinforce the need for early intervention and beyond. In short, promising new agents in reducing lipid that is currently being developed but need to be tested with realistic expectations of patients selected according to the pathophysiology of dyslipidemia and the specific pharmacology of the drug. Hoping to find a drug that is used for each of the risk of vascular disease called. „Other statin“ must be considered a challenge because statins significantly reduce the so-called residual risk. Which is especially important in patient populations such as individuals with high LDL - C to a maximum of tolerating doses of statins, those with high or dysfunctional HDL, high lipoprotein (a), selected patients with high triglycerides or patients with atherogenic LDL. Care must be taken not to eliminate the study of drugs that could save lives, selected sub-groups design of clinical trials on the basis of erroneous expectations for drugs that would be an adjunct to statins.³⁶

Table 1. Recommendations for lipid analysis in the assessment of cardiovascular risk (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	CLASS	LEVEL OF EVIDENCE
Total HOL is recommended to assess the overall risk of the SCORE system.	I	C
LDL-C in the primary screening and risk assessment.	I	C
TG provide additional information on risks and indicated in his assessment.	I	C
HDL-C is a powerful risk factor is indicated in his assessment.	I	C
Non-HDL-C as an alternative risk factor, particularly in combined hyperlipidemia, DM, MetS kidney disease	IIa	C
Lp (a) to be considered in high-risk patients with a family history of early occurrence of CVD	IIa	C
Apo B as an alternative risk factor, particularly in combined hyperlipidemia, DM, MetS kidney disease	IIa	C
ApoB/apoA1 ratio can be recommended as an alternative to risk assessment. Combines both risk factors.	IIb	C
Non-HDL-H/HDL-H ratio can be recommended as an alternative to risk assessment.	IIb	C

Table 2. Recommendations for lipid analysis in the assessment of dyslipidemia before treatment (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	CLASS	LEVEL OF EVIDENCE
Determination of LDL-C as the primary lipid analysis.	I	C
TG provide additional information about the risks and benefits for the diagnosis and treatment choices.	I	C
HDL-C should be determined before starting therapy.	I	C
Non-HDL-C for further characterization of lipid disorders especially in combined hyperlipidemia, DM, MetS kidney disease.	IIa	C
Apo B for further characterization of lipid disorders especially in combined hyperlipidemia, DM, MetS kidney disease	IIa	C
Determination of Lp (a) to be considered in high-risk patients with a family history of early occurrence of CVD	IIa	C
Total HOL may be considered but is usually insufficient for the characterization of lipid disorders before treatment.	IIa	C

Table 3. Recommendations for the analysis of lipids as targets for the prevention of CVD (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	CLASS	LEVEL OF EVIDENCE
LDL-C as the goal of treatment.	I	A
Total cholesterol as a target in the treatment is recommended only if other analyzes are not possible.	IIa	A
TG should govern the treatment of dyslipidemia with high TG.	IIa	B
Non-HDL-C as an alternative target for the treatment of combined hyperlipidemia, DM, MetS kidney disease	IIa	B
Apo B should be considered as a secondary endpoint in the treatment.	IIa	B
HDL-C is not recommended as the treatment goal.	III	C
ApoB/apoA1 ratio and the ratio ne-HDL-H/HDL-H are not recommended as the treatment goals.	III	C

Table 4. The influence of lifestyle changes in order to reduce total and LDL-HOL C (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	EFFECT SIZE	LEVEL OF EVIDENCE
Reducing saturated fat food	+++	A
The reduction of input trans-unsaturated fat food	+++	A
Increased fiber intake	++	A
The reduction of food intake of cholesterol	++	B
The use of food enriched with phytosterols	+++	A
Reduction of body weight	+	B
The use of soy protein products	+	B
Increase daily physical activity	+	A
The use of fermented red rice	+	B
Use products with polikosanolom	-	B

Table 5. The influence of lifestyle on reducing TG levels (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	EFFECT SIZE	LEVEL OF EVIDENCE
Reduction of body weight	+++	A
Reducing alcohol intake	+++	A
Reducing intake of mono-and disaccharide	+++	A
Increase daily physical activity	++	A
Reducing carbohydrate intake	++	A
The use of supplements with n-3 polyunsaturated fats	++	A
Replacing saturated fats with mono-and polyunsaturated fats	+	B

Table 6. The influence of lifestyle on increasing HDL-C (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	EFFECT SIZE	LEVEL OF EVIDENCE
The reduction of input trans-unsaturated fat food	+++	A
Increase daily physical activity	+++	A
Reduction of body weight	++	A
Reducing carbohydrates and replacing them with unsaturated fats in the diet	++	A
Moderate alcohol intake	++	B
The carbohydrates rich foods onus choose a low glycemic index and high in fibers	+	C
Stop smoking tobacco	+	B
Reducing intake of mono-and disaccharide	+	C

Table 7. Therapeutic goals depending on the level of cardiovascular risk (adjusted by the European guidelines for the treatment of hyperlipidemia 2011)

Total CV risk (SCORE) %	LDL-C levels				
	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.5 mmol/L	100 to <155 mg/dL 2.5 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	>190 mg/dL >4.9 mmol/L
<1	No lipid intervention	No lipid intervention	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled
Class/Level ^b	I/C	I/C	I/C	I/C	IIa/A
≥1 to <5	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled
Class/Level ^b	I/C	I/C	IIa/A	IIa/A	I/A
>5 to <10, or high risk	Lifestyle intervention, consider drug*	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class/Level ^b	IIa/A	IIa/A	IIa/A	I/A	I/A
≥10 or very high risk	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class/Level ^b	IIa/A	IIa/A	I/A	I/A	I/A

Table 8. Determination of lipid profiles depending on cardiovascular risk (modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	CLASS OF EVIDENCE	LEVEL OF EVIDENCE
The lipid profile is indicated in patients with type 2 diabetes	I	C
Confirmed CVD	I	C
Hypertension	I	C
Smokers	I	C
BMI ≥ 30 kg/m ² or waist circumference >94 cm (90) in men, >80 cm for women	I	C
Family history of early cardiovascular disease	I	C
Chronic inflammatory diseases	I	C
Chronic kidney disease	I	C
Family history of familial dyslipidemia	I	C
Lipid profile may be considered in men >40 years and women >50 years	IIb	C

Table 9. Recommendations for the pharmacological treatment of hypercholesterolemia (Modified according to the European guidelines for the treatment of hyperlipidemia 2011)

	CLASS OF EVIDENCE	LEVEL OF EVIDENCE
Recommend statin highest recommended dose or maximum dose that is tolerated to achieve the target level.	I	A
In case of intolerance to statins, bile acid sequestrants or nicotinic acid terebalo to be taken into account.	IIa	B
Cholesterol absorption inhibitor, alone or in combination with bile acid sequestrants or nicotinic acid can be considered in case of intolerance to statins.	IIb	C
If the target value is reached, the statin in combination with cholesterol absorption inhibitors, bile acid sequestrants or nicotinic acid should be considered.	IIb	C

Table 10. Recommendations for therapeutic target LDL-C Depending on the level of cardiovascular risk (Modified according to the European guidelines for the treatment of hyperlipidemia 2011)

Recommendations	Class^a	Level^b
In patients at VERY HIGH CV risk (established CVD, type 2 diabetes, type 1 diabetes with target organ damage, moderate to severe CKD or a SCORE level $\geq 10\%$) the LDL-C goal is <1.8 mmol/L (less than ~ 70 mg/dL) and/or $\geq 50\%$ LDL-C reduction when target level cannot be reached.	I	A
In patients at HIGH CV risk (markedly elevated single risk factors, a SCORE level ≥ 5 to $<10\%$) an LDL-C goal <2.5 mmol/L (less than ~ 100 mg/dL) should be considered.	IIa	A
In subjects at MODERATE risk (SCORE level >1 to $\leq 5\%$) an LDL-C goal <3.0 mmol/L (less than ~ 115 mg/dL) should be considered.	IIa	C

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6. ZNAČAJ ISHRANE U PREVENCIJI KARDIOVASKULARNIH BOLESTI 6. IMPORTANCE OF DIET IN PREVENTION OF CORONARY HEART DISEASE

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Objectives: To review metabolic, epidemiologic, and clinical trial evidence regarding diet and CHD prevention.

Materials and methods: We searched MEDLINE for epidemiologic and clinical investigations of major dietary factors and CHD.

Results: Numerous evidence from epidemiological and clinical studies indicates that at least 3 dietary strategies are effective in preventing CHD: substitute nonhydrogenated unsaturated fats for saturated and *trans*-fats; increase consumption of omega-3 fatty acids; and consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grain products. However, simply lowering the percentage of energy from total fat in the diet is unlikely to improve lipid profile or reduce CHD incidence. Many issues remain unsettled, including the optimal amounts of monounsaturated and polyunsaturated fats, the optimal balance between omega-3 and omega-6 polyunsaturated fats, the amount and sources of protein, and the effects of individual phytochemicals, antioxidant vitamins, and minerals.

Conclusion: Substantial evidence indicates that diets using nonhydrogenated unsaturated fats as the predominant form of dietary fat, whole grains as the main form of carbohydrates, an abundance of fruits and vegetables, and adequate omega-3 fatty acids can offer significant protection against CHD. More studies of genetic variation in relation to CHD are needed.

Key words: diet, prevention, coronary heart disease

Because of the great public health importance of coronary heart disease (CHD), numerous studies have been focused on prevention and early detection of risk factors for atherosclerosis.

Diet is a key modifiable risk factor in the prevention and risk reduction of coronary heart disease (1,2) and the World Health Organization (WHO) and other international and national organizations invest a lot of effort in healthy eating promotion among population. Dietary guidelines have been constantly changing and harmonizing with the current scientific evidences and the characteristics and living conditions of the local population.

The relationship between diet and CHD has been studied intensively for nearly a century. Until recently, most epidemiologic and clinical investigations of diet and CHD have been dominated by the diet-heart hypothesis (3). Although the search for the optimal diet for prevention of CHD is far from over, more specific and firmer evidence on diet and CHD is now available.

The European Society of Cardiology shows that the lifestyle of people with high cardiovascular risk is a major cause of concern with persistent smoking and high prevalence of both obesity and central obesity (4). Although information about healthy diet are available, patients with CHD are experiencing dietary changes mainly as the bans and they do not followed the dietary advice received from their physicians (5).

In Serbia, the situation is probably more complex because the national dietary pattern does not follow the healthy eating guidelines. The dishes of Serbians contain too much fat, especially saturated and cholesterol, and sodium, and not enough dietary fiber, calcium, iron, polyunsaturated fatty acids and vitamin A (6).

The objective of the paper to review metabolic, epidemiologic, and clinical trial evidence regarding diet and CHD prevention.

For this review, we searched MEDLINE for epidemiologic and clinical investigations of various dietary factors (fat, cholesterol, omega-3 fatty acids, trans-fatty acids, carbohydrates, glycemic index, fiber, folate, specific foods, and dietary patterns) and CHD. We selected 147 original investigations and reviews of metabolic studies, epidemiologic studies, and dietary intervention trials relating to diet and CHD.

Certain nutrients have a special significance in the prevention of CHD, especially those with effects of different dietary fatty acids on serum cholesterol levels. All analyzed studies confirm early reports by Keys (7) that saturated fatty acids increase and polyunsaturated fatty acids decrease total and LDL cholesterol. When monounsaturated or polyunsaturated fats replace saturated fat, LDL-C decreases and HDL-C changes only slightly. Moreover, substituting polyunsaturated fat for saturated fat may have beneficial effects on insulin sensitivity and type 2 diabetes (8). However, palmitic acid and myristic acid increase the LDL cholesterol more than that of stearic acid. Thus, people who eat relatively often red meat and other foods with a lot of stearic acid have lower blood cholesterol levels than would expected. On the other hand, those who eat a lot of whole dairy products increase the risk of atherosclerosis. The optimal amounts of monounsaturated and polyunsaturated fats in the diet are still unclear. Intake of linoleic acid is usually recommended not to exceed 10% of energy, in part because of little long-term human experience with such diets, although benefits from higher intake exist for blood lipids.

In numerous controlled metabolic studies, *trans*-fatty acids (found in stick margarine, vegetable shortenings, and commercial bakery and deep-fried foods) have been shown to raise LDL-C levels and lower HDL-C relative to *cis*-unsaturated fatty acids (9) and the increase in the ratio of total to HDL cholesterol for *trans*-fat is approximately twice that for saturated fat.

Adherence to the Mediterranean dietary pattern seems to be related to a lower heart rate (10). In the Lyon Diet Heart Study (11), higher α -Linolenic acid (ALA) consumption in the context of a Mediterranean diet dramatically reduced total and cardiovascular mortality as well as nonfatal myocardial infarction. Other trials also strongly support the protective effects of omega-3 fatty acids, including both ALA and fish oil, in secondary prevention of CHD. Both omega-3 and omega-6 fatty acids have important roles in reducing CHD risk, probably through different mechanisms. Thus, a good strategy is to substantially increase intake of omega-3 fatty acids from fish and plant sources (because intake for many people is clearly suboptimal) without decreasing intake of linoleic acid. This will improve the ratio and maximize the cardioprotective benefits of both omega-3 and omega-6 fatty acids.

In several epidemiologic studies, higher consumption of whole grains was associated with lower risk of CHD. Also, prospective cohort studies have consistently found an inverse association between fiber intake and risk of CHD. Several studies have found a stronger association for cereal fiber than for fruit or vegetable fiber. The low glycemic index foods with a high level of fiber and numerous micronutrients in whole grains may also contribute to the benefits (12).

Much evidence suggests that adequate folate consumption is important for the prevention of CHD (13). The role of phytochemicals and antioxidants in the prevention of CHD is promising

but unsettled. Although a body of experimental evidence has demonstrated the role of antioxidant vitamins in reducing oxidative stress and substantial epidemiologic evidence has linked intake of vitamin E with a lower CHD risk, results from published clinical trials of vitamin E supplements, primarily among patients with clinical CHD, have been largely disappointing (14). Finally, a large and inconclusive literature has examined the relationship between dietary minerals such as calcium, magnesium, zinc, and selenium and risk of CHD (15). Future researches should be directed on the role of genetic factors in modulation of effects of nutrients on CHD.

CONCLUSION

Compelling evidence from metabolic studies, epidemiologic investigations, and clinical trials in the past several decades converges to indicate that at least 3 dietary strategies are effective in preventing CHD: substitute unsaturated fats (especially polyunsaturated fat) for saturated and trans-fats; increase consumption of omega-3 fatty acids from fish oil or plant sources; and consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grains. A combination of these approaches can confer greater benefits than a single approach. However, simply lowering the percentage of energy from total fat in the diet is unlikely to improve lipid profile or reduce CHD incidence. A variety of options exist for designing attractive and heart-healthy diets. Such diets, together with regular physical activity, avoidance of smoking, and maintaining a healthy weight, may prevent the majority of cardiovascular disease in Western populations.

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7. PREVENTION OF CARDIOVASCULAR DISEASES IN GENERAL PRACTITIONER'S OFFICE

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ABSTRACT

In accordance with the Regulation on the scope and level of services to be provided to the adult population, conduction of physical examination, which has the task of precisely detecting present risk factors (RF), it has been planned once in every five years for the population age 35 years and once in every two years for the population of age 35 - 64 years and once in a year for elderly people over age of 64. The protocol treatment of patients during physical examination implies, among other procedures, the procedures for the prevention of cardiovascular diseases with a focus on primary prevention (detection, elimination and reduction of modifiable risk factors) and secondary prevention (early detection, adequate treatment and prevention of any complications). In order to improve the prevention of cardiovascular diseases since 2006, in some health centers in Serbia, the new way of organizational approach to the preventive activities has been revived with the establishment of the Health Prevention Center. This method of organization and delivery of program activities has resulted from the need for preventive action, applicable legislation and the fact that a far greater number of covered patients can be achieved by engaging all staff in primary care with appropriate coordination. The success of prevention and treatment of cardiovascular disease depends to a large degree on the health professionals. However, the decision whether the chosen physician will conduct program activities or not, has not left solely his choice, but also the choice of the patient, who if does not respond to a scheduled check-up has no responsibility and bears no sanctions. It is therefore essential that the country provides financial support of program activities at the primary level, supports the active participation of patients in their own health and penalizing them if they do not.

Keys words: prevention of cardiovascular disease, general medicine, treatment protocol

INTRODUCTION

Given that cardiovascular disease (CVD) are the major socio-economic problems that are associated with high rates of morbidity and mortality in recent years, a number of published clinical recommendations for the prevention of cardiovascular diseases, which are based on the conclusions of national and international group of experts in the field (1).

In countries where the concept of health by eliminating harmful habits dominate health policy, morbidity and mortality rates, use of health services and the demand for emergency admissions or interventions are being gradually reduced, and hence the cost of health care.

For all these reasons it is important that all specialties of doctor's who are in a situation to diagnose and treat cardiovascular disease in their daily work, diagnose and appropriately treat risk factors for their development.

The thesis of the present factors interact in the development of high risk for coronary heart

disease and the thesis of introducing changes in lifestyle as the primary therapy is common for all the recommendations that despite the presence of risk factors emphasize the importance of organ damage, the presence of clinically established cardiovascular disease to assess the risk profile of a people and setting target values present FR to be pursued.

For these reasons, in Serbia in the promotion of preventive the activities of 2004, it is an active search for FR, their complete reduction and elimination, in order to preserve the health of the population.

PROTOCOL OF ACTION IN ORDER TO PREVENT CARDIOVASCULAR DISEASE

In accordance with the Regulation on the scope and level of services to be provided to the adult population, carries out a physical examination which has the task of precisely detecting present FR. The plan is once every five years for the population aged 35 years and every two years for the population of age 35-64, and once a year for population over 64 years (2).

Protocol treatment of patients in the systematic review implies, inter alia, procedures for the prevention of cardiovascular diseases with a focus on primary prevention (detection, elimination and reduction of modifiable risk factors) and secondary prevention (early detection, adequate treatment and prevention of any complications) (3).

Health assessments shall be conducted through a physical examination on the basis of:

- Medical documents not older than 6 months
- Collecting data on personal and family history

The personal history to find out information about the disease (if people with CVD), formerly the usable therapy, the success of previous therapeutic interventions, type and dose of drugs that are currently used, the maximum values of blood pressure and duration of illness.

- Perform a physical examination that includes a review of the systems, blood pressure and anthropometric measurements: body weight, body height and waist
The degree of nutritional status assessed on the basis of waist circumference and body mass index's (BMI). If you are a person with increased body weight learned duration of the presence disorders, data on the effects of previous non-pharmacological and pharmacological health interventions, provide data on pre-existing disorders of lipid metabolism and carbohydrate.

- Perform a survey to detect the presence of behavioral risk factors: alcohol consumption, inadequate diet with excessive intake of salt, the presence of smoking habits as inadequate, the smokers of the degree of nicotine dependence, psychosocial status and estimate the level of physical activity, as well as information on the identification of factors risk to health.

- Determines the presence of risk factors for stratification 10 yearly risk of developing IHD (ischemic heart disease) and other risk factors that are not taken in stratification but may contribute to the emergence of diseases and health damage.

Identify the major risk factors for ischemic heart disease (IHD) implies the presence of: cigarette smoking (with no level of smoking is not acceptable), presence of hypertension (if systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg, or Persons taking antihypertensive medications, the presence of low HDL cholesterol

(<1.0 mmol/L (40 mg/dl)), having a family history of early coronary heart disease (in male first degree relative younger than 55 years old, female relatives in the first degree younger than 65 years) and age (men over 45 and women at 55 years). investigate also the presence or absence of coronary heart disease or its equivalents. necessary to identify and equivalents for IBS which is the presence of clinical atherosclerotic disease, diabetes mellitus and factors that give the 10-year risk for CHD greater than 20% since their presence automatically puts the patient in a high risk category, and also people with coronary disease at high risk for recurrent coronary events. The task is to determine the specific risk factors and risk factors for life habits, that are not imposed on stratification but may contribute to the occurrence of diseases and health damage and may affect the assessment of risk, such as elevated fibrinogen which contributes to hypercoagulated condition, elevated lipoprotein (a) concentrations as a genetic marker of early atherosclerosis, elevated homocysteine, micro albuminuria in diabetes or insulin resistance, obesity, physical inactivity, inadequate style and lifestyle that includes an inadequate diet, excessive intake of alcohol and salt, use of certain drugs can improve the already present factors and failure of therapy. During risk stratification and decision treatment decisions (non-pharmacological/and pharmacological treatment) should be kept in mind that although obesity is a major risk factor for coronary heart disease is not, as such, considered as its impact on risk is considered unaccounted for by other risk factors (diabetes, low HDL cholesterol and hypertension). Should also take into account the fact that HDL cholesterol > 1.6 mmol/L (60 mg/dl) and cardio protective effect is calculated for a "negative" risk factor, and in setting the target LDL cholesterol is one of the risk factors used risk stratification can take in the presence of the HDL cholesterol. Diagnosis of abnormalities in terms of the existence of specific risk factors (LDL, homocysteine, prothrombotic factors and pro-inflammatory factors may affect the intensification therapeutic intervention. quest for a specific risk factors is recommended in patients with moderate risk for ischemic heart disease (≥ 2 main FF and 10 - year risk $\leq 20\%$) or in patients with low-risk (0-1 FR and 10-year risk $<10\%$) with family hypercholesterolemia (indicated by very high LDL cholesterol ≥ 4.75 mmol/l) when necessary and control of lipids in other family members.

- The patient is sent to the laboratory tests (CBC, SE, urine, urea, creatinine, electrolytes (K, Na, and Ca), protein, AST, ALT, gamma GT, lipid (HOL, TGL, HDL-c, and LDL-c) and ECG.

- Are evaluated 10-year risk of fatal cardiovascular events using SCOR model for a country with high risk (4).

This interactive system for risk control provides physicians and patients with information about the regulation of the overall risk of a particular therapeutic intervention and change of lifestyle. Unlike other SCORE model to determine the risk for cardiovascular disease included 10-year risk of fatal cardiovascular event. This model allows determining the risk of cardiovascular disease is projected at 60 years, which allows management of younger patients with low absolute risk but with inadequate style and lifestyle and risk profile, which will be much higher in later years. Determination of the relative risk compared to an absolute risk is of interest for some population groups. So asymptomatic healthy by "risk" of preventive measures to reduce the risk of illness should be provided in accordance with the level of overall risk for cardiovascular disease. People who are at high risk should be according to the target set in the intense change of style and way of life and eventually to medical. Patients with existing cardiovascular disease are classified as very high risk for future vascular events and intensive non-pharmacological and pharmacological treatment is required. SCORE project is the result of a large database of prospective European studies and predicts any fatal atherosclerotic event as a fatal cardiovascular event in the next 10 years. Sex, age, smoking, systolic blood pressure, total cholesterol and total cholesterol/HDL cholesterol are taken as

factors in risk assessment. Limit high-risk was defined as $\geq 5\%$. Based on the SCORE system in the country with reliable information on cardiovascular mortality have already made the national patterns of risk.

- Perform a patient education about healthy style and way of life and reduction of risk factors present at the current official guidelines.
- In accordance with this water and adequate medical records and preventive map where the record all the information obtained in the course of a systematic review.

CENTER FOR PREVENTION-NEW WAY OF ORGANIZING APPROACH TO PREVENTIVE ACTIVITIES

Center for Prevention DZ represents a new way of organizing the provision of access to preventive activities at the health center. This operation started in 2006 in certain health centers. The center has three departments: Resource coordinating educational unit, which role is in patient education, preventive educational unit (which is an each office of a selected general practitioner) to carry out program activities and a mobile unit which main task is to promote health in the community. In the absence of funds to organize health promotion in the community (the state does not allocate funds for these purposes), means that it works by the attending physician within the mobile units providing support to local governments and other actors from the local community. How will he succeed depends on the skill, relationships, goodwill of individuals from the community... and the free time physician has to devote improving population health. Is health promotion obligation only to the medical professionals - as happened in practice or obligation of all: the state, the entire society, health professionals and the individuals themselves? This system of operation of the Centre, came about precisely for these reasons and the need for preventive action, applicable legislation and the fact that a far greater coverage of patients can be achieved by engaging all staff in primary health care in coordination with the Center to coordinate monthly plans, the use of available equipment, analysis of results, analysis of the current problems...

CONCLUSION

Programs on the prevention of cardiovascular disease are introduced at the national level, but their implementation is only at the level of recommendation, one could say, at the level of liability of the chosen doctor but without the active participation of the state, especially in the field of financial support. There is much talk about the importance of FR for the health of the population and the planning of services that must be carried out at the primary level and in accordance with good clinical practice recommendation is to work on the disclosure and modification. It is significant that none of the risk factors should be considered individually but in the context of global risks that provides guidance on the method of treatment and the achievement of the target values of the most important risk factors for coronary heart disease modified the degree of global risk. However, we should bear in mind that the risk factors used in the stratification variables that change and risk calculators can be used to motivate the patient as a guide to treatment, but can't replace clinical judgment. The final decision should be made after a complete clinical evaluation.

What should be noted is the fact that the presence of risk factors does not have to be absolutely high risk over the next year but says the lifetime risk from repeated exposure. The importance of determination and no other risk factors that are present in a person and in

routine practice do not apply or were not taken for the calculation of risk calculators may give false negative results or falsely reassure a person at high risk.

The success of prevention and treatment of cardiovascular disease depends largely on health professionals and application protocols for treatment for the prevention of CVD. However, the decision whether the attending physician conducts program activities or not is left solely his choice but also the choice of the patient, who if does not respond to a scheduled check-up has no responsibility and bears no sanctions. It is therefore essential that the government and financial support for prevention activities at the primary level with the introduction of the active participation of patients in their own health and even sanctioning them if they do not.

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II POSTER PREZENTACIJE

II POSTER PRESENTATIONS

1. PROMOCIJA ZDRAVLJA NA RADNOM MESTU

1. HEALTH PROMOTION AT WORKPLACE

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The health of the modern workforce is changing. The aging of the labor force contributes to the complexity of health needs; chronic disease has become a significant concern for employers, due to escalating health care costs. Preventive medicine has vast unused possibilities for improving the health of the population. Public health in Serbia can be improved by building workplace “cultures of health” that support healthy lifestyles. This paper discusses the possibilities of occupational health future orientation toward holistic medicine, for the sake of workers’ well-being and better quality of their lives, then creation of more humane society and vocational affirmation. Health promotion at workplace and salutogenic concept may have crucial roles. Approaches to changing behavior in the work place may be directed at the levels of individuals, groups of individuals, organizations, or work environments. Ideally, programs are implemented at multiple levels simultaneously because individual efforts at changing behavior tend to more successful if they are complemented by supportive environments. This concept is a huge challenge for academic public and vocational practitioners in poor countries in transition that are already burdened with the current economic and financial crisis. Each in their own way, helped by self-education and education, without big material investments, together they may take their countries to the road of health, the road still rarely taken, yet more secure.

Key words: Public health, Holistic medicine, Occupational health, Salutogenesis, Health promotion at workplace

2. EPIDEMIOLOŠKE KARAKTERISTIKE INFARKTA MIOKARDA U SRPSKIM
SREDINAMA SEVERNOG DELA KOSOVA I METOHIJE
**2. EPIDEMIOLOGIC CHARACTERISTICS OF MYOCARDIAL INFARCTION IN
SERBIAN AREAS OF NORTHERN KOSOVO AND METOHIIJA**

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The Aim: Show the most important epidemiological characteristics of myocardial infarction in the Serbian areas of the northern part of Kosovo and Metohija.

Materials and Methods: As the epidemiological method we used a cross sectional study. As a material for writing paper we used data from the Register of chronic diseases-Bureau of Public Health Pristina, Kosovska Mitrovica.

Results: In the period from 2004. to 2011. on Kosovo and Metohija (Serbian enclaves) 421 patients and 166 deaths from myocardial infarction were reported. In the same period in Serbian municipalities in northern part of Kosovo and Metohija a total number of 349 patients were reported (255 men, 94 women). Most affected were persons aged 55-59 years, 70(20,1%). The highest non-standardized incidence rate was recorded in 2008. year (110,25/100,000 population). The linear trend of incidence rates showed a statistically significant increase ($y = 9.050 x + 21.73$). In the period from 2008. to 2011. year, 97 individuals (54 men and 43 women) died of myocardial infarction. The largest number of deaths were reported in the Kosovska Mitrovica 34(35.1%), with the highest non-standardized mortality rate (60,13/100,000) 2008. year. The linear trend shows a decline in the mortality rate ($y = -13.88 + 69.43 x$).

Conclusion: During 2008. year the largest number of patients and deaths from myocardial infarction was recorded in the Kosovska Mitrovica, among the male sex, age over 55 years.

Keywords: myocardial infarction, Serbian municipalities, Kosovo and Metohija.

3. KARDIOVASKULARNI FAKTORI RIZIKA U SRBIJI 3. CARDIOVASCULAR RISK FACTORS IN SERBIA

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¹Dom Zdravlja Bela Palanka

Introduction: Cardiovascular diseases are coronary heart disease, cerebrovascular disease and peripheral arterial disease. Those are the major causes of mortality among people in the world. They are caused by risk factors- are, sex, genetic, higher blood pressure, smoking, higher LDL- cholesterol, lower HDL-cholesterol, diabetes, obesity.

The aim of the study: The aim of the study was to determine risk factors for cardiovascular disease in Serbia and to recommend the best way of prevention.

Materials and Methods: This study is analysis of prevalence of risk factors, cardiovascular disease morbidity and mortality in Serbia.

Results: According to current statistics, cardiovascular disease (CVD) are the leading cause of death worldwide (50% of total mortality). In our country, according to study from 2001th year, about 56% died from CVD. Regarding mortality by sex, CVD was the cause of death in the world with 55% of men and 43% of women. According to the indicators in the 1996. in our country, the mortality rate was 800 for men and 600 for women aged 45 to 70 years, which has put our country in the top countries ranked by the amount of rates. As for mortality from cardiovascular disease by age, the greatest incidence in men aged between 40 and 60 years, and women between 60 and 70. In recent years it became more frequent in younger patients (the third and fourth decades). It is more common in men than in women in the fourth decade ratio is 7-8:1, and then the frequency increases the women's side. In the eighth decade, the incidence is equal in both sexes. The leading risk factors are higher blood pressure and smoking.

Conclusion: This study find out that the major cause of cardiovascular disease is higher blood pressure. The best way to prevent it, is a screening for hypertension once in two years, even if the blood pressure is normal. The second risk factor is smoking, and the third is higher LDL-cholesterol. The prevention of CVD is first mission in medical practice, and the most important is primary prevention.

Key words: cardiovascular, disease, risk, prevention

4. STOPA INCIDENCIJE OBOLELIH OD DIABETES MELLITUSA U NIŠAVSKOM OKRUGU U PERIODU OD 2006. DO 2011. GODINE
4. THE INCIDENCE RATE OF DIABETIC PATIENTS IN NISAVSKI DISTRICT FOR THE PERIOD FROM 2006TH TO 2011TH YEAR

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Diabetes mellitus (DM) is one of the most common chronic disease and a major public health problem. The WHO (World Health Organization - WHO) and the International Diabetes Federation (International Diabetes Federation - IDF) estimates that 2011th, the worldwide suffer from DM 366 million people, and that the number of patients to the 2030th increase to 552 million. The study was designed to examine the basic epidemiological characteristics of DM (in rates) population Nisavski District of DM type 1 and type 2 by sex and age, in the period since 2006. to 2011th. Data on all patients and analysis were performed using data from the population register of DM Nisavski District. Incidence rates were calculated per 100 000 population.

In the period from 2006 to 2011th in Nisavski District, a total of 92 registered people newly diagnosed with type 1 DM (48 men and 44 women) and 4873 of type 2 DM (2170 men and 2703 women). Average annual non-standardized rate for men with DM type 1 was 14:32, 10:33 for women, while men with DM type 2 was 196.18, and 236.67 for women. The incidence rate was 1.2 times higher among women with type 2 DM. In terms of age, patients with type 1 DM, the maximum average incidence rate was registered in the age group 5-9 years (17:20). In type 2 DM, the maximum average incidence rate was registered in the age group 55-59 years (648.67). In general, with increasing age and incidence rates, so that the lowest incidence rates observed in younger children.

Although the highest incidence rates recorded in developed countries, the largest increase in the number of cases expected in developing countries, where one of our country. Therefore, the time to take appropriate preventive measures to prevent the increase in the incidence and mortality of DM

Keywords: diabetes mellitus, incidence, prevention

H. SESIJA: SOCIJALNA MEDICINA
H. SESSION: SOCIAL MEDICINE

I PREDAVANJA PO POZIVU
I INVITED LECTURES

1. JAVNO ZDRAVLJE DANAS
1. PUBLIC HEALTH TODAY

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The World Health Organization (WHO) defines health as follows:

"Health is not merely the absence of disease, but psychological, physical and social well-being."

Over the years, the WHO has debated and developed a revised definition (1984) as follows:

"Health is the extent to which an individual or group is able to, on the one hand, realize aspirations and satisfy needs, and on the other hand, changes or eliminates the environment.

Health is a source of daily life, not just a case of life: it is a positive concept that emphasizes social and personal resources, as well as physical capacities."

The oldest definition given by Professor Charles Edward Winslow, a professor at Yale University:

"Public health is the science and art of preventing disease, prolonging life, improving physical health, efficiency through organized community efforts for the protection of the environment, control of infection in the community, educating individuals about the principles of personal hygiene, the organization of health services for the early diagnosis and preventive treatment of disease and development of social mechanisms that will ensure that every individual in the community has a standard of living that will allow it to maintain health. "

The American glossary states that public health " science and practice of protecting and improving the health of the community through preventive medicine, health education, control of communicable diseases, sanitary control and monitoring of environmental hazards."

According to the World Health Organization public health can be defined as " the science and art of improving health, preventing disease and extending the lives of people through organized community efforts."

It is primarily engaged in public health " risks to health and resolution of infectious, toxic and traumatic causes of death," and now a new public health approach combines the traditional with the social concept of health, highlighting the socio - economic determinants of health.

The new public health seeks to address issues relating to fair use of health services, environmental protection, public health policy, health correlation with social and economic development.

Basic features of the new public health are:

- Prevention as a primary intervention strategies
- To build upon the many disciplines
- To build on the idea of social justice
- Connection with government and public policy.

The Government of the Republic of Serbia in 2002 adopted the document " Health Policy of the Republic of Serbia ", starting from the premise that the health of the people of the general public interest and the most important resource for development.

This begins the process of advocating for health, in line with the strategy of the European Union in this field.

Ministry of Health formed a National Expert Group on Public Health, whose main task of drafting the strategy of public health.

The first draft of the Public Health Strategy has been prepared for public consultation in the second half of the 2003rd, and Strategy, the Government of the Republic of Serbia adopted on 26 marta 2009. year. Later that year, the Serbian Parliament adopted the Law on Public Health.

Public Health Act defines public health as " the public interest by creating conditions for the preservation of public health through organized comprehensive social activities aimed at the preservation of mental and physical health, and environmental stredine and prevention of risk factors for disease and injury, which are achieved by using health technologies and measures aimed at promoting health, preventing disease and improving the quality of life. "

Strategic Directions for public health, in addition to the focus on health promotion, are directed to the organization with management, continuous quality improvement and measurement of outcomes of all activities related to the conservation and unapredjenjem health of the population, as well as the functioning of social systems associated with health.

Public Health encourages the responsibility of the state and society in ensuring the welfare of all citizens by improving the health and preservation of a healthy environment.

Based health promotion and primary prevention, and instrumentalized through team work and interdisciplinary, multisectoral cooperation, as well as all forms of partnership.

Health problems in the public health in the Republic of Serbia shall be resolved at all levels, but the most effective troubleshooting is achieved in local government.

Formulation of policy and strategy in this area is in compliance with recognized functions of public health, in accordance with the recommendations of the World Health Organization.

Activities undertaken in the field of public health, including:

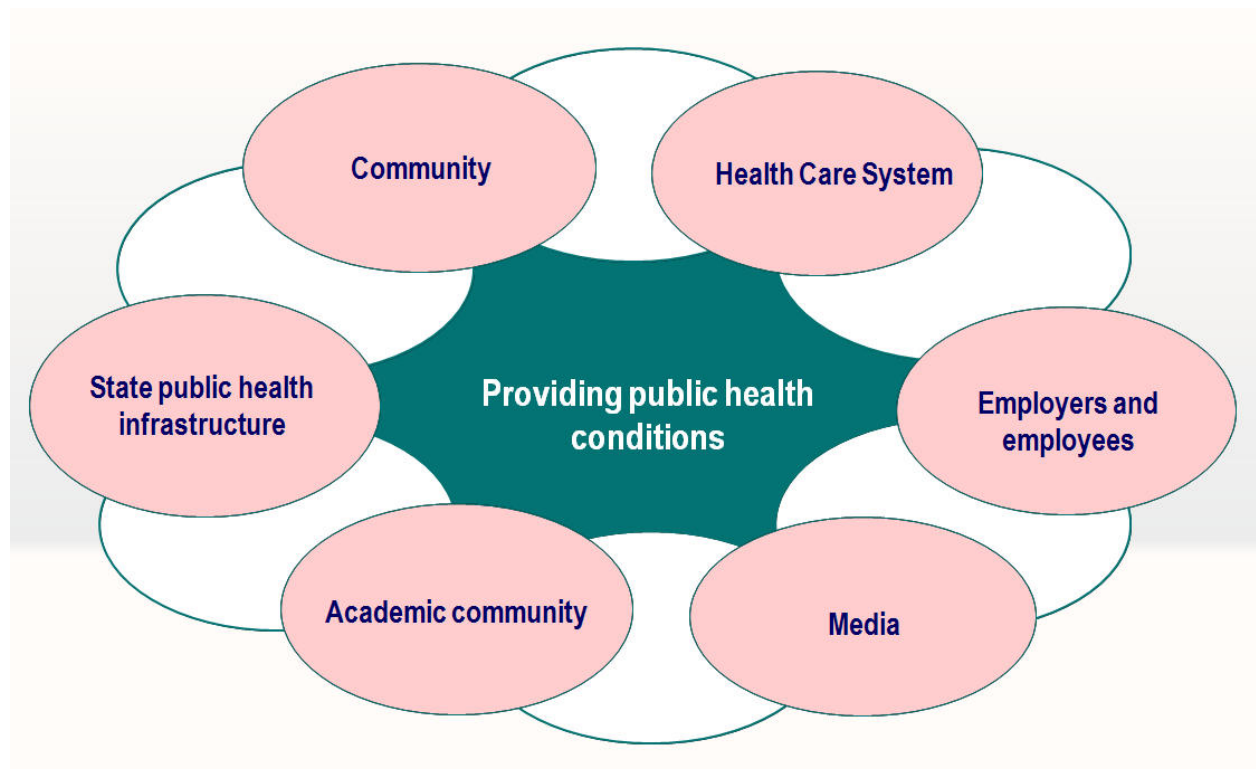
- Monitoring, evaluation and analysis of the health status of the population;
- Health surveillance, investigation and control of risks and threats to public health;
- Health Promotion;
- Social participation in health;
- Policy development for health through participatory processes within the existing socio-economic relations;
- Strengthening institutional capacity for planning and management in public health;
- Support the provision of equal access to necessary health care;
- Development and training of human resources in public health;
- Providing quality health services to the individual and population levels;

- Research in public health;
- Reducing the impact of emergencies and disasters on human health, including prevention, mitigation, preparedness, response and rehabilitation.

Department of Public Health disposed of population depending on the needs in a cost effective manner that corresponds to the reality and quality of evidence-based, which is the entire service focused not only on the individual but the entire population.

The strategy is aimed at promoting a holistic approach to health that will be achieved through integrated strategic approaches and activities. It identifies priority areas and provides guidance health services and other sectors to those issues whose resolution of will achieve the greatest benefit for the population, especially in orienting health inequalities.

It is part of the strategy of development of the health system and part of the development strategy of the company.



Scheme 1: the public health system

The Ministry is responsible for the organization of the public health system in Serbia.

Part of the responsibility for the area of public health, in addition to the Ministry of Health, and the Ministry are responsible for the areas of education, environment, social welfare, science, sports, agriculture, economy, employment, etc..

General objectives have the greatest potential for improving health and reducing health inequalities and specific objectives, as further development and operationalization of general, are measurable, achievable, realistic and time-bound.

The overall objectives of the Strategy are:

- Monitoring, evaluation and analysis of the health needs and expectations of the community
- Prevention and control of communicable and non-communicable diseases and injuries

- Promote and support healthy lifestyles
- The promotion, development and support of public- health policy
- Developing and training human resources in the field of public health
- The establishment and development of partnerships in addressing public health problems
- Promotion, development, support and launch actions to provide a safe and healthy living and working environment
- The promotion, development and support of health at all ages
- The promotion, development and support actions to improve the health status of socially vulnerable groups of the population
- Support the development of affordable and quality health care

In implementing the strategy, the Ministry of Health is working with all partners in the health system, as with all other partners outside the health sector.

Monitoring the implementation of the Strategy performs Institute of Public Health of Serbia " Dr Milan Jovanovic - Trampoline ", together with institutes of public health, as well as institutions that have a general overview of all sectoral activities.

Evaluation of the implementation of the Strategy will be performed in each phase of the implementation of the Action Plan. To evaluate the use of European Union health indicators (ECHI -2) and indicators selected by the experts responsible for specific activities and programs.

Annual reporting is required and includes: the results of the implemented activities, the difficulties and problems in implementation.

Action plan for the implementation of the Strategy for the period since 2009. the 2013th years as its integral part.

Activities coordinated by the Institute and the public health and the implementation of the activities carried out according to priorities and availability of funding.

According to the public health activities in the field of public health provided by the Institute of Public Health of the Territory of the Republic of Serbia, for the city and the territory of several municipalities, in accordance with the law governing health care.

The provision and implementation of public health in the Republic of Serbia actively participate:

- health service,
- organization for health insurance,
- educational and other institutions,
- companies,
- public enterprises,
- entrepreneurs
- Red Cross of Serbia,
- associations, churches and religious communities,
- citizens, local governments,
- autonomous province and the Republic of Serbia.

Activities in the implementation of public health are carried out within the following areas:

- Physical, mental and social health of the population;
- health promotion;

- Environment and human health;
- Operating environment and public health;
- Health management, quality and efficiency of the health system;
- An integrated public health information system for monitoring, evaluation and analysis of the health status of the population and report the authorities and the public;
- Public Health in natural or other major disasters and emergencies.

Action Plan for the period since 2009. the 2013th the

New public health

Funds for carrying out activities in the field of public health shall be provided:

- From the budget of the Republic of Serbia, autonomous provinces, cities and municipalities;
- The organization of health insurance;
- The sale of products and services that are directly related to the activities of health institutions;
- Carrying out scientific research and educational activities;
- From legacies, gifts, bequests;
- From other sources in accordance with the law.

Leading role in the field of public health of the Republic of Serbia have institutes of public health. They are organized at the national, district and city level. The main task is to coordinate the overall area of public health and are directly involved in health promotion, disease prevention, promotion of physical and mental health of the population, environment and working environment in collaboration with other relevant institutions and organizations outside the health sector, and nongovernmental organizations.

According to the Health Care, Institute/“Zavod” Institute of Public Health:

- 1) monitors, evaluates and analyzes the health status of the population and report to the relevant authorities and the public;
- 2) monitor and analyze health problems and health risks;
- 3) The proposed elements of health policy, plans and programs of measures and activities dedicated to the preservation and improvement of public health;
- 4) to information, education and training of the population to take care of their own health;
- 5) assesses the effectiveness, accessibility and quality of health care;
- 6) plans to develop professional training of health workers and associates;
- 7) Encourage the development of an integrated health information system;
- 8) perform applied research in the field of public health;
- 9) cooperate and develop partnerships in the community to identify and solve health problems of the population;
- 10) perform other duties in accordance with law.

Institute/“Zavod” Institute of Public Health is a health facility that performs social - medical, hygienic - ecological, epidemiological and microbiological health care.

Department of Public Health conducted bacteriological, serological, virological, chemical and toxicological examinations and tests in connection with the production and sales of food, water, air and items of general use, as well as in relation to the diagnosis of infectious and non-infectious diseases.

Department of Public Health, co-ordinate, harmonize and associated professional health care institutions in the Network Plan for the territory for which it was established.

Department of Public Health is working with other health care institutions in the territory for which it was established, as well as with the relevant local authorities and other institutions and organizations of the importance of improving public health.

Serbian public health perspective can be traced through several important development directions:

- development of the scope of activities and the activities of the Institute and the Institute;
- improving the health status of the population and troubleshooting environment/working environment;
- strengthen the position and fixing the links in the health care system;
- strengthening cooperation with the local community;
- development and training of staff to work in the field of public health;
- strengthening links with national and international organizations and institutions in the field of research and other programs and projects;
- retrieval and dissemination of the source of funding for the activities of the Institute and the Institute of Public Health.

Today, the main weaknesses in the implementation of the objectives of public health are the incompletely defined action plan for the implementation of public health, the low level of awareness in the local community and uncertain funding sources.

2. MOBILIZACIJA ZAJEDNICE I MOTIVACIJA U PROCESU PROMOCIJE ZDRAVLJA 2. COMMUNITY MOBILIZATION AND MOTIVATION IN THE PROCESS OF HEALTH PROMOTION

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Introduction

Access to the new public health conceptual provides health promotion as one of its basic elements, in terms of the integration of social, environmental and bihevioral aspects of public health. Health promotion is defined as the process of enabling people to take control of their own health in order to improve it. It is becoming increasingly important in the current period in which the governments of most countries worry about the gap between the high cost of health care and positive health outcomes. Health promotion in the community, in the concept of new public health should support efforts to move the main focus of the health system and the entire community from illness to health and essential for the development of sustainable health care system, as well as coordination and integration of health policies with the health sector. This concept is focused to the whole population, instead of focusing only on high -risk group for the development of certain diseases, and disease prevention. The focus of health promotion in the community is the healthy population, the study of the health needs and health - promotion programs, in order to reach those people in the community who have never been identified as a risk group. Health promotion activities in the population include health information, health education, and developing of healthy lifestyles, as well as a set of activities whose goal is the establishment of healthy communities, cities, workplaces and schools.

Health Promotion is the art and science of helping people discover the synergies between their core passions and optimal health, enhancing their motivation to strive for optimal health, and supporting them in changing their lifestyle to move toward a state of optimal health. Optimal health is a dynamic balance of physical, emotional, social, spiritual, and intellectual health.



Fig 1. Optimal health

Source: Michael P. O'Donnell (2009) *Definition of Health Promotion 2.0: Embracing Passion, Enhancing Motivation, Recognizing Dynamic Balance, and Creating Opportunities*. *American Journal of Health Promotion*: 9/10 2009, Vol. 24, No. 1,

Levels of optimal health are: Physical (fitness, nutrition, medical self-care, control of substance abuse), Emotional (care for emotional crisis, stress management), Social

(communities, families, friends), Intellectual (educational, achievement, career development) and Spiritual (love, hope, charity).

Challenges in Serbia and possibilities for motivation in the process of health promotion

Some of the major challenges for health promotion in the community are increasing poverty and unemployment, global environmental threat to survival of humanity, epidemiological changes - a steady increase in the incidence of infectious and chronic diseases, injuries and violence (HIV/AIDS, influenza, CV disease, depression and suicide), demographic changes - the large number of elderly people, as well as the development and progress of biotechnology, communications (especially the revolutionary changes in information technology), the globalization of transport, travel, values, and ideas, with the dominance of consumerism and privatization.

Current access to the new public health is also present in the national public health strategies within the health system reform in the Republic of Serbia, which is oriented towards the promotion of health. Promotion and preservation of public health, the development of a healthy environment and promotion of healthy lifestyles are the goals of the national health promotion programs that are continuously implemented in the Republic of Serbia since 2001. Program activities are carried out across the network and coordinate district institutes of public health and community health through teamwork, multi-sectoral and multi-disciplinary approach and partnerships with the education system, social security, local communities, work organizations, the media and non-governmental organizations. Challenges in health promotion in Serbia are factors that make motivations difficult but not impossible. Motivation is the term used to refer both to our reasons for action: „What is your motive?” and to our enthusiasm for doing it: „How motivated are you? The forces that direct our actions are highly complex and there are many ideas about how motivation operates. Concepts relating to motivation and formation of goals and intentions can be found in a number of theories. Some theories emphasise conscious decision-making others more subconscious urges, impulses and inhibitions. Few have tried to synthesise or integrate the different elements (West 2006). It has been defined in the psychology literature as ‘the psychological forces or energies that impel a person towards a specific goal’ (Sheldon et al 2000).

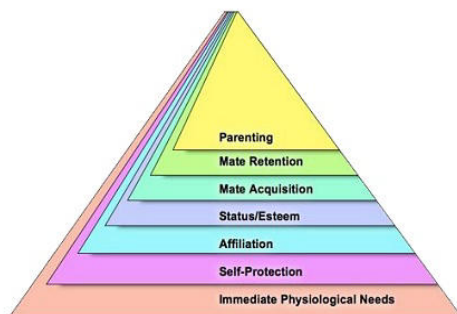
Income and social status affects the health and determinate the degree of control people have over their life circumstances, as well as their ability to react and make decisions that are important to them in life. Poverty and transitional crises increase the differences, deepen inequalities in health and may increase morbidity and mortality rates. Possible consequences is the lowered motivation of individuals and communities for actively participating in health promotion programs in the circumstances of the social determinants of health.

Results of the research indicate that the support of family, friends and community are important in stronger motivation and help people to cope with difficult situations and to maintain a sense of control over their lives. Also, the results of research on the effect of support for the poor and homeless show positive effects on the health status of these categories. Revised Maslow pyramid of needs indicated importance of partnership and family for human health and wellbeing (Fig 2 and Fig 3).



Maslow's original pyramid of needs

Fig 2: Maslow's hierarchy of needs



Revised pyramid of needs

Fig 3: Revised Maslow's hierarchy of needs

New approaches and possibilities of community motivation for health promotion

Numerous challenges of modern health promotion require new approaches, new research opportunities and resources, particularly with regard to the possibilities of new technologies, social and commercial marketing, finding new resources in the community, including marginalized groups in the process of health promotion, research in the field of motivation for health promotion and promotion health -based evidence. New resources in the community related to the development of an academic network of health promotion, developing partnerships with the community, intense involvement of students and students of medical school, volunteer work in the field of health promotion, as well as associations into action to promote health in the community. Motivation and private sector involvement in community partnerships for health promotion is of high importance as it contributes to better health outcomes and greater program effectiveness. Partnership encourages social learning and innovation in individuals who are involved in this process, with a focus on partnership with the health service sector and non-health -sector development programs. Sharing experiences through a network of healthy cities is also an opportunity to innovate and enrich the practice of health promotion and community motivation.

New approaches in order to motivate individuals and communities to cooperate include the use of new technologies, such as the availability of information via e - mail and phone SMS, a website dedicated to promoting health or health promotion process simulation using information technology.

One possible approach is contemporary and the use of social and commercial marketing to inform as many people in the community, the integration of health promotion and social marketing and commercial marketing that aims to healthy lifestyles, initiatives supported by the public and private sectors.

General question is: How to motivate our community to choose healthy lifestyles? Firstly, we have to answer the following questions: What is our community? And what have we experienced in our community? Then, to define strategies and theories of motivation: e.g. How do we help someone stop smoking? Or start a new fitness program? Fight Childhood Obesity? Also, we define resources and programs to help motivate our community. Associated elements are: personal motivation, health behaviours and participation in a community-level health intervention.

The key areas of health promotion in the community in the future are focused on politics of health promotion in the community, health promotion services, financing of health promotion and availability of resources, motivation for community participation, as well as research and information available information in this area. Priorities and recommendations in this regard are contained in the document Shaping the future of health promotion: Priorities for action statement. Preconditions for success in the future as the application of health policy in practice, strengthening the structure and process of health promotion, the move towards a knowledge-based practice, building competent force for health promotion and community empowerment.

Partnership for health (Health for All Policy) is recommended, by connecting individuals, groups and organizations in all government and private sectors, civil associations, unions and co-workers in the field of health. The health sector should be engaged in work on the active motivation, promotion and advocacy of health and to give incentives to other sectors to join in the multi-sector activity. Public policy should be directed to health, and activities are focused on the determinants of health. It is a process which recognizes that most of the factors that influence health is determined by factors outside the health sector, and examines the importance of health and non-health sectors partnership. The main policy objective is to create a health oriented environment that enables healthy lifestyle and this policy facilitates a healthier choice for all members of the community.

Conclusion

Health promotion is a process that enables individuals and communities to increase control over the determinants of health and to improve their health. One of its main objectives is to enable community members to learn how to be healthy and improve their health, emphasizing positive potentials and capabilities of individuals and communities. Community organizations include community capacity to make positive changes of their own. The partnership for health is an essential tool for solving health problems in the community and to create a healthier community. Health professionals play very responsible role in the partnership for the community health, as well as in the processes of its motivation and mobilization. Requires a good knowledge of theories of motivation and their application in practice in order to increase the number of community well-motivated people with clearly defined objectives that are taking action for health and persistent in achieving these goals. Processes of community motivation and mobilization requires a good knowledge of theories of motivation and their application in practice. The main goal is to increase the number of community well-motivated people with clearly defined objectives in order to take action for health and staying persistent in achieving these goals.

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II ORAL PRESENTATIONS
II USMENA IZLAGANJA:

TOPIC 1: MOTIVATING THE LOCAL COMMUNITY IN HEALTH PROMOTION
TEMA 1: MOBILIZACIJA LOKALNE ZAJEDNICE U PROMOCIJI ZDRAVLJA

1. FIZIČKA AKTIVNOST I PONAŠANJE ADOLESCENATA
1. PHYSICAL ACTIVITY AND ADOLESCENT BEHAVIOR

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Objectives: Physical education has a positive effect on the adoption of healthy lifestyles, improving health and quality of life. Based on the research results, objectives was to show the behavior of adolescents in Sombor, for future targeted planning preventive interventions.

Materials and methods: In a sample of 225 young people, 147 high school students, of which 115 girls and 32 men and 78 students, 43 girls and 35 men, we conducted a survey of diet, physical activity and behavior.

Results: About 50% of male population from high school and college, are never physically active, students do not visit a theater and do not read on regular bases. More than half of respondents often do high intensity physical activity, sports. Most of them are relaxing in front of the TV and computer. 70% of high school students (both sexes) are daily physically active. Normal weight adolescents applies to over 80% of high school students, 50% of man sand almost 100% women.

Conclusion: Education and promotion of healthy lifestyles will help to reduce sedentary behavior of young people, and learn them about the importance and benefits of from physical activity.

Key words: youth, physical activity, behavior

2. ULOGA LOKALNE ZAJEDNICE U PREVENCIJI POVREĐIVANJA STARIH U SAOBRAĆAJU

2. THE ROLE OF LOCAL COMMUNITY ON TRAFFIC INJURY PREVENTION OF ELDERLY

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Due to increasing life expectancy and decreasing birth rates, in majority of European countries, including Serbia, there will be a drastic increase of elderly population in the forthcoming period and in twenty years the majority of road users will be from the age group of 65 years or more.

According to the WHO data, every day over 500 road users of age 65 and more are injured or killed in traffic accidents. Risk of causing traffic accident triples and the risk of fatal injury is nine times greater for drivers older than 65.

In Serbia, according to the data of National Road Traffic Safety Agency referred to age group of the participants in traffic accidents, category of age 65 and more most commonly suffers from severe and fatal injuries. Out of the total number of road users with fatal injuries during the 2012. (684), 27% was older than 65.

Injuries of elderly in traffic have not been only the emotional and financial burden for the family, but also have an impact on our society in general, primarily reflected in the costs of their often long-term treatment and rehabilitation as well as permanent disability.

The aim of this paper is to define joined activities of local communities and institutes of public health in creating and implementation of different preventive programs primarily focused on education of road users about the psycho-physical characteristics of elderly that make them particularly vulnerable in traffic.

Further activities should be education of educators (medical professionals, etc), the elderly in their homes as well as in primary health care centers, education of novice drivers in driving schools, and public awareness campaigns.

Evidence based good practice from developed countries towards this issue have shown that educational programs together with health promotion campaigns significantly increase public awareness and consequently decrease number of traffic injuries in elderly.

Key words: traffic accidents, elderly population, local community, preventive programs

3. THE NEED FOR A COMMUNITY ORGANIZATION IN SUBSTANCE ABUSE PREVENTION IN SCHOOL CHILDREN

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School children are a vulnerable population groups. Their physical and mental growth and development are influenced by environmental factors. In particular, a major problem in this population is abuse of psychoactive substances.

In Europe, smoking is the most common in Estonia, where 65% of school children smoke. In Eastern Europe, 30% -60%, and in Western Europe, 7% -30% of school children smoke. In Serbia, 23% of school children aged 12-16 years and 30% of school children aged 17 smoke.

Under age 13 35% of school children in Estonia began to drink, 24% of school children in England and 3% in Israel. The average age at first alcohol consumption in Serbia is 14.6 years, and the average number of alcoholic drinks per week was 4.7.

In Western Europe 5% -30%, and in Eastern Europe 20% -30% of adolescents use psychoactive substances. Between a third and a half of the adolescents in our country have tried a drug at least once.

The main reasons for the increase in substance use among school children in Serbia are:

- failure to recognize a healthy lifestyle as socially acceptable behavior
- under-developed life skills in all phases of growing up,
- lack of health education in the official curricula of primary and secondary schools,
- infrastructure of the health system is not sufficiently tailored to the needs of young people,
- health workers are not educated enough in the field of health promotion among youth and improve their life quality
- lack of continuous and comprehensive monitoring of the health behavior of young people,
- underdeveloped teamwork, inter-sectoral cooperation and participation of young people in the field of health preservation and health promotion.

Therefore, there is a need for community-based organizations in the prevention of addiction among school children. It includes prompt information and education, recognizing the importance of peer education. It is necessary to develop the life skills of young people, particularly in deciding on the possible choices. It is necessary to provide services for the maintenance and improvement of youth health, and a safe and supportive environment.

4. PROMOCIJA ZDRAVLJA PORODICE I ZAJEDNICE KROZ METOD PORODIČNOG RASPOREDA

4. HEALTH PROMOTION IN FAMILIES AND COMMUNITIES USING THE METHOD OF THE FAMILY CONSTELLATIONS

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Integrative health care is the new direction in medicine, the answer to the limitations of official, allopathic medicine, but also of some branches of traditional, complementary and alternative medicine (TCAM). The basic purpose of an integrated (holistic) approach to health improvement is in the use of the best methods and official procedures (the so-called Western, formal) and traditional (alternative, complementary) medicine. The Ministry of Health of the Republic of Serbia, on 14 December 2007, adopted the Rules on the conditions, manner and procedure for carrying out the methods and practices of traditional medicine. One of this methods is Family constellations, developed and methodologically framed in early 80s, adapting it to the modern therapeutic approach by a German psychotherapist, philosopher, theologian and educator, Bert Hellinger. It is systemic family therapy, which health and disease models are close to socio-medical model, as well as the modern concept of health promotion in the community. It is individual-centered, in the context of different systems - family, school, workplace and the wider community. Healing method involves transpersonal approach, internal mental/soul, and relationships within the family and social environment. Areas of application are: family relations in general; partnership relations; diseases and disorders ; business constellation; social work, adopting. Experience during over 30 years, has shown that this method is efficient, cost effective and safe, specially in the field of health promotion in families and communities.

5. UTICAJ ORGANSKI GAJENE HRANE NA ZDRAVLJE POJEDINCA I ZAJEDNICE
**5. INFLUENCE OF ORGANICALLY GROWN FOOD ON THE INDIVIDUAL AND
COMMUNITY HEALTH**

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Organic food production needs support from health care providers and social stakeholders involved in the public health system. The number of organic food production followers in the world is growing. The motivation is found in decreased risk of modern age diseases, and in preservation of the environment. Up-to-date, there are no evidence based data that organically grown food is nutritively superior compared to food produced by conventional methods. It is concluded after systematic review of literature published between January 2000 and Decembar 2010 that focused on the effects of xenobiotics, pesticides, hormones, antibiotics and genetically modified organisms on health, as well as known data about connection of organically grown cultures and human health. Harmful effects of xenobiotics are well documented. Xenobiotics are various chemical compounds, but also parts of the transgenic plant species genome that are used in nutrition. They show various biological effects: toxic, carcinogenic, disruption of various body functions, especially regarding immune, nerve and endocrine systems. Health promotion and health education topics should provide this information to the target groups, especially during the “Healthy food” and “October 16th - World Food Day” campaigns

6. FOOD AT WORKPLACE

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Too often the workplace nutrition programme is either an afterthought or not even considered by employers. Work, instead of being useful, is frequently a harmful to proper nutrition. Health nutrition programme is designed to be useful for proper nutrition and improve health among employees. And workplace is determined like a key point of intervention. Poorer nations, like ours, remain in a circulus vitiosus of poor nutrition, poor health, low productivity, low wages and no chance for development. Obesity, inadequate calories and iron deficiency result in fatigue and lack of dexterity, which leads to an increased number of accidents at work. Employees and employers must understand that their health and thus job security is dependent upon proper nutrition. The workplace can be an excellent locus for health promotion nutrition programme.

Key words: workplace, health promotion, healthy eating, employees

7. IMPORTANCE OF LIVING CONDITIONS TO THE HEALTH OF THE ELDERLY

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People who are older than 65 represent a growing segment of the population, taking into account the demographic trends in our country. Our whole society and the Healthcare Department are faced with requirements from a greater share of the total healthcare, social and economic problems that the elderly population is faced with. Among the most significant factors concerning the healthcare concerns of the elderly are factors of living conditions related to the healthcare culture, possibilities for satisfying the needs concerning nourishment, residence, social support, availability and the use of all healthcare types, including private practice services. Our aim was to research the most significant segment of the living conditions of the elderly, which is significant for their healthcare status, in order to recognize the factors which bring greater benefit to the whole community from the healthcare system.

The material and methods involve the category of the elderly from the region of the City of Nis (a total of 1295, as a representative sample, while sub-groups were made based on sex and age), covered by the survey. The following were analyzed: literacy, economic conditions, housing conditions, marital state, quality of communications with family and friends, religious beliefs and social support.

Results: The elderly belong to the least educated category (illiterate: 4%). They are in the least favorable economic position (the rate of poverty of the elderly in Serbia is 14.8%: 10.6% of the whole population). In Nis, most of the respondents in the survey have a RSD 20,000 pension, which is one fourth of all the social expenditures intended for the elderly and, in the Republic of Serbia, these expenditures had continually been deducted from the GDP (from 18% in 2003 to 15% in 2010). Widowhood is almost three times more frequent in women. 72% of the elderly have children and most of them live in the same household or the same city. However, one third of men and 38% of women assess mutual relationships as poor or even non-existent: $\chi^2=31.66 > \chi^2(3 \text{ i } 0.05)=7.815$; $p < 0.95$. The estimation of the quality of contacts with friends and acquaintances also shows statistically significant differences dependent on sex and age group. One third of the elderly stated that the housing conditions (architectural designs) are sometimes or always unfavorable. The elderly mostly feel useful and active in the family, but least in the community, with statistical differences according to age sub-categories: $\chi^2=40.13 > \chi^2(4 \text{ i } 0.05)=9.488$; $p < 0.05$. The church mostly has a role in the sense of respecting tradition, and less frequently as a social category which may be viewed as a social support generator. Statistically speaking, women declare that they are religious more frequently. Social support is closely expected from family and friends, irrespective of the sex and one's health, while the readiness to provide social support is more frequent in women (48%: 32.3%).

The research conclusions indicate the requirement of being familiar with the monitored indicators, for the purpose of acquainting oneself more fully with the living conditions of the elderly, as well as the risk factors they are faced with at a later age. This would most certainly complete the image of their overall living and health requirements, which is significant for taking appropriate measures on the part of the Healthcare Department and the community as a whole.

Keywords: the elderly, living conditions

8. AKTIVNOSTI STUDENATA UNIVERZITETA U KOSOVSKOJ MITROVICI

8. THE FREQUENCY OF STUDENTS' PHYSICAL ACTIVITY AT THE UNIVERISTY IN KOSOVSKA MITROVICA

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Introduction: Students represent a population with a particular risk of physical inactivity consequences since they usually spend most of the daysitting in closed stuffy rooms, listening to lectures or learning; and instead of recreating they spend their free time in a coffee shop or by the television or computer.

Aim: The aim was to determine the frequency of physical activity among the students at the University in Pristina, with a temporary headquarters in KosovskaMitrovica, and to examine the association of this habit with the basic socio-economic and demographic characteristics of the respondents.

Methods: This was a cross sectional study of a representative sample of students at the University of Pristina, with a temporary headquarters in KosovskaMitrovica, in March and April 2011.

A list of students enrolled at the faculties of the University of Pristina in the school year 2010/2011 servedas a source of sample information which was available toRectory legal service at the University of Pristina. The mechanism, that was used to obtain a random sample, is a combination of two techniques of sampling:stratification andmulti-stage sampling; representativeness was determined by a nomogram (7% of students). The survey instrument was the Questionnaire on behavior and health. The frequency differences were tested by hi-square test. The criterion for statistical significance was $p < 0.05$.

Results: Apart from attending physical education classes, only 16.9% of students at the University of Pristina are engaged in physical activity. A greater proportion of males are daily engaged in physical activity ($\chi^2=116.694$, $df=5$, $p=0.000$), students at the Faculty of Sport and Physical Education ($\chi^2=167.860$, $df=45$, $p=0.000$), students coming from the central Serbia ($\chi^2=24.173$, $df=10$, $p=0.007$), those living with relatives during the studies ($\chi^2=27.896$, $df=15$, $p=0.022$) as well as students who are "very" satisfied with the faculty ($\chi^2=36.571$, $df=20$, $p=0.013$).

Almost half (45.9%) of the students at the University of Pristina spend up to 5 hours sitting, and almost a quarter (23.5%) even up to 8 hours a day. Most of the students at the Faculty of Natural Sciences and Mathematicsspends up to 5 hours a day sitting, while a fifth of medical students and the same proportion of law students sit for more than 8 hours a day ($\chi^2=121.158$, $df=36$, $p=0.000$). Among the students who sit for 5 hours a day, there is slightly higher proportion of male students ($\chi^2=9.122$, $df=4$, $p=0.058$) as well as students who are "in general" satisfied with the faculty, while the students who are not "at all" satisfied with the faculty sit more than 8 hours a day ($\chi^2=80.744$, $df=16$, $p=0.000$). Almost half of the students

who said that they would "enter postgraduate school" after the faculty, spent up to 5 hours a day sitting, while half of the students who "would not do anything for a while" after the faculty spent more than 8 hours a day sitting ($\chi^2=35.776$, $df=16$, $p= 0.003$).

Conclusion: Promotion of physical activity as a good way to maintain and improve health should be the basis of public health activities and a task not only for health sector, but for a number of social sectors too.

Keywords: frequency, physical activity, students

TOPIC 2: SOCIO-MEDICAL ASPECTS OF HEALTH
TEMA 2: SOCIJALNO-MEDICINSKI ASPEKTI ZDRAVLJA

9. POVEZANOST SOCIJALNO-EKONOMSKIH I DEMOGRAFSKIH FAKTORA SA
MENTALNIM ZDRAVLJEM STANOVNIKA
**9. CONNECTIONS BETWEEN SOCIO-ECONOMICS AND DEMOGRAPHICS
FACTORS WITH MENTAL HEALTH**

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Objectives: were to determine the prevalence of certain aspects of mental health and relationship of socio-economic and demographic factors of residents in northern Mitrovica with the impact of mental health problems in social relationships.

Method: The study was conducted as a cross-sectional study of a representative sample of the residents of northern Kosovska Mitrovica in the 2012. We examined 328 patients. As the survey instrument was used a questionnaire that was used in the National Health Survey in Serbia in 2006. For the assessment the significance of the difference between these variables, was used the chi-square test, with a significance level of 0.05.

Results: A sense of anxiety and nervousness was present in 72.8% of respondents, despondency and depression in 58.8%, sleep problems in 57%, and problems with concentration and memory were present in 44.5% of respondents. The before mentioned emotional problems more often affected the social relationships in elderly patients, widows and widowers, those with lower education, lack of social support and those with poor economic condition

Conclusion: The results present a high proportion of people with a mental health problem. Determining the population groups in which these problems affect social relationships more often is an important step in planning and then implementation health-promotion programs that aim at reducing these problems.

Keywords: emotional problems, socio-economic factors, demographic factors, mental health

10. URGENTNA STANJA KOD DECE U BEOGRADSKIM BOLNICAMA
10. EMERGENCY CASES INVOLVING CHILDREN IN BELGRADE HOSPITALS

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Introduction: Emergencies are always traumatic for the patient and his environment, especially in childhood and they require prompt medical service.

Objective: To determine the characteristics of patients and the burden of hospital services which are taking care of emergency cases involving children.

Methods: There was performed retrospective analysis of data about the management of emergency cases involving children for 2012., in the five hospitals in Belgrade (University Children's Hospital, Institute for Health Protection of Mother and Child Serbia "Dr Vukan Cupic", KC "Zemun-Belgrade", "Zvezdara" and "Dragisa Misovic-Dedinje").

Results: In the 2012. in the hospitals who take care about emergency cases involving children and young people aged up to 18 years 102.549 emergency patients were examined (51% of pediatric surgery and 49% pediatric). About 12% of patients were reviewed in hospitals at the secondary level, and 88% in tertiary hospitals. There is seasonality in terms of increased number of emergency patients examined in the autumn-winter period. Daily frequency of examined pediatric patients ranged from 26 to 117, and that depends on hospital. Most patients, 54% viewed without a referral, while 40% of patients had a primary health referral, and only 6% of the patients brought emergency care unit. 86% of patients after reviewing returned from hospital to home. 22% of pediatric and 5% of pediatric surgical patients were held for hospital treatment. Children aged 1-4 are mostly taken care for in pediatric department and children aged 10 and more are majority in pediatric surgery department.

Conclusion: Health services that perform emergency patient care in the field of pediatrics and pediatric surgery are burdened with a large number of patients who do not require urgent review. There is need for greater involvement of primary health care in the management of patients who are not critically ill, and education of parents.

Keywords: emergency cases, Pediatrics, Pediatric Surgery, receiving days

11. EMPLOYEE SATISFACTION IN BELGRADE HOSPITALS - WHAT HAS CHANGED IN THE LAST 5 YEARS?

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INTRODUCTION: Job satisfaction is the level of contentment a person feels regarding their job. It affects work performance, absenteeism, staff turnover, customer satisfaction.

OBJECTIVES: The aim of this study is to determine the level of employee satisfaction in Belgrade hospitals and changes from year 2008 to 2012.

METHODS: A retrospective analysis of employee satisfaction in all 26 public hospitals in Belgrade. Data were obtained from surveys about employee satisfaction that has been carried out according to the methodology of the Institute of Public Health of Serbia, for the period of five years, from 2008 to 2012. Statistical analysis included descriptive statistics methods, χ^2 test and ANOVA (F).

RESULTS: In observed period percentage of dissatisfied with their jobs was increased from 23.5% to 26.4% and percentage of satisfied was reduced from 36.9% to 34.7%. Overall satisfaction was reduced from 3.1 to 3.03 ($y=-0.016x + 3.094$).

Employees are least satisfied with salary, and the average score was reduced from 2.12 to 2.03 ($y=-0.016+2.054x$). Overall satisfaction with interpersonal relationships is reduced from 3.14 to 3.08 ($y=-0.012+3.102x$), and the time available to do the work from 3.29 to 3.13 ($y=-0.035+3.287x$). The average level of satisfaction with the work equipment is increased from 2.78 to 2.83 ($y=0.009x+2.797$) and opportunities for education from 2.82 to 2.98 ($y=0.051 x +2.745$).

Technical workers are least satisfied with their job and administrative workers are most satisfied ($\chi^2 = 92.126$, $DF=12$, $p=0.000$). In all reviewed years, the most satisfied were employees in psychiatric hospitals ($F=14.484$, $DF=25$, $p=0.000$).

CONCLUSION: Throughout the years covered in this study, the level of satisfaction has not been improved. Also, reduced response throughout the years indicates a loss of confidence of employees in this study.

KEYWORDS: employee satisfaction, quality, hospital

12. ULOGA ZDRAVSTVENOG SEKTORA U PREVENCIJI SAOBRAĆAJNOG TRAUMATIZMA

12. THE ROLE OF HEALTH SECTOR IN THE PREVENTION OF ROAD TRAFFIC INJURIES

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Road traffic injuries are one of the three leading causes of death in age group 5-44 years. Only in Serbia during the past 10 years more than 9,000 people were killed, and over 188,000 injured in traffic accidents.

Followed by high mortality, morbidity and resulting disability, traffic accidents place major burden on the health system, with proven effectiveness of preventive measures. However, in Serbia, when creating preventive measures the impact of this system is insufficient.

Therefore, in order to have more comprehensive consideration of the size of the problem and to create adequate preventive programs, for health sector it is necessary to develop a functional system for collecting, updating and analyzing injury data, and to carry out the harmonization of its road traffic injury database with the database of the Ministry of Internal Affairs.

Prevention activities of health sector should take place at multiple levels- primary, which means prevention of occurrence of injury, secondary that includes pre hospital and hospital care to prevent complications, and tertiary (physical and psychological rehabilitation) to prevent subsequent disability.

Activities of the health sector within the primary prevention should be based on:

- Continuous implementation of educational programs aimed at the general population about high-risk behaviors and health conditions that can cause road traffic injuries,
- Design and emphasizing the consulting role of physicians and pharmacists in daily patient contact,
- Change of legislation on medical examinations for drivers, and
- Continuous education of all road users about the basic life support techniques.

In health sector, the important role in the design, organization and implementation of educational programs in order to prevent road traffic injuries should primarily have Institutes of Public Health.

Keywords: road traffic injuries, health sector, educational programs

13. KVALITET RADA GINEKOLOŠKO-AKUŠERSKIH ODELJENJA U BEOGRADU, 2008-2012.

13. WORK QUALITY OF MATERNITY WARDS IN BELGRADE, 2008-2012.

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Introduction: The work quality of maternity wards becomes a must in conditions of ever decreasing birth-rate and ever increasing financial restrictions.

Objectives: to determine whether there are some differences among the quality work indicators in 5 maternity wards in Belgrade and the change in quality in period 2008-2012.

Materials and methods: The retrospective data analysis from reports on quality work indicators of maternity wards in Belgrade hospitals in period 2008-2012, by using descriptive statistics and linear trend methods.

Results: 19,785 Deliveries were carried out in Belgrade in 2012 (by 18% more than in 2008). 70.6% of delivering women had normal deliveries. The average length of hospital stay for normal deliveries was 3.6 days, with almost 2 days difference among maternity wards. 27% of deliveries were done by Caesarean section, slightly less than in previous years ($y = -0.03x + 27.33$). The incidence of Caesarean section was 12% in CHC "Zemun" and up to 34% in CCS. Epidural anaesthesia was used in 28% of deliveries (5% in CHC "Zemun" and CHC "Zvezdara", up to 54% in CHC "Dr D. Mišović"). A partner or a family member of a delivering woman was present only in 352 deliveries (1.8%).

2453 Delivering women and 516 babies suffered injuries during delivery. In period 2008 – 2012 the percentage of delivering women who suffered injuries during delivery was increased from 2.4 to 12.4 ($y = 2.1571 + 3.2333x$), whereas the percentage of children who suffered injuries during delivery was decreased from 3.3 to 2.56 ($y = -0.0463x + 3.3087$).

The percentage of children who were born alive but died before discharged from hospital was decreased from 0.19% to 0.17% ($y = -0.012x + 0.244$).

Conclusion: There are some differences in quality indicators among maternity wards in Belgrade. The quality improvement should be directed towards the decrease of incidence of delivering women's and babies' injuries and the increase of incidence of deliveries carried out in epidural anaesthesia and those where partner is present.

Key words: quality indicators, maternity ward

14. PATIENT SATISFACTION WITH WORK OF FAMILY DOCTORS IN NIŠAVA AND
TOPLICA DISTRICT IN 2012

**14. ZADOVOLJSTVO PACIJENATA RADOM IZABRANIH LEKARA NA
NIŠAVSKOM I TOPLIČKOM OKRUGU U 2012. GODINI**

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Objectives: One of the prerequisites of the quality of work of health institutions is the patient satisfaction with the health care provided. Assessing the degree of patient satisfaction with work of family doctors in health care institutions for adult population (stated in the questionnaire as general medicine), women (gynecology) and children (pediatrics) in Health Care Centers in Nišava and Toplica Districts, in 2012.

Materials and Methods: An anonymous questionnaire was conducted on 03.12.2012. in 12 Health Centers in Nisava and Toplica Districts, using a uniform questionnaire, made by professional methodological instructions defined by the Institute for Public Health of Serbia.

Results: 4701 people were surveyed. 96.9% of surveyed patients declared that they have a family doctor. Patients consider that general practitioners have the best knowledge of their personal situation (73.4%) and of their medical history (81.1%), listen to them patiently (86.7%), and they prefer going to their family doctor when they have new health issues (88.3%). The majority of patients consider that gynecologists spend enough time talking with them (80.9%), give explicit explanation of diseases and prescribed medications (88.7%), and after visiting their gynecologist they feel more capable to deal with their health problems (81.4%). The highest degree of overall patient satisfaction was with gynecologists (4.13±0.78), then with general practitioners (4.13±0.78), and the lowest degree was with pediatricians (3.98±0.74). It was determined that there exists statistically relevant difference in the overall satisfaction among general medicine, gynecology and pediatrics (F=5.895, p=0.003).

Conclusion: The results of the assessment of patient satisfaction themselves are not the goal of the research, but should serve as the guidelines and recommendations for appropriate activities in integrated approach in improving the quality of work of health institutions.

Key words: patient satisfaction, quality of work, social medicine

15. PSYCHOSOCIAL FACTORS OF WORKING ENVIRONMENT AS AN ASPECT OF HEALTH

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Psychosocial hazards or risk factors are those ways of workplace organization and business management, as well as the social environment, which can produce bad mental and physical consequences.

Univariate regression analysis confirmed that the following domains of COPSOQ questionnaires are significantly associated with IRS values : emotional demands, obligations in the workplace, predictability, prizes, role – definition, job satisfaction, work - family conflict, self-estimated health, burnout and stress.

Univariate regression analysis confirmed that the increase in the value of IRS significantly correlates to: non-exposure to threats of violence, non- exposure to physical violence and non-exposure to abuse.

The decline in the value of the IRS significantly correlates to: exposure to threats of violence by clients/patients, exposure to physical violence several times, exposure to abuse several times and exposure to abuse by the customer/patient.

CONCLUSION

Extremely successful business people are different from average ones because of their exceptional level of empathy, self-discipline and initiative, all of which are part of emotional intelligence.

The contents of emotional intelligence - developing self-awareness, self-esteem, empathy, social communication, optimism, good mood, should become a legitimate target for the employees in the health sector.

Raising the level of emotional intelligence is a guarantee of prevention of psychosocial risks.

16. DESET GODINA AUTOMATIZACIJE IZVEŠTAJA VANBOLNIČKOG MORBITETA NA ODSEKU ZA STATISTIKU ZDRAVSTVENE SLUŽBE INSTITUTA ZA JAVNO ZDRAVLJE NIŠ

16. TEN YEARS IN AUTOMATICALLY DATA PROCESSING REPORTS ABOUT OUT-PATIENT MORBIDITY IN DEPARTMENT OF STATISTICS IN PUBLIC HEALTH INSTITUTE NIS

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The Evidential law and Statistical Researchment law are defined reports out-patient morbidity that health care institutions are obliged to generate. They are processed in the Department of Statistics in Public Health Institute Nis. The annual report 1525 is treated outpatient morbidity with two districts (of Nis and Toplica) from 28 health care institutions, with the corresponding territory of about 500,000 inhabitants, and consists 314 six-months reports and 462 annual reports have been made every year..

Data of the number and type of services, organizational structure and human resources are generated in all health care institutions of Nis and Toplica quarterly. Statistics Division also performs quarterly formal and logical control of the received reports, and prepares summary reports for municipalities, Nis District and Toplica. After that summary reports for municipalities and districts for six-months period and annuals have been made too.

Since 2003. the whole process has been made using computers instead of paper reports. Computer program anticipates tree-months input of all the data. After that, every tree-months, six-months and annual reports form every institutions, municipalities and districts have been made automaticly. Using this program, everyday work in Department of Statistics has been increased significantly.

17. STEPEN NEZAVISNOSTI U DNEVNIM AKTIVNOSTIMA KOD STARIH I STEPEN DEPRESIVNOSTI

17. THE INDEPENDENCE INDEX IN DAILY ACTIVITIES AMONG THE OLD AND THE DEPRESSIVENESS

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Objectives: Depressiveness is more common among the old than among the general population. Investigating the cause of depressiveness, in this particularly sensitive population, becomes an important matter of national health. The aim of this paper was to determine the connection between depressiveness and independence index among the examinees in daily activities.

Materials and methods: The study included 249 examinees (169 women and 80 men). All the examinees were 65 or over 65 years old, with the average age of $80,93 \pm 6,63$. Depressiveness is estimated by means of score on Geriatric Depression Scale (GDS). Score 6 and above points to depression. The independence index is determined by the total Katz score (Katz index of independence in activities of daily living). A lower Katz score indicates a lower independence index.

Results: Depression symptoms have been discovered among 57,7% of examinees. The average GDS score in the total sample is high ($6,79 \pm 3,76$). Katz score in the group of patients with depression is $2,9 \pm 1,95$, whereas in the group of patients without depression the score is $3,94 \pm 1,95$, which is significantly higher in comparison with the other group ($U=4731,5$, $p=0,00$), statistically speaking.

Conclusion: The examinees who are incapable of taking care of themselves in an adequate way are more depressed. It takes planning and realization of concrete programs from the field of not only mental hygiene, but also physical medicine and rehabilitation, for us to be able, on the one hand, to contribute to preservation and improvement of mental health among the old, and on the other hand, to accelerate their independence index in daily activities, which would greatly contribute to a significant advancement of their health.

Key words: Katz score, depressiveness, GDS, elderly.

18. PUBLIC HEALTH ASPECTS OF SEXUAL AND REPRODUCTIVE HEALTH

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Objectives: 1. Analysis of determinants of SRH which contribute to inequalities in health; 2. Proposal of new approach in promotion of SRH through implementation of health in all policies.

Materials and methods: Review of literature and analysis of determinants of SRH and models of good practice in this area.

Results: Sexual and Reproductive Health (SRH) is state of complete physical, mental and social welfare, not only absence of reproductive and sexual diseases and dysfunctions. SRH has an impact on people's life and it is influenced by different factors/determinants: socioeconomic and cultural factors, educational level and access to education, employment, family conditions, gender equality, tradition and cultural norms, legal framework, availability and quality of health care and social services, NGOs and efficacy of local authorities and policies.

Renewal of the population in Serbia is jeopardized due to decreasing of birthrate and average number of children per woman and family as well as to increasing age of first time mothers.

Conclusion: Actual approach in promotion of SRH implies adequate response to social determinants through implementation of health in all policies and integrated multilevel leadership based on intersectoral and interdisciplinary approach.

Key words: Sexual and Reproductive Health, Health determinants, Health in all policies

19. BETWEEN SOCIO-ECONOMICS AND DEMOGRAPHICS FACTORS WITH SELF-RATED HEALTH

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Objective: was to determine the connection between socio-economics and demographic sfactors of residents in northern Mitrovica with their self-rated health.

Method: The study was conducted as a cross-sectional study of a representative sample of the residents of northern Kosovska Mitrovica in the 2012. For creating the sample was used voters' list for the presidential elections in 2008. The sample consisted of 328 respondents. As the survey instrument was used a questionnaire that was used in the National Health Survey in Serbia in 2006. For the assessment connection between social-economics and demographics factors of residents in northern Mitrovica with their self-rated health was used a single linear regression, with a significance level of 0.05.

Results: Those who have declared that they have not enough income for recreational and go out, who were in bad financial situation, who declare that there is an interruption in the supply of water and are not connected to the city sewer, and older respondents, were significantly more likely to declared a state of health poor or very poor.

Conclusion: Considering that the self-rated health, although subjective indicator, as the number of studies showed is a good predictor of morbidity and mortality, study of factors affecting it are also important, especially factors which derived from the social environment, and that can be change in order to improve the subjective feeling of health of the residents.

Keywords: self-rated health, socio-economics factors, demographics factors, connection

20. DIRECT RELATIONSHIPS BETWEEN CLUTTER AND PRODUCTIVITY

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Objectives: The aim of this study was to examine the impact clutter have on capability and effectiveness of the working man.

Materials and methods: For the purposes of this study researches published in indexed biomedical journals in the last 5 years were used.

Results: People collect things for a number of reasons. Scholars at Yale recently identified that two areas in the brain associated with pain - the anterior cingulate cortex and insula - light up in response to letting go of items people own and feel a connection towards. Neuroscientists at Princeton University found when they looked at people's task performance in an organized versus disorganized environment that excess things in one's surroundings, whether it be theirs closet or office desk can have a negative impact on its ability to focus and process information. A team of UCLA researchers found that similar to what multitasking does to people's brain, physical clutter overloads their senses, making people feel stressed, and impairs their ability to think creatively.

Conclusion: The results of the study showed that physical clutter in one's surroundings competes for the attention, resulting in decreased performance and increased stress. But clutter isn't just physical – there is also a digital, computerized form of clutter that erodes people's ability to focus and perform creative tasks. Cleaning out the closet, emptying the inbox, putting things where they “belong” may master the clutter.

Key words: clutter; multitasking; stress

21. HISTORY OF MEDICINE - GIANTS OF MEDICINE II

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On the occasion of 47-days they Preventive Medicine in Nis and 110 years of the Public Health Institute Nis decision was taken on the organization of the exhibition at the institute that would unite and a permanent exhibition on the subject of Giants Medicine "They treat people" in honor of Elizabeth Ross. In this way, the Public Health Institute Nis and thus contributes to the celebration of the 100th anniversary of Serbian liberation wars. On this occasion, we present the biographies of some doctors from the exhibition.

Abraham Jacobi 1830- 1911 American physician, scientist, professor, dean and revolutionary. Considered the father of pediatrics, the founder of the first pediatric clinics in the United States. He gave his great contribution to the study and later in the application of the proper treatment of children. His work was noted on the proper nutrition of children. He was first professor at New York School of Medicine and later Professor of Medicine at Columbia University.

Hans Christian Joachim Gram 1853- 1938 was a Danish bacteriologist. According to this doctor staining techniques in microbiology called and systematization baktertja against Gram positive and Gram negative bacteria. Hans Christian Gram will contribute and dedicated to the study of pernicious anemia.

James Parkinson 1755-1824 was an English apothecary surgeon in London. According to him Parkinson new disease called because he was the first to describe the disease. Parkinson's was first described gout as well as a detailed description of peritonitis. He was a great erudite because besides medicine dealing with the geology and paleontology.

Charles Bernard Carpenter 1933- 2011 A pioneer of transplant medicine and immunology. Carpenter in 1958. graduated from the Medical School of Harvard University. He is the founder of immunogenetics. He pointed in particular to the first kidney transplantation. The founder of the Society of Transplantation and the American Society of Nephrology.

III POSTER PREZENTACIJE:

III POSTER PRESENTATIONS:**1. HEALTH INFORMING IN STUDENTS POPULATION REGARDING MEDICAL ASPECTS OF TOBACCO USE**

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Students, as a part of the youth population, are characterized by numerous health risks (smoking, use of psychoactive substances, unhealthy diets, use of alcohol, risky sexual behavior, physical inactivity...). One of the major risk is the use of tobacco. The identify the characteristics of the student health information regarding harmfulness of tobacco use. For the purpose of this study, the unique questionnaire has been designed. The survey included 519 examinees. 51.1% of the students were obtaining information about health aspects of tobacco use several times, 42.2% were obtaining information from doctors and other health workers. In generally the students are informed about the health aspects of tobacco use. The doctors are most common persons from whom students were get information about health aspects of tobacco use.

2. IMPORTANCE OF EMPLOYEE SATISFACTION IN HEALTH FACILITIES MANAGEMENT

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Employee satisfaction in health facilities in the Republic of Serbia has been assessed year by year, since 2007. It is a part of Ministry of Health Program activities, related to Health facilities Quality of work. Employee satisfaction is dynamic; it changes, and affects the performance. Methodology of assessment was unique for all facilities and results have been gathered in Institute for Public Health “Dr Milan Jovanovic Batut”.

Unfortunately, many weaknesses associated with this assessment have been recognized, especially related to the use of results of assessment. The results represent a valuable material for the management of health facilities. Respecting the principles of good management, certain segments that are a source of un-satisfaction, sometimes it is very easy to upgrade. The most important is the awareness of managers of health facilities about the importance of motivation and employee satisfaction, as a prerequisite for a better quality of work, achievement of health services plan and well-being of patients.

3. HEALTH INFORMING IN STUDENTS POPULATION REGARDING MEDICAL ASPECTS OF ALCOHOL USE

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Alcohol use is the social and health problem in global level. Alcohol use among young people is one the permanent rise regardless of the the available information on the harmfulness of acohol. One of the major health risk in students population is alcohol use. The aim of the work was to identify the characteristics of student health informing regarding harmfulness of alcohol. For the purpose of this study, the unique questionnaire has been designed. Solid knowledge about medical aspects of alcohol use (65.2% group of biomedical students, 58.5% other students). 51.6% of students were obtaining information about alcohol use several times, 37.1% were obtaining information from doctors and other health workers mostly. In generally students consider that they have excellent or solid level of knowledge about the health aspects of alcohol use. The doctors are most common persons from whom students were get information about health aspects of alcohol use.

4. ORGANIZACIONE MERE PREVENTIVNOG KARAKTERA KAO DETERMINANTA ZDRAVLJA KOD BOLESTI U VEZI SA RADOM

4. PREVENTIVE ORGANIZATIONAL MEASURES AS A DETERMINANT OF HEALTH IN WORK-RELATED DISEASES

Katarina Bulatović¹, Nikolić D.¹, Rangelov T.¹, Marjanović S,¹ Ristić S,¹

¹Public Health Institute Nis

Occupational diseases result from long-term exposure to harmful substances and gases that adversely affect the overall health of the workers. The most common adverse agents include : nitrogen compounds, carbon monoxide, cyan or it's compounds, aliphatic hydrocarbons, cyclic hydrocarbons or their homologs, nitro and amino derivatives of hydrocarbons, halogenated hydrocarbons, carbon disulphide, alcohols, ethers, esters, aldehydes, ketones and pesticides. According to the established ability to work and the amount of recurrent rates of occupational poisoning we distinguish temporary inability to work, which is determined by the current, relevant criteria, and permanent inability to work. Depending on the duration of the clinical manifestations, poisoning can be divided into acute and chronic, based on which we determine work capacity.

The most frequent occupational lung diseases include: pneumoconiosis, lungs byssinosis, asthma, allergic bronhiolonveolitis, chronic obstructive bronchitis and tuberculosis These. diseases result from inhalation of coal dust and the accumulation of the particles of hard metal, dust of vegetative origin etc. Occupational asthma is defined as asthma caused by exposure to agents in the workplace, while tuberculosis as an infectious disease is caused by Mycobacterium tuberculosis. As a result of these diseases permanent lungs and airways damages arise, that manifest as pulmonary fibrosis, lung obstruction, lung insufficiency...

The most common occupational skin diseases that occur as a consequence of the allergens from the environment are allergic contact dermatitis and urticaria.

Malignant diseases caused by long-acting ionizing and ultraviolet radiation, as well as exposure to chemical and biological agents, are classified as serious occupational diseases. Most often they occur at the point of direct contact of the body with a carcinogenic substance or it's active metabolite. When it's absorbed, it usually attacks the skin, respiratory tract and less frequently the digestivetract, and when it's eliminated, the urinary tract. Clinically they are no different than other cancers.

5. ORGANIZACIJA I REZULTATI SKRINING PROGRAMA NA NIŠAVSKOM OKRUGU

5. ORGANIZATION AND RESULTS OF THE SCREENING PROGRAM IN NIS COUNTY

Saša Ristić¹, Nikolić D,¹ Marjanović S,¹ Bulatović K,¹ Rangelov T,¹

¹Public Health Institute Nis

Aim: The aim of the study is to overview the extent and content of providing screening services in health centers in Nis and Doljevac and short-term indicators of the screening program (process and outcome) in Nis district health centers, during the period between January-June 2013.

Methodology and data source: The study uses a retrospective comparative socio-medical scientific method applied to data from the monthly reports of the screening program provided by health centers.

Results: Screening program of cervical cancer in the Nis Health Center started in 18.02.2013. at the Department of gynecology. Since then 25 women were diagnosed with ASCUS and afterwards proposed a detailed control. In this reporting period through colon cancer screening, all 16 out of 16 policyholders who were referred to the specified clinic for colonoscopy responded; 13 colonoscopies were performed, and 3 are waiting for diagnosis (untreated), with the following results :1 neo sigma (waiting for PH test), 1 ulcerative colitis (waiting for PH test) and 3 polypectomies were performed. Breast cancer screening program at the Health Center Nis started in 01.03.2013. at the Department of X-ray and ultrasonography, with the engagement of the team consisting of four radiologists and one x-ray technician. So far, the Nis HC, 9 CA changes have been detected throughout the screening program (12 women with the same changes were discovered beyond the screening in this period and have been referred to mammography).

Conclusion: It should be noted that there isn't an adequate feedback from the secondary level to general practitioners and that it is an imperative in the upcoming months, because only that level of organized effort will allow screening programs to survive in the future.

Key words: screening, cervical cancer, breast cancer, colon cancer

6. POKAZATELJI PRUŽANJA PREVENTIVNIH ZDRAVSTVENIH USLUGA U SLUŽBI ZA ZDRAVSTVENU ZAŠTITU ŽENA NIŠAVSKOG OKRUGA (2008.-2012.)

6. INDICATORS OF WOMEN'S HEALTHCARE PREVENTIVE SERVICES IN NIŠ DISTRICT (2008.-2012.)

Tamara Rangelov,¹ Bulatović K., Nikolić D.¹ Ristić S,¹ Marjanović S,¹

¹Public Health Institute Nis

Aim: The aim of this study is to assess the extent and trend of providing preventive services in the Departments of Women's Healthcare in Nis district during the period between 2008 - 2012.

Method: The study used a retrospective comparative socio-medical examination of data from the annual reports on the realization of the work Plan of Health Centers in Nis. Preventive health services of women's healthcare are shown collectively, without analyzing the structure of individual services.

Results: During this period, the average number of preventive services by insured women (over 15 years) at Nis District was 0.46, and average 2231 provided preventive services by a physician of this Department. However, there are wide variations among health centers from those who show a constant growth trend of providing preventive services, such as HC Doljevac, to those who have little variation by years (HC Sokobanaja) to eg. HC Ražanj in which the peak of provided services was achieved in 2009., after which it returned to the average value for the district. Average percentage of realization of the Plan of preventive health services in the Departments of Women's Healthcare in Nis District is 86.76%. Although there are differences in most health centers the Plan was accomplished in a percentage between 80% and 100% for the entire period, which is a solid implementation of planned services.

Conclusion: Promoting, improving and protecting the health of women were already outlined as major goals of health policy in Serbia, but everyday medical practice testifies to certain deficiencies. Although women make up 51.4% of the total population of Serbia and also the majority of employees in the health sector, healthcare for women is not always appropriate in terms of organization, methods and access to services. The protection is more focused on the treatment than prevention of neglected diseases and conditions, and health promotion.

Key words: prevention, women's healthcare, socio-medical analysis

ADDENDUM TO THE BOOK OF ABSTRACTS

1. KORELACIJA PRODUKCIJE SERUMSKIH ANTITELA I KLINIČKE SLIKE KOD ENTEROKOLITISA IZAZVANOG *C. JEJUNI*

1. CORRELATION BETWEEN ANTIBODY DETECTION AND CLINICAL PRESENTATION IN ENTEROCOLITIS CAUSED BY *CAMPYLOBACTER JEJUNI*

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Introduction: Thermophilic *Campylobacter* species, especially *Campylobacter jejuni*, have been recognized as a major cause of acute bacterial gastroenteritis in humans.

Aim: To detect correlation between clinical presentations and serum antibodies in patients with *C. jejuni* enterocolitis.

Material and methods: Humoral immune response to *C. jejuni* was monitored within group of 30 patients suffering from confirmed *C. jejuni* enteritis diagnosed at the Public Health Institute, Niš. For IgA, IgM and IgG antibody detection ELISA technique was performed (Serion Immundiagnostica GmbH Würzburg, Germany, VIRION TEST EVALUATION ver. 4.0). At the same time, data of clinical manifestations of enterocolitis (fever, headache, number of diarrheal stools, duration of diarrhea, presence of blood and watery stools), were obtained by questionnaire.

Results: Positive values of total immunoglobulins, were found in 18 (60%) patients. Increased levels of IgA were detected in seven (29.2%) patients with moderate fever (up to 38°C) with diarrhea lasting up to 5 days. In three patients with all 3 classes of immunoglobulins the number of diarrheal stools was higher than 10 with an average duration of illness of 6.33 ± 0.94 days.

Conclusion: In this investigation, moderate clinical presentation of *C. jejuni* enterocolitis was associated with the presence of serum IgA.

Key words: *Campylobacter jejuni*, enterocolitis, humoral immune response

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