

53 Days of Preventive Medicine

International Congress

24-27. September 2019.
Niš, Serbia



BOOK OF ABSTRACTS



Public Health Institute Niš



Faculty of Medicine,
University of Niš



Serbian Medical Society, Niš

Niš, 2019.

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- **Informatics in the health system**
- **Current parasitosis**
- **Microbiology today**
- **Nutrition and Health**
- **Environment and health**
- **Theoretical and practical problems of communicable diseases**
- **Theoretical and practical problems of non-communicable diseases**

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PLENARY SESSION

An operational Framework For Promoting Adolescent And Community Health

Luca Rosi PhD, MC, MHM, MPH

What is health?

According to WHO, Health is a state of physical, mental, and social well being, and not merely the absence of disease or infirmity; where a clean environment is essential for good health well-being

While to some, the terms preventive medicine and health promotion are used synonymously, Preventive Medicine focuses on the health of individuals, communities, and populations. Its goal is to protect, promote, and maintain health and well-being and to prevent disease, disability, and death

Health promotion is the action that enable people to increase control over their own health. Therefore, it covers a wide range of social and environmental interventions that are designed to benefit and protect individual people's health and quality of life by addressing and preventing the root causes of ill health, not just focusing on treatment and cure.

According to WHO, since Ottawa, there are 3 key elements that make health promotion effective.

Namely:

Good governance for health so that policymakers should make health a central line of government policy.

Health literacy so that people have the necessary knowledge, skills and information to make healthy choices, and have financial, social and environmental opportunities to make these choices.

Healthy Cities/Urban Health which means leadership and commitment at both central and municipal level for planning and build up preventive measures in communities (and primary health care facilities).

Health promotion implies a strong understanding of the interaction of these 3 elements, because suddenly everyone is an actor in the system. In other words, a well constructed approach to health should take into account cultural, social and psychological perspectives among the others.

Those of you that are psychologists, sociologist, epidemiologists and/or population health scientists understand pieces of this puzzle, how people become engaged with these pieces, how community support this process, and how this process can promote individual and community health.

Health promotion and adolescent's misbehavior

One of the most critical element to be considered in making effective Healthcare promotion and prevention is the so-called vulnerable/fragile population. And among these the adolescent and their role in the community.

Let me clarify the term adolescent. By this term I mean those who are neither children nor adults but they have social needs belonging to both. The adolescent is therefore a quite complex psycho-social individual!!

When children advance from elementary through middle school, they face new and challenging social, family, and academic situations. Often during this period, children are exposed to substances such as cigarettes, drugs and alcohol for the first time. When they enter high school, teens may encounter greater availability of drugs, drug use by older teens, and social activities where drugs are used.

We have been there! Risk-taking is a normal part of the human development. The desire to try new things and become more independent is healthy, but it may also increase teens' tendencies to fail in this trial and errors growth due to also vulnerability to peer pressure.

Moreover, adolescents have a different set of developmental goals and needs that make it a relevant stage to understand how community participation affects healthy development.

For example, according to Erikson¹, a major developmental task of adolescence is identity formation, which includes defining one's role in relation to society, suggesting that youth engagement within their communities is an important part of development.

Communication suddenly represents one of the most effective tool of engagement to sustain a correct growth of the adolescent. And overall the growth of the all community, teachers, parents, students as part of one system.

According to the evidence an effective engaging action should include:

Family prevention programmes: e. g. strengthening protective factors through the family, including increasing family bonding and using appropriate discipline.

Community/school prevention programmes: e. g. introducing programmes at an early-age (pre-school/first grade) to address risk factors for later substance abuse.

Role of healthcare providers: e. g. introduce and perform at primary care provision level screening for substance abuse and counselling at early stages.

Health Promotion and effective communication

Today, thanks also to the new media, we live an historical period in which a good communication is fundamental to connect to the younger generation.

Interpersonal Communication and social marketing serve to influence and empower individuals, populations, and communities to make healthier choices promoting positive changes in attitudes and behaviors.

They can address elements such as:

Increase risk perception

Reinforce positive behaviors

Influence social norms

Increase availability of support and needed services

Effective health communication strategies should therefore include components such as:

¹ Erikson EH, Identity: youth and crisis. New York, NY: WW Norton & Company, 1968.

Use of research-based strategies to shape materials and products and to select the best channels that deliver them to the intended audience.

Understanding of language and priorities for different cultures and settings.

Consideration of health literacy, internet access and social/mass media exposure of target populations (including exposure to fake news very common not only among the young generation).

Recommendations

The Maslow's hierarchy of needs demonstrates that individual's basic needs (food, water and shelter) have to be met before people can achieve independence. Therefore individuals are healthy when they meet their basic needs, and by doing so they can realize their personal potential development and the potential development of others.

Create a supportive system that will encourage adolescents to visit health facilities (plan the environment WITH them rather than plan for them). According to C. Rogers a supportive (social) system is a set of interrelated units that are engaged in joint problem solving to accomplish common goals for health and well being;

Enhance client-provider development by empowering health care providers (i. e. on interpersonal communication and counseling);

Increase adolescents access to information by using their language (i. e. social media) and start introducing innovative communication approaches and channels to disseminate key health messages;

Favor change on health perspective. The One Health approach helps recognizing the inherent interdependence of human, animal and environmental health. In fact it calls for collaboration across many sectors, scientific disciplines, and communities of practice;

Promote good public-private partnerships on health promotion.

Take a proactive approach to patient care.

SESSION: PROMOTING HEALTH IN FAMILY AND SOCIETY

INVITED LECTURES

1. USING BEHAVIOURAL NUDGES TO IMPROVE CHILDREN'S FOOD CHOICES AT SCHOOL

Mihela Erjevec

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A diet rich in fruit and vegetables offers protection from many non-communicable diseases [1]. We know that eating habits are established in childhood and that they are more malleable early in life [2]. However, despite a plethora of information- and education-based campaigns delivered over several decades, most children do not eat the recommended quantities of fruit and vegetables [3].

Like their peers around the globe, children in the UK are not eating well enough to support optimum health. Their diets are full of energy-rich nutrient-poor foods, such as fatty snacks filled with salt and sugar. In Wales, it is estimated that only 23% of children eat their recommended five daily portions of fruit and vegetables. These percentages are considerably lower for children from poorer areas or families.

Clearly, evidence-based interventions are needed to change this trend. In the present talk, I will be telling the audience at the Congress about the research that had been done under my supervision in Bangor University, to address this issue.

Because of their broad scope and reach, school-based interventions have been considered a convenient way to improve children's diets [5], but many of these interventions are complex to administer and costly to implement. Therefore, relatively few schools choose to employ them. Recently, some simple changes to the choice architecture of dining environments have been shown to improve dietary behaviour of children and adults [6], offering a promise of an inexpensive approach that may be more acceptable to cash-strapped, busy schools.

One definition of 'nudges', which we adopted, is that they consist of environmental changes that make it easier to choose well, but do not involve restriction of choices or provision of incentives. We first conducted a systematic review of the existing literature and found that only a few studies took this approach [7]. We concluded that there is now some evidence that children's *choices* can be influenced by behavioural nudges, but very few studies have looked at children's *consumption*, which is the real variable of interest. It was important to determine whether the latter could be measured in primary school children.

Our first challenge was lack of reliable, validated measures that could establish children's consumption of fruit and vegetables, and more generally give us the nutrient content of their meals. Therefore, we developed a digital photography estimation method that was practical, sensitive to changes, reliable, and valid [8].

Next, in a series of studies (still ongoing), we investigated whether children's consumption of fruit and vegetables could be improved using a set of simple nudges. We enlisted help from local schools and catering team from the Conwy Council. The research team consisted of one PhD student, nine Masters students, and five undergraduate interns (so far); a colleague was also assisting us with his knowledge of inferential statistics. The intervention was so simple that we did not have to find external funding for this research. We hypothesised that children would consume more fruit and vegetables if these foods were presented more attractively and conveniently as a part of the school lunch.

Children's lunchtime choices and consumption of fruit and vegetables was examined at two time points, at baseline and post-intervention. We also recruited matched control schools where no intervention took place. Photographs were taken of children's lunchtime servings

and plate waste at each point. School menus were matched across schools on the observation days. In all schools, children were able to take and eat a portion of vegetables (e.g., peas, served with potatoes and meat patties) and a piece of fruit (e.g., an apple, on demand), in line with the Welsh school catering practices.

The choice architecture intervention, implemented over three consecutive weeks in the intervention schools, included the following ‘nudges’:

There was improved presentation and provision; chopped up fruit and salad vegetables were served in colourful reusable pots, arranged on cake stands

There were attractive advertisements – we used prominent posters announcing fruit and veg of the day, and placed them in the canteen

We also used attractive labelling of fruit (e.g. Funky Punky Fruit; Hearty Sporty Pears) and vegetables (e.g. Dinosaur Tree Broccoli; Ringing Bell Peppers).

Children were prompted to choose fruit and vegetable by adult staff; we briefed the caterers how to do this effectively (e.g., asking children whether they wanted some peas, sweetcorn, or both – rather than asking them whether they wanted vegetables, to which the answer could be ‘no’).

To estimate weights of fruit and vegetables served and eaten in each meal, the researchers calculated portion sizes based on average weights of provided foods (e.g., an average serving of peas was 58 grams; a child-sized apple was 60 grams; fruit and vegetable pots were 40 grams each). Percentage eaten was estimated on an 11-point scale (0-100%) from photographs of servings and plate waste. Finally, total consumption of fruit and vegetables was calculated for each child, at baseline and at follow-up.

We were the first research group to report that behavioural nudges can lead to a significant increase in fruit consumption of children taking school lunches [9;10; 11]. This result had been replicated and extended in research that is still ongoing. Overall, we found that children taking school dinners ate vegetables but seldom fruit, whereas those bringing their lunchboxes from home mostly ate neither; some had fruit but virtually none had vegetables. In this group, an increase in vegetable uptake and consumption was recorded.

We consider that our research has relevance for other scientists, public health practitioners, schools and caterers. In the EU and England, for example, there are presently costly fruit school schemes that have no evidence for their effectiveness; more targeted and subtle approach, such as that shown in our research, may give better, cost effective results.

In the next stage, we plan to work with the caterers to roll out this approach more widely to schools, providing free downloadable materials and instructions for cooks interested in providing a better service to their children, and schools who want to act to improve their pupils’ diets.

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2. PROMOTION OF HEALTH AND HEALTHY LIFESTYLES IN THE COMMUNITY

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Definitions and concepts

Health promotion was defined in the Ottawa Charter as “the process of enabling people to increase control over, and to improve, their health” (1). Health, as defined by WHO, as a state of complete physical, mental and social well-being could be reached if the individuals or groups are able to identify their aspirations, needs, determinants that influence their health, to practice healthy living and to change or cope with the environment.

World Health Organization in its document „Healthy living“ define healthy lifestyle as a way of living that lowers the risk of being seriously ill or dying early(2). Healthy lifestyle helps people to enjoy more aspects of their life, not just to avoid a disease or illness, but to achieve physical, mental and social well-being and to live longer. Adopting a healthy lifestyle could provide a more positive role model for other people in their families and in their close or distant surroundings, in their community.

Building of healthy communities is today a leading goal of modern health systems and health institutions that recognise the importance of prevention of illhealth statuses through the development of healthy life styles and healthy environment (3).

Community concept itself is differently explained depending on discipline that is handling this term. Therefore, even in 1955, Hillery collected and analysed 94 definitions of this term, noticing three basic components of the community (4):

- people in social interaction;
- within geographical area, and
- those that have one or more common relations.

Nutbeam’s definition (5) explains community as „specific group of people who often live in defined geographical zone, share common culture, values and norms, and is organised through social structure according to the relationships that community developed over the time“. Members of the community gain personal and social identity by sharing common beliefs, values and norms that are developed in past and can be modified in future. Individuals in community are aware of their identity as a group and share common needs and dedication to satisfy those needs. In modern communities, especially in developed countries, individuals do not only belong to one isolated community, but rather join into larger number of communities based on different features such as territory, occupation, social interests and use of spare time. Examples of these are business communities, working communities or different children’s communities. In last years, idea of community that reside a certain physical space is more and more received with reserve and the advantage is given to „virtual“ communities (6).

Promoting healthy lifestyle in the community

The world we live in, our surroundings, neighborhoods, our communities are instrumental in determining our health status. Education, access to services, family life, and work all play a role in shaping individual health and lifestyles. The kinds of health messages that people

receive close to home, in their own "world," also are among the most influential in determining their health behaviors. Many witnesses, therefore, argued that interventions in schools, the workplace, and the community at large can be powerful tools in implementing the principles of the European policies Health for All and Health 2020 (7).

Health behaviour is any activity undertaken by an individual, regardless of actual or perceived health status, for the purpose of promoting, protecting or maintaining health, whether or not such behaviour is objectively effective towards that end (8). Health behaviours and risk behaviours are often related in clusters in a more complex pattern of behaviours referred to as lifestyles.

Lifestyle is a way of living based on identifiable patterns of behaviour which are determined by the interplay between an individual's personal characteristics, social interactions, and socioeconomic and environmental living conditions (8). These patterns of behaviour are continually interpreted and tested out in different social situations and are therefore not fixed, but subject to change. Individual lifestyles, characterized by identifiable patterns of behaviour, can have a profound effect on an individual's health and on the health of others. If health is to be improved by enabling individuals to change their lifestyles, action must be directed not only at the individual but also at the social and living conditions which interact to produce and maintain these patterns of behaviour (8).

Closely related to the community is a concept of the community development. It is a process in which special place is given to community actions for health that represent collective efforts directed towards the increase of control over health determinants, and therefore over the health improvement (9). In Ottawa Charter, the significance of concrete and effective community in establishing priorities for health, adoption of decisions, planning of strategies and their implementation for achievement of better health is emphasized. Concept of enabling (strengthening, recuperation) of the community is closely related with definition of community actions for health, in accordance with Ottawa Charter. Capable community is the one in which individuals and organisations apply skills and resources in collective efforts directed towards health priorities and meeting of health needs.

In process of community development, special place is given to community actions for health that represent collective efforts directed towards the increase of control over health determinants, and therefore over the health improvement (9). In Ottawa Charter, the significance of concrete and effective community in establishing priorities for health, adoption of decisions, planning of strategies and their implementation for achievement of better health is emphasized. Concept of enabling (strengthening, recuperation) of the community is closely related with definition of community actions for health, in accordance with Ottawa Charter. Capable community is the one in which individuals and organisations apply skills and resources in collective efforts directed towards health priorities and meeting of health needs.

That means participation of its members in actions for health, through the active partnership with different sectors of society. Therefore, efficient community based approach must ensure partnership of its members with health professionals in identifying and solving community issues and must orientate towards health determinants in the way community sees them, even when it comes to the prevention programmes for specific diseases.

Community participation and active partnership is a central tenet of health promotion practice, stemming from an ideological position that seeks to shift power over health away from professional dominance within a bio-medical paradigm towards a social model that creates the conditions where people have greater control over their health and wellbeing (10). People create healthy communities by demonstrating unity and by operating as accelerants of positive changes, finding new modes for actions with the goal of creating an environment that enables healthy life styles and encourages people to fulfill their own potentials (11).

Many studies has shown scientific evidences that the main elements of healthy lifestyle are regular physical activity, healthy nad balanced diet, non-smoking environment, and moderate or non use of alcohol (12, 13). Also, othher factors, as oral health, safe patterns of beahaviour, responsible reproductive health, appropriate amoun of sleep, stress coping skills, appropriate use of health service especially preventive services, social support, are of essential impotance for good health through the lifecourse.

Health promoting projects and programmes in Novi Sad – example of a good parctice

The City of Novi Sad enforces health promotion and disease prevention policy through its bylaw – Rules on Modality and Procedure of Allocation of Assets from the City of Novi Sad Budget for Health Programs and Projects (Official Herald of the City of Novi Sad no. 51/2009 and 3/2011). This bylaw provides financial support for local health systems and NGO’s in addressing major health problems and public health issues.

Relevant competitions are published in the following fields: public health, non-communicable diseases prevention, prevention of drugs abuse, and pronatalist policy, separately for health institutions and for NGO’s. The City of Novi Sad has established Committees in the areas above mentioned (membered by professionals who are recognized due to their professional and/or academic work in relevant areas on local, regional, national and/or international level) with help from more specialized working groups, assess technical and professional quality of applications received, and after discussion and conclusions of working groups, decide on received competition applications and projects. Competitions are public (published in the official herald and on the City web page) as well as results.

Priority is given to the projects and programmes that are directed to health education and health promotion particularly for vulnerable population groups, educating educators, providing appropriate amount of health education tools and educational materials, facilitating partnership within health sector as well as interdisciplinary and multi-sectoral partnership, empowering health professionals in the area of public health and health promotion, empowering local community and NGO’s, and continuously providing information about public health issues for the public (14).

The City of Novi Sad is dedicated in enforcing health promotion and disease prevention programs for over a decade through its policies, strategies and financial support. Since the City of Novi Sad have become Healthy City in December 2012. we expect to grow awareness and commitment to health, resulting in mobilizing all citizens to take a „Whole of Society“ approach.

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SESSION: PUBLIC HEALTH TODAY

3. PUBLIC HEALTH PRACTICE IN SERBIA AND NEW PUBLIC HEALTH CHALLENGES IN THE 21ST CENTURY

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Abstract

The field of public health is constantly changing. Public health practice aims to adapt to the global disease pattern changes, which are closely linked to changing lifestyles. Lifestyle also has a significant impact on all aspects of health, including major public health problems with their high prevalence and incidence in all regions of the world.

In the 21st century there is a change of leading health problems in the human population all over the world, including Serbia. Chronic and noncommunicable diseases, as well as injuries, are overtaking communicable diseases as a leading health problem. Still, communicable diseases must not be overlooked. Changes of the leading health problems should inform changes of the public health programs and strategies. These, in turn, have to be implemented at the population level in order to lead to a favourable public health outcome.

In the Republic of Serbia there are 25 public health institutes that systematically implement different public health programs by collecting, analysing, and making available data concerning health status of the population at the district and population level. These data consist of health status statistics, community or population health needs, and epidemiologic and other assessments of health problems. This function of public health institutes is of utmost importance for the proper planning of public health activities and measures aimed at improving public health situation in the country. Public health surveillance is a basic instrument for policy decision making in the field of public health and healthcare in general.

Strengthening public health surveillance at population level requires, in general, continual change of public health institutions' activities aimed at improving public health. These changes in PHI's methodology of work have to be properly selected, evidence-based and in line with international recommendations, and have to include a multidisciplinary approach.

Public health surveillance is the key task of the public health institutes and it encompasses systematic collection, management, analysis, and interpretation of data concerning health, followed by dissemination of the data to public health programs. So far, the best recognized use of public health surveillance data is the detection of epidemics and other health problems at population level, but there are many other uses that are critical to public health practice. The data is used to estimate the scope and the value of public health problems, which facilitates public health planning. Surveillance data can also be used to detect changes in health practices, monitor changes in infectious and environmental agents, evaluate control measures, and describe the natural history of a health event in a community that will generate hypotheses and stimulate applied research. Public health surveillance is the fundamental source for decision-making in public health. Information technology and capacity building of public health workforce are important strategies for the modification of public health surveillance as well. Public health institutes will probably have to face new challenges in the 21st century to meet new demands in the field of public health.

Introduction

The field of public health is constantly changing. Main challenges are changes of life styles, changing patterns of mortality and morbidity, changing demographics, climate change, digital and medical technology changes, challenges made by political influence on public health, change produced by influence of big corporation on habits, community influence on public health and others

Changing of life styles

A lack of physical activity, an unhealthy diet and other such habits that the modern era entails have brought on changes in the entire population when it comes to decision-making in these areas. Continuous implementation of various health promotion strategies has led to a positive shift in behavior where healthier choices are concerned.

According to the WHO definition health promotion enables people to increase control over their own health. It covers a wide range of social and environmental interventions that are designed to benefit and protect individual people's health and quality of life by addressing and preventing the root causes of ill health, not just focusing on treatment and cure (1).

There are 3 key elements of health promotion:

1. Good governance for health

Health promotion requires policy makers across all government departments to make health a central line of government policy. This means they must factor health implications into all the decisions they take, and prioritize policies that prevent people from becoming ill and protect them from injuries.

These policies must be supported by regulations that match private sector incentives with public health goals. For example, by aligning tax policies on unhealthy or harmful products such as alcohol, tobacco, and food products which are high in salt, sugars and fat with measures to boost trade in other areas. And through legislation that supports healthy urbanization by creating walkable cities, reducing air and water pollution, enforcing the wearing of seat belts and helmets.

2. Health literacy

People need to acquire the knowledge, skills and information to make healthy choices, for example about the food they eat and healthcare services that they need. They need to have opportunities to make those choices. And they need to be assured of an environment in which people can demand further policy actions to further improve their health.

3. Healthy cities

Cities have a key role to play in promoting good health. Strong leadership and commitment at the municipal level is essential to healthy urban planning and to build up preventive measures in communities and primary health care facilities. From healthy cities evolve healthy countries and, ultimately, a healthier world.

Individual measures are important as well. Changing life habits is a process that involves several stages. Sometimes it takes a while before changes become new habits. Adopting new, healthier habits may protect people from serious health problems like obesity and diabetes. New habits, like healthy eating and regular physical activity, may also help people to manage their weight and have more energy. After a while, if people stick with these life style changes, people may become part of your daily routine.

Changing patterns of mortality and morbidity

Throughout the 20th century, there have been rapid and profound changes in morbidity and mortality in both the developed and the developing countries. These changes are clearly demonstrated in the values of many indicators commonly used for a general description of

both these processes, such as life expectancy, infant mortality rates and cause-specific prevalence and incidence rates.

Tracking the aforementioned indicators and taking initiative through measures aimed to improve the overall health of the population are a task fit for public health institutions, including public health institutes.

Changing demographics

The population in Europe is ageing very fast and we expect the proportion of people aged 65 and older to increase to 25% in 2050 (2). People will live longer, but not necessarily in good health and well-being. In the same time, we are facing an increasing of the burden on health care systems to treat multimorbidity and chronic diseases. There is a need to address these changing demographics to mitigate their impact.

The Serbian population has been shrinking for decades. The number of newborn children on an annual basis has been dropping, all the while estimated life expectancies have lengthened. Public health institutions are bringing in new priorities and programs into their line of work in order to counter this challenging trend.

Climate change

Although global warming may bring some localized benefits, such as fewer winter deaths in temperate climates and increased food production in certain areas, the overall health effects of a changing climate are likely to be overwhelmingly negative. Climate change affects social and environmental determinants of health – clean air, safe drinking water, sufficient food and secure shelter.

Climate change has affected the Republic of Serbia in equal measure as the rest of the world. Many diseases transmitted by different vectors call for the cooperation of numerous sectors including professionals from the fields of environmental and veterinary science, meteorology, etc.

Digital and medical technology changes

The modern-day method of prevention and treatment of disease, as well as the tracking of medical data associated therewith via modern informational technologies, are a trademark of the 21st century and a great privilege, but simultaneously a challenge for all those employed in the healthcare system. The benefits of new medical technology in healthcare are very beneficial for prevention as well as for treatment. We are aware of the advantages and challenges of new technology and digitalization.

Political influence on public health

Public health workers and experts need an understanding of the political system and should be willing to work with politicians. Public health experts need to invest in collaborating and coordinating with politicians to make sure our evidence-based voice is heard (3).

The influence of political climate on the development of different areas of public health is a challenge for both the healthcare workers and the decision-makers in all fields of politics.

Influence of big corporation on habits

The financial support for numerous health organisations in even developed countries by powerful and reach companies that are producers of products that are not healthy, is more often in place globally.

The public healthcare sector is faced with many challenges, as a consequence of big corporations continually putting new products onto the market, in terms of preserving healthy habits and public health in general.

Community role

The role the community plays in the upkeep of public health is of great importance in society's quick and efficient reaction to public health needs.

Forming a Council to deal with health-related questions on a local and municipal level, and putting together local public health programs, are the tools of choice in improving public health.

New challenges in public health in new century

The fight against premature mortality—the health problems that continue to affect the life expectancy of children. We're mainly talking about infectious diseases—such as malaria, tuberculosis, and respiratory and diarrhoeal diseases—but obesity is also a problem. It is needed to be solved. It seems clear that the public health network needs to adapt to 21st century challenges. The 21st century public health professional needs to be smart, persistent and innovative, be able to be a diplomat and a negotiator at the same time (2). The approach of health in all policies is essential and the recently published manifesto: 'All policies for a healthy Europe' is a step in the right direction (4).

The most important action is to ensure that this science is translated into action, and that solutions are implemented which will contribute to the transformation and improvement of people's lives and health" (5).

Influence of international agency on public health

Some international agencies like CDC and ECDC do have public health influence globally. Main goal of those institutions is to protect public health and safety through the control and prevention of disease, injury, and disability in the US, Europe and internationally. These institutions make influence world widely and they are focusing on applying disease control and prevention. It especially focuses its attention on infectious disease, food borne pathogens, environmental health, occupational safety and health, health promotion, injury prevention and educational activities designed to improve the health globally. In addition, these institutions are in charge for the researches, and as well as these provides information on non-infectious diseases such as obesity and diabetes and is a founding member of the International Association of National Public Health Institutes (IANPHI).

The role of WHO is, as well, of great importance in actualizing healthcare policy and reaching the set goals of sustainable developments.

In lieu of a conclusion

Public health surveillance is the fundamental source for decision-making in public health. Information technology and capacity building of public health workforce are important strategies for the modification of public health surveillance as well. Public health institutes will probably have to face new challenges in the 21st century to meet new demands in the field of public health.

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4. NATIONAL ACCOUNT OF HEALTH WORKERS FOR BETTER POLICY PLANNING AND DECISION MAKING

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At the end of the second decade of the 21st century, health system stakeholders were concerned with achieving universal health coverage (UHC) and health-related sustainable development goals (SDG). The implementation of health programs and plans is directly related to dedicated resources, including health resources for health. By 2030, the global shortage of human resources for health is estimated at over 17.4 million over the identified minimum staffing level (threshold of 4.55 doctors, nurses and midwives per 1000) needed to achieve the Sustainable Development Goals of the World Health Organization in 2013 (1). Most of the global needs are for over 9 million nurses and midwives (52%) and for almost 2.6 million doctors (15%), and in Southeast Asia (about 40%) and Africa (about 24%). It is also estimated that current trends in production and employment will not sufficiently reduce the need-based shortage of healthcare professionals by 2030 (2). In fact, in 2005, the estimated health workforce shortfall was eight times lower, aka 2.4 million professionals, based on the threshold of 2.28 healthcare professionals required to reach the Millennium Development Goals by 2015, most of which were identified in Southeast Asian countries and Africa.

Although the thresholds or methods used in calculations are not comparable, from the socially accountable perspective, considerably different estimates raise a number of questions. In 2006, the threshold was achieving 80% coverage of assisted deliveries while in 2013, the threshold was an aggregate coverage indicator (SDG index), which weighted the importance of specific indicators based on the contribution of the diseases they track to the global burden of diseases. In addition, cautious interpretation of projections of workforce shortages is necessary because they are as good as the data and assumptions underpinning projections. Almost every health system in the world strives to have valid and update information on its main resource, health workforce. The quality of health care policies and decisions depends on the quality of data. In this regard, what data we better monitor and collate today than in 2005, and why? Using the data on health workers in national accounts, can we explore the evidence of the alignment of the health workforce policy with plans and policies for health services provision?

Another issue is related to the governance of the health workforce. The health workforce situation in 2005 (3) characterized: *“inappropriate or inadequate training, with curricula that are not needs-based; poor access to information and knowledge resources; inadequate numbers and skills of health workers; uneven distribution of workers at different levels of service delivery, from national programme officers through to health facility personnel; low morale and motivation; unsafe conditions in the workplace; poor policies and practices for human resources development (poor career structures, working conditions and remuneration); lack of supportive supervision; lack of integration of services with the private sector; high attrition of health workers, as a consequence of death from the very disease they work to cure or because of migration.”* Based on current data, is the situation of the health workers today different from 2005? So, what types of interventions have been implemented in the meantime, at the institutional or national level, and with what impact? Do we have any evidence on the governance impact on the health workforce situation?

It is also important to learn from each other. Does national health workforce information system enables knowledge and experience translation? Do we have a standardized tool that can be applied to international and time comparisons, that is, it can help to learn and transfer best practices?

Both the Global strategy on health workforce by 2030 (1) and the High-Level Commission on Health Employment and Economic Growth (4) promote the concept of having national health workforce accounts (NHWA) as important means to support countries in their national HWF policy and planning (5). Implementing NHWA will bring national and international benefits. At national level, it supports labour market analysis, policy design, and examine the causal impact of policy change, and as such it can serve as a guiding and supporting tool for countries to inform national evidence-based HWF policy decisions. At international level, it is to facilitate the standardization of health workforce information systems for interoperability.

The NHWAs, a harmonized, integrated approach for annual and timely collection of health workforce information, are designed to support of strategic workforce planning and global monitoring with core indicators to provide full coverage of all health workforce components and policy domains. The core indicators are set up in 10 NHWA modules including (5):

the most crucial information on the health workforce (Module 1: Active health workforce stock);

information and data to support policies on the education and training component, being the base and ‘input’ of health workforces (Modules 2: Education and training; Module 3: Education and training regulation and accreditation; Module 4: Education finances);

for tracking policies that address inflows and outflows in the health workforce (Module 5: Health labour market flows; Module 6: Employment characteristics and working conditions; Module 7: Health workforce spending and remuneration); as well as

health workforce information and data information in relation to serving population health needs (Module 8: Skill mix composition for models of care; Module 9: Governance and health workforce policies; Module 10: Health workforce information systems).

Finally, the NHWA can track and support countries’ health workforce efforts towards UHC, the SDGs and the national /global health workforce milestones. In doing so, Serbia can apply NHWA in a flexible, modular way and according to its own specific needs and priorities with clear policy relevance in mind, and eventually work towards selecting and covering the entire NHWA.

In conclusion, rapid aggregation and display of health workforce data using the NHWAs can inspire optimizing planning systems, through: developing health workforce available, accessible, acceptable and of the appropriate competencies to provide good quality health services, better allocation of resources, increasing productivity, effective retention policies, replacement the health worker loss caused by exits effective public–private partnerships increasing investments in education and production, and/or increasing immigration financing and financial incentives for a more balanced geographical distribution of the HWF across the country or region negotiations with the government as well as negotiations with the private sector

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5. PUBLIC HEALTH IN THE COMMUNITY IN REPUBLIKA SRPSKA

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Introduction

Health and well-being are basic need of all people. All countries of the world, including the Republic of Srpska, face challenges to health and well-being of the population, and their governments have a great responsibility to promote health. The future is uncertain, and today's political and economic system can be deeply transformed (1). Although ideals are difficult to achieve, they need to be constantly pursued.

The World Health Organization (WHO) defines health as "a state of complete physical, psychological and social well-being, not just the absence of illness or disability." The WHO has been continuously proclaiming its goal of "health for all" in documents, starting from 1948 until today (2). The WHO has highlighted the importance of essential public health functions for achieving sustainable development goals and full coverage of health care as well as the implementation of international health regulation (3).

Development of health can be partly influenced by the developed health system, while other sectors have a greater involvement (4). It is important to emphasize intersectoral cooperation and partnerships in health care constantly (5). So it is no wonder that the Banja Luka Charter was signed at the Third Ministerial Forum of Southeast Europe 14.10.2011. which was held in Banja Luka, in which the signatory countries pledged to strengthen public health capacities and implement a "health in all policies" approach (6).

The leading causes of mortality in the Republic of Srpska in 2016 are cardiovascular diseases (49.53%) and malignant diseases (21.10%), which together account for more than half of the total mortality (70.63%). The implementation of public health activities stopped the trend of increasing mortality from cardiovascular diseases in the period 2007-2016. The increase in life expectancy in the last ten years from 74.43 for both sexes in 2007, to 77.24 in 2016, is a result of public health achievement.

The aim of this paper is to present public health in Republika Srpska with special reference to public health in the local community.

Development of a political and strategic health framework in Republika Srpska

The context of development in the Republic of Srpska carries with it numerous opportunities and challenges for health and health system, especially related to demographic, epidemiological, economic, political, legal and regulatory, socio-cultural and technological changes. An unfavorable demographic trend will have significant consequences for the health of the population in terms of the epidemiological transition to chronic non-communicable diseases.

Health was recognized in the Constitution of the Republic of Srpska (7). The Law on Health Care regulates the provision of health care for the population of the Republic of Srpska based on the principles of equality, availability, inclusiveness and continuity (8). This law follows a number of by-laws, such as the Rulebook on the content, scope and way of right to health care regulation (9), which prescribes measures for the promotion of health, prevention and early detection of diseases.

According to the leading causes of diseases and deaths in the last year in the Republic of Srpska, many legal and strategic documents dedicated to the prevention and early detection of non-communicable diseases are prepared.

Mental health promotion is regulated by the Republic of Srpska Mental Health Policy (10). The production and sale of tobacco products is regulated by the Law on the prohibition of

smoking tobacco products in public places (11), and the Strategy on substance abuse and control of narcotic drugs and drug abuse in 2016 - 2021 (12).

The Program for the early detection and prevention of the risk factors of cardiovascular and malignant diseases and other mass non-communicable diseases and the early detection of these diseases have been implemented in the Republic of Srpska, since 2004 (13).

Of particular importance to public health are the Policy for the Advancement of Early Childhood Growth and Development in the Republika Srpska (14) and the Policy for the Advancement of Nutrition of Children by the Age of Five in the Republika Srpska (15), making the Republika Srpska Government one of the first countries to have dedicated themselves to this topic.

According to the European "Health 2020" policy (16) and the European Action Plan for Strengthening Public Health Capacities and Services (17), the Republic of Srpska Health Policy until 2020 was adopted in September 2012 (18). The policy includes reducing disparities in population health; investing in health; involving citizens in health decision-making and creating healthy local communities; control of non-communicable and infectious diseases and promotion of safety; creating a healthy and supportive environment for health and well-being; strengthening a customer-oriented health system; strengthening public health capacities and emergency preparedness and promoting and adopting a "health in all policies" approach.

In 2018, the Government of the Republic of Srpska adopted an "Action Plan for the Prevention and Control of Non-communicable Diseases in the Republic of Srpska for the period 2019 -2026" (19). The Action Plan is based on previously announced Policy for improvement of population health in the Republic of Srpska and Action Plan for the Prevention and Control of Noncommunicable Diseases in the European region WHO for the period 2016-2025 (20).

Organization of public health in the Republic of Srpska

Health care is provided at primary, secondary and tertiary level of health care centres which have a contract with the Health Insurance Fund.

A special form of public health care is provided by the public health organization (8). Institutions of the public health system are organized at the level of the Republic of Srpska and local self-government units. The main actors in the field of public health in Republika Srpska are the Ministry of Health and Social Welfare and the Public Health Institute of the Republic of Srpska. The Public Health Institute of the Republic of Srpska is organized through regional centres located in Dobož, Istočno Sarajevo, Foča, Zvornik and Trebinje.

At the local level, public health activities are under responsibility of local authorities which carried out by family medicine teams and hygienic-epidemiological services of health centres. Responsibility for improvement of health of the population in community through promotion of healthy lifestyles and reduction of risk factors for health are provided by family medicine teams in collaboration with local government institutions.

At the level of local authorities, in area of health promotion are active mental health centres as well as physical rehabilitation centres.

Monitoring of risk factors and protective factors for non-communicable diseases

In order to adequately plan public health strategies and action plans, studies are continued provided in the Republika Srpska. Studies of monitoring of risk factors of patients with coronary diseases in Republika Srpska (21) conducted in health centres during 2003 and 2006 showed high prevalence of risk factors among respondents. Thus, a 2006 study found that 40% of subjects smoked, 77% had hypertension, 36% had hyperlipidemia, 20% had diabetes, and 27% were obese.

According to the RepublikaSrpska Population Health Survey conducted by the Public Health Institute of the RepublikaSrpska in 2010 (22), the prevalence of smoking (daily and occasionally) was 31%. According to the findings of the Multiple Indicators Survey in BiH 2011-2012, 51% of women and 58% of men aged 15-49 used tobacco for a lifetime (23). A global youth smoking survey conducted in 2013, found that 7.9% of young people ages 13 to 15 are daily smokers (24). In terms of alcohol consumption, according to previous survey (22), an increasing rate (20,6%) from 2002, of no alcohol consumption, so 55.7% do not consume alcohol. Among alcohol consumers, 16.8 consume it daily. The findings of the same survey indicate poor eating habits (22), because every fifth resident does not think about health when choosing a diet. Fresh fruits are consumed daily by 38.9% of the adult population and 48.2% consumed fresh vegetables. Every tenth inhabitant salts food before tasting it. According to the Multiple Indicators Survey 2011- 2012, 95.3% of children under six months old were breastfed at least once. According to the Population Health Survey, 57.9% of the population had a low level of physical activity and only 19.7% had a high level (22).

Prevalence of risk factors for non-communicable diseases in neighbouring Croatia and Serbia are similar to those in our country. According to Health and Health Data in Croatia (25), a quarter of adults smoke tobacco daily, and occasional excessive alcohol consumption, especially among young people, is steadily increasing. The prevalence of obesity, especially in children, has increased, and since 2001, it has doubled. According to a 2013, Serbian Population Health Survey, prevalence of tobacco smoke exposure is more than 50% in population over the age of 15, and rate of alcohol consumption compared to a previous 2006 survey, has increased (26). More than half of the population (56.3%) was overweight and compared to 2006, prevalence of obesity has increased. One of the reasons was the insufficient consumption of fruits and vegetables by 54.4% of the population, while 19.7% did not think about health when choosing a diet. Interventions regarding leading public health challenges are essentially, not only in our country, but also in the region.

Challenges in public health in the Republic of Srpska

Key public health challenges in Republic of Srpska are related to malnutrition in early childhood, the high incidence and mortality of non-communicable diseases, and diseases that are effectively prevented by vaccines.

With an adaptation of the "Nutrition Friendly School Initiative" material developed by WHO experts, "Schools / Preschools-Friends of Good Nutrition Habits" program was launched in 2014. The program is being implemented in 10 pre-schools. The Rulebook on conditions for providing nutrition, social and health care in preschools was adopted, and most of the initiative was introduced, it is expected to be implemented in all preschool institutions in the future.

The program is an excellent example of cross-sectoral cooperation between health and education sectors, families and local authorities.

In cooperation with the World Bank and the Swiss Development Agency, a project on reducing health risk factors in two local communities, Doboje and Zvornik, is focused on four risk factors (tobacco smoking, alcohol consumption, physical inactivity and unhealthy nutrition). The activities of the project are based on the Model Approach of Communities that Care (CTC) (27), which is a widely adopted evidence-based approach worldwide, including in several European countries. The project is entering in final phase and it is expected to show positive effects in local communities. Also, it will be the possibility of implementing "good practice" across the RepublikaSrpska.

Within the Project "Strengthening and improving modern and sustainable public health strategies, capacities and services for improving population health", a number of activities

were carried out. One of them is a self-assessment evaluation using the self-assessment tool for the evaluation of essential public health services in the WHO European Region 2014, version September 2014. All 16 ministries appointed their representatives to the Public Health Network, and representatives of all sectors participated in a series of public health capacity-building events and policy-making initiatives.

A Study of the description of the food environment in Banja Luka according to the WHO/EURO FEED cites methodology was also conducted. Samples of the most commonly prepared street food were collected and analyses were conducted in Portugal.

The contents of the training / intervention package in the assessment and management of individual cardiovascular risk for family medicine teams in the Republic of Srpska were agreed with training of 23 educators from two training centres, two departments of family medicine in the Republic of Srpska provided by Finnish consultants. Seven guidelines have been prepared for: arterial hypertension, diabetes, cardiovascular disease, hyperlipoproteinemia, obesity in children and adults, promotion of physical activity and quitting smoking.

With monitoring and evaluation of the implementation of the individual cardiovascular risk assessment and management program in family medicine have been developed 13 indicators by the Agency for Certification, Accreditation and Quality Improvement of Health Care of the Republika Srpska, which are not routinely collected in practice. The Agency has taken steps to assess their fulfilment by family medicine teams, and conducted a study based on 13 selected indicators before and after education.

The Action Plan for the Prevention and Control of Noncommunicable Diseases in Republika Srpska for the period 2019 to 2026 is of high priority for implementation. Currently in preparation is a detailed financial plan for the implementation of those activities. In general, the Action Plan is divided into 32 activities, of which in 26 the Public Health Institute of the Republic of Srpska has the key role. One of the activities concerns the establishment of local health committees, which will be the working bodies of the Federation of Municipalities and Cities of Republika Srpska. The Action Plan also envisages the establishment of a network of healthy cities with the aim of increasing local community involvement in public health.

The growing distrust of parents in the measles vaccine has led to epidemics of measles in the Republic of Srpska and in the region countries. With the professional and financial assistance of UNICEF, a number of trainings of pediatricians, family doctors and nurses on immunization on interpersonal communication on immunization were held.

Conclusion

The Republic of Srpska Government has created good grounds for improving the health of the Republic of Srpska population. Good health and well-being requires greater involvement of all actors in the communities of the Republic of Srpska

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6. SERBIA AND THE THIRD HEALTH PROGRAM OF THE EUROPEAN COMMISSION (2014-2020)

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In order to ensure protection of population health and to improve public health, prevent diseases and eliminate risk factors that affect physical and mental health, the European Union decided to develop Health Programme that will be implemented within the EU countries and some non-EU countries that joined this Programme.

The Health Programme is an instrument of funding aiming to support and develop health related activities in participating countries.

Previous Programmes

In 1993 the Commission presented a Communication on the Framework for Action in the Field of Public Health as an initial strategy document to develop work on public health. On this basis, eight action programmes on health promotion, cancer, drug dependence, AIDS and other communicable diseases, health monitoring, rare diseases, accidents and injuries, and pollution-related diseases, were agreed.

These programmes have been replaced by the Public Health Programme (2003–2008) and the Health Programme (2008-2013), that were generated knowledge and evidence i.e. best practice, tools, and methodologies to be used as a basis for informed policymaking and further research and to secure benefits for population.

Third Health Programme (2014-2020)

This Programme is based on Regulation (EU) 282/2014. It's budget is €449.4 million and has 23 priority areas, and four specific objectives: to promote health, prevent disease and foster healthy lifestyles through “health in all policies”; protect EU citizens from serious cross-border health threats; contribute to innovative, efficient and sustainable health systems, and facilitate access to high quality, safe healthcare for EU citizens.

There are two main funding mechanisms: grants and tenders. Grants for projects, operating grants, direct grants with international organisations and grants to EU authorities and bodies for co-financed actions (called joint actions). The Consumers Health Agriculture and Food Executive Agency (Chafea) organises calls for proposals for projects and operating grants, as well as calls for joint action and tenders. Direct grants are signed with international organisations active in the area of health.

All EU countries, Iceland, Norway, Serbia, Moldova and Bosnia & Herzegovina participate, meaning that entities registered there are also eligible to participate in the calls for proposals. Participation is open to a wide range of organisations, including: public authorities, public sector bodies, in particular research and health institutions, universities and higher education establishments, and NGOs.

Joint Action Projects

This type of projects is co-financed by European Commission and participating countries/institutions have to provide finance at the amount of 20% to 40% of the whole budget amount.

The ministries of Health of participating countries nominate Competent authorities, the institutions that represent country in the projects. Besides that, there is possibility to include some institutions as an affiliated entity or collaborating partner.

Republic of Serbia joined to the Third Health Programme at 2016, and since than participate in numerous Joint Action (JA) projects.

Since 2017, for the period of 2017-2020, Serbia participates in three JA projects – Implementing good practices for chronic diseases – CHRODIS+, Joint Action on Tobacco Control - JATC, and Joint Action on integrating prevention, testing and link to care strategies across HIV, viral hepatitis, TB and STIs in Europe – INTEGRATE.

“CHRODIS+ is a high-level response by the EU to support member states by stepping up together and sharing best practices to reduce the burden of chronic diseases. This three-year initiative (2017-2020) under the Third health programme (2014-2020) is funded by the European commission and the participating partner organisations”.

In CHRODIS+ participate 42 institutions from 21 European countries. They collaborate in order to implement pilot projects and generate practical lessons in the field of chronic diseases.

JATC is a collaborative action with the aim to implement an action-oriented initiative based on evidence-based tobacco control policies and implementation at the national, regional or European level with the overarching aim to improve the protection of EU Public Health.

The actions to be performed during JATC bring significant added value to the existing public health knowledge as the vast majority, if not almost all of the data submitted, has never been evaluated on a comprehensive scale. In JATC is involved 30 partners/institutions.

The Institute of Public Health of Serbia leads Work Package 2 responsible for the dissemination of project results.

„The main objective of INTEGRATE is to integrate early diagnosis and linkage to prevention and care of HIV, viral hepatitis, TB and STIs in EU member states by 2020. INTEGRATE has been focusing on how effective tools for diagnosis and linkage to care in one disease area can be used in others. This will be done through review of existing tools followed by adaption and piloting of the tools in other disease areas. Further, INTEGRATE will focus on capacity building and knowledge sharing among the partners and central to the work will be a focus on identification of best practices in testing and linkage to care and efforts to improve sustainability at the national level through policy development“. In the INTEGRATE participate 29 partners from 15 countries.

In 2018, European Commission launched 6 new JA projects and Serbia participates in all of them - Innovative Partnership for Action Against Cancer – iPAAC, Joint Action on Health Equity Europe – JAHEE, Joint Action on Health Information – INFACIT, European Joint Action on Vaccination – EU - JAV, EU Healthy Gateways Joint Action Preparedness and Action at Points of Entry (Ports, Airports, Ground Crossings), and Joint Action supporting the eHealth Network – eHAction.

„The general objective of the iPAAC is to develop innovative approaches to advances in cancer control. The innovation that will be covered within the JA consists of further development of cancer prevention, comprehensive approaches to the use of genomics in cancer control, cancer information and registries, improvements and challenges in cancer care, mapping of innovative cancer treatments and governance of integrated cancer control, including a new analysis of National Cancer Control Plans“. In the iPAAC JA is involved 24 countries with 44 institutions, including 7 institutions from Republic of Serbia.

„JAHEE represents an important opportunity for Member States to work jointly to address health inequalities and achieve greater equity in health outcomes across all groups in society, in all participating countries and in Europe at large. The effects of health inequalities within and between European countries are widely recognized, and reducing health inequalities is on the agenda of many countries. Despite an increasing concern and awareness on health inequalities, a wide gap exists in Europe in terms of political response. The general objective of JAHEE is to improve health and well-being of European citizens and achieve greater equity in health outcomes across all groups in society in all participants countries and in Europe at large. In addition JAHEE will also include a specific focus on both vulnerable groups and migrants“. 25 countries with 48 institutions participate in this project. Serbia is represented by 5 institutions.

„The goal of INFACIT is to strengthen national and EU health information systems by establishing a sustainable research infrastructure to support population health and health system performance assessment, strengthening European health information and knowledge bases, as well as health information research capacities to reduce health information inequalities, and supporting health information interoperability and innovative health information tools and data sources“. In the INFACIT project has been involved 28 countries with 39 institutions.

„The EU-JAV project aims at building concrete tools to improve vaccination coverage in EU and therefore improve population health. The JA Vaccination proposes to address several important issues, common to many countries such as establishing a sustained cooperation of relevant Member State authorities, defining basic principles for vaccine demand forecasting, developing a concept and prototype for a data warehouse for EU-wide sharing of vaccine supply and demand data among dedicated stakeholders, defining common stages and criteria for priority-setting of vaccine research and development, developing a concept and prototype for a vaccine R&D priority setting framework, defining structural, technical and legal specifications as regards data requirements for electronic vaccine registries/databases/immunisation information systems and providing a framework to cooperate on confidence from research to best practices and implementation“. 34 partners from 20 different countries are involved in realization of the activities of the EU-JAV project. Serbia is represented by 3 institutions.

“The EU HEALTHY GATEWAYS Joint Action aims to support cooperation and coordinated action of Member States to improve their preparedness and response capacities at points of entry. This includes ports, airports and ground crossings, in preventing and combating cross-border health threats from the transport sector. This Joint Action will produce guidelines, catalogues of best practices and validated action plans to be implemented by Member State health authorities at operational level in the field of transport, covering all

types of health threats, risk communication, advice for public health event management and contingency planning.

Online and face-to-face training on contingency planning and management of events (due to infections, vectors, chemical, environmental, and other agents) at points of entry will be provided at the European, national and local level, while the Joint Action will also support the execution of hygiene inspections on ships and airplanes". One of the specificities of the HEALTHY GATEWAYS Joint Action is that among 37 authorities from 30 countries, partner from Taiwan participates in the project, as well.

„Ageing population and increased prevalence of chronic conditions combined with limited human and financial resources are putting health systems under increasing strain. Digital tools, however, bring an opportunity to improve health care sector. Integrating eHealth into health policy and aligning eHealth investments with health requirements is of high importance, especially when recommendations and practices can be transferred across countries. Targeting Members States and Countries of the EU and eHealth stakeholders, as well as the general public, this project aims to improve health care with the use of ICT“.

In 2019 has been launched only one Joint Action - Strengthened International Health Regulations and Preparedness in the EU – SHARP.

„The SHARP Joint Action will strengthen implementation of Decision 1082/2013/EU, supporting the EU level preparedness and responses to health threats and the implementation of the International Health Regulations (2005). Through the Joint Action special efforts will be employed to fill gaps that have been or will be identified in priority countries (countries that have biggest gaps in the capacity required for full IHR capability). The partnership of the joint action consists of 26 Associated Partners and 33 Affiliated Entities, which all will receive Commission co-funding. In addition there are 9 Collaborating Partners that will self-fund all activities that they participate in. Totally 30 countries (24 EU members, 3 EEA/EFTA members and 3 European neighborhood countries) participate in the Joint Action. The SHARP JA will liaise with and collaborate with the ECDC, the WHO EURO regional office and the WHO Health Emergency and IHR unit in Lyon, and IANPHI in relevant activities“. The Institute of Public Health of Serbia leads the Work Package 8 – Training and local exercises, exchange of working practices.

Three new Joint Action that will start in 2020, are in the phase of preparation - Joint Action on the implementation of digitally enabled integrated person-centred care, Joint Action to strengthen health preparedness and response to biological and chemical terror attacks, and Joint Action on the Implementation of validated Best Practices.

The expectations from the European Commission from new JA projects are to

„enable the digital transformation of health and care in the Digital Single Market“, and to build the capacities of national and regional authorities to organise and deliver integrated person-centred care;

strengthen health preparedness and response to terrorist attacks across the health, security and civil protection sectors, focusing on biological and chemical agents;

focus on adapting, replicating and implementing evaluated effective health interventions (i.e., practices that have proven to work) in the areas of food reformulation monitoring, the framing of aggressive marketing of food, and public procurement of healthy food in public settings.

Next programmes

Last May the European Commission adopted a legislative proposal for a new European Social Fund Plus (ESF+) Programme for the period 2021-2027 aiming to become the financial instrument for the implementation of Health Policies while facilitating synergies with other EU instruments financing health-related projects.

The other EU financial instruments as the European Regional Development Fund, Horizon Europe, Digital Europe, InvestEU Fund or Connecting Europe Facility will also tackle public health priorities.

Health-related resources will be part of the budget of several priority areas: social protection, research and innovation, the digitisation of society, cohesion and global responsibility. The main objectives of new programme are: Improving crisis preparedness and response against cross-border health threats; Strengthening health systems (digital transformation, EU health information, support to national reforms); Supporting EU health legislation (medicines, HTA, tobacco, cross-border care); Supporting integrated work (European Reference Networks, implementation of best practices for health promotion and disease prevention).

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SESSION: INFORMATICS IN THE HEALTH SYSTEM

7. ELECTRONIC HEALTH DOCUMENTATION - BENEFIT OF THE HEALTH SYSTEM

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Abstract

"Health Document" is an original or reproduced document, received or created in health institutions, private practices and other legal entities. Healthcare Information System - ISIS (Healthcare Information Systems - HIS) is one of the basic components in the modern healthcare system. The benefits of the HIS over the classical approach are multiple: economic, qualitative, organizational, healthcare and research. On the example of the Health Center Niš and the Public Health Institute Niš it has been shown the application of information and communication technologies into practice. In 2011, the Health Center Niš became a user of the medical information system MEDIS.NET, which was implemented in the Laboratory for Medical Informatics of the Faculty of Electronic Engineering in Niš. Thanks to the software developer seamless integration of the software with minimal changes was enabled and officially started in March 2016. Since March 2019, paper prescriptions for prescribing medicines have been replaced by electronic ones. Due to the continuous advancement of communication information technologies, the functioning of healthcare institutions has been considerably facilitated. The efficiency and quality of healthcare delivery, its organization and contact with patients are significant strengths and direction in which the healthcare system will move in the future.

Introduction

Health documentation is used to: patient's health monitoring; monitoring and studying the health status of the population; monitoring the fulfillment of obligations of all health care entities; monitoring environmental risk factors and assessing their impact on population health; monitoring of health care resources; monitoring and continuous improvement of the quality of health care; health care financing; health care planning and programming; monitoring and evaluating the implementation of health care plans and programs; conducting statistical and scientific research; informing the public; fulfillment of international obligations in the field of health and for the development of health care and health insurance systems.

"Health Document" is an original or reproduced document, received or created in health institutions, private practices and other legal entities. Health documents consist of patient's medical records and basic documentation of a health care institution, private practice and other legal entities. Health records may be kept in written or electronically form;

"Medical records" contains observable, measurable and reproducible findings obtained from a patient's examination, as well as laboratory and diagnostic tests, assessments or diagnostic formulations. Medical records chronologically record patient care, diagnostic or reasons for a visit to a healthcare facility, support preventative procedures, screening, and treatment. It represents a forensic medical document so it must be complete.

The health information system is defined as a set of people, material resources and procedures for the production and communication of information for the needs of the health system. According to the definition of the World Health Organization, it is part of the general information system and it implies a mechanism for the collection, processing, analysis and reception of information necessary for the organization and implementation of health care, but also for research and organization.

The application of information technology in healthcare system is continuously growing worldwide. The use of health and communication technologies is not a novelty; their use has been ongoing for the last twenty years. Information system significantly improve the health care system by increasing efficiency, by reducing paperwork, speeding patients flow through the system, keeping records of all health care segments.

The pace of life, the development and application of technological advances in medicine, the emergence of new and expensive drugs, and the population aging are leading to a steady increase in health care costs, therefore a number of appropriate measures are needed to limit or control this growth.

The application of information and communication technologies in the healthcare system is a significant factor in the development and progress. Due to continuous advancement of information technologies, the functioning of healthcare institutions has been considerably facilitated. The efficiency and quality of healthcare delivery, its organization and contact with patients are significant strengths and direction in which the healthcare system will move in the future.

Health information system with e-records provides the following:

1. Electronic entry and data updating related to the provided health services,
2. Working with medical, financial and technical documentation,
3. Connection to specialized information systems, such as, for example, laboratory or radiological information systems,
4. Connection with electromedical devices, such as Magnetic Resonance Imaging, X-ray, ECG, laboratory analyzers, etc.
5. Review of all collected medical data and the ability for monitoring medical histories,
6. Support the healthcare staff in making the right decisions at the right time.

Health information systems contain detailed information about the health services, therefore it is significant in health, financial and administrative terms. Healthcare workers have registered the benefits and capabilities of the information system, using it on a daily basis.

Health care costs have increased significantly, so there is a need for more effective and quality healthcare at all levels. One of the steps in reducing the cost of health care delivery is the creation of a national health system. Healthcare Information Systems - ISIS (Healthcare Information Systems - HIS) is one of the basic components in the modern healthcare system.

The organizational structure of health care involves different entities, which should develop and have its own information system, designed to meet the internal needs and needs of other institutions. Today's trend in this area is mainly based on two strategies:

Integration of local information systems into an ununique health information system

Development and improvement of quality of IT services in healthcare.

The benefits of the Healthcare Information System over the classical approach are multiple:

A. Economic: increasing the volume and quality of services, increasing the efficiency of treatment by reducing hospitalization, greater utilization of available capacities, better quality records of health services provided and accurate monitoring of their implementation, less burden on healthcare professionals

B. Qualitative: reducing the scope of administrative activities with more efficient execution, increasing the level of knowledge and modernization of health technology, systematic planning, execution, introduction, monitoring, collection, analysis and interpretation of work activities, increasing discipline in material and accounting operations and increasing the reliability of information

C. Organizational: standardization of the process of service delivery, support for the implementation of health care programs, quick access to information on the financial and other institution resources, shortening the time in planning the provision of health care and monitoring the flow of activities, effective communication between participants in

health care, timely provision of necessary information relevant to the provision of health care.

D. Healthcare: updating and standardizing methods and procedures in the healthcare delivery process, increasing diagnostic and therapeutic quality through greater use of good guidelines, timely and easy access to all diagnostic and anamnestic data, quality control and reliability of healthcare delivery in accordance with modern diagnostic and therapeutic procedures.

E. Scientific-research: constantly use of modern scientific achievements, simpler and accessible data from practice for writing scientific papers, easier access to many data and libraries, possibility of constant contact with colleagues.

These are all facts that support the assertion that the health information system installed in an actively used healthcare facility is an excellent teaching and research database and a prerequisite for effective education and successful research.

Continuing education is a mandatory segment in the work of every employee in the healthcare system. Namely, for the license renewal, it is necessary for each health care professional to collect a sufficient number of points from continuing education. The reliance on classical methods of education, where preference is given only to "ex-chair" lectures with practical exercises with patients, is increasingly difficult to meet the increased demands and scope of medical education. Therefore, all additional forms of education in medicine have become extremely important. Health information systems can also play an important role in this process designing and implementing appropriately and providing the necessary functionalities that extend the traditional set of options that health information systems offer, which have previously been largely focused on patient-related administrative data and health services provided to them.

Electronic documentation content

User/Patient Identifier: A universal code that uniquely identifies each user in the healthcare system.

Institution identifier: A universal code that uniquely identifies each institution or department, accredited to provide health care services.

Provider ID: A universal code that uniquely identifies a provider in a healthcare system.

New health care programs are being introduced, with the overriding goal of preventing disease and directing the population to change their attitude to health, promoting healthy lifestyles and strengthening responsibility for their own health. There is a need to strengthen preventive and primary health care, decreasing the expensive treatment and reducing the number of patients.

The application of information technology is very useful and effective in health promoting. The promotion of healthy lifestyles arises from the need to strengthen primary and preventive health care and aimed at improving the quality of health of the population, changing the attitude of the population and society as a whole, towards health, raising the level of awareness of the population about chronic diseases and strengthening the responsibility for one's own health.

For good functioning, it is necessary to create a *National Health Information System*.

1. This implies a change in the way medical information is created, used and accessed.
2. Acceptance of electronic health records as a technology in the healthcare delivery process.
3. Application of international standards in the conditions of new technological solutions of information and communication technologies.

Computerization and the introduction of information systems in healthcare facilities have paved the way for the creation of the concept of an electronic health record, which enabled all

patient data to be in electronic form. This way of storing health information creates the potential to significantly improve the quality of health services and increase effectiveness. Healthcare institutions that have introduced e-records have shortened the administrative route to the lowest possible level, with completely accurate insight from the services provided to prescription data. Increasing the efficiency of health care and safety with the widespread use of electronic records also results in huge financial savings.

Advantages of introducing E-cartons:

- Replaces traditional medical records that can often be unfinished, illegible, torn and lost.
- The security of the data collected is increased and their integrity and absolute confidentiality insisted.
- Duplicate prescription is prevented.
- The possibility of medical error is avoided.
- Computerized writing and control of laboratory analysis instructions.
- All laboratory findings are archived into the electronic file itself.
- Facilitate comparisons of patient demographics, utilization of these data for statistical purposes and, consequently, enhancement of the quality of healthcare services.
- Availability of records of services provided and much better control of material consumed.

Results

We will show on the example of the Health Center Niš and the Public Health Institute Niš, how far the application of information and communication technologies has been put into practice and what is their contribution to a daily work.

The Health Center Niš is constantly striving to improve the provision of health services to its users, simultaneously increasing the level of satisfaction of its employee. In 2011, the Health Center Niš became a user of the medical information system MEDIS.NET, which was implemented in the Laboratory for Medical Informatics of the Faculty of Electronic Engineering in Niš.

The first contact with the healthcare system was made in primary health care which should be able to handle at least 80% of all health problems. As a participant in the pilot program, Health Center Niš was among the first which integrate the existing MEDIS.NET program into IZIS (Integrated Information System). This project of the Ministry of Health of the Republic of Serbia covers all health care institutions (primary, secondary and tertiary institutions) as well as pharmacies.

Thanks to the software developer from the Faculty of Electronic Engineering in Nis, seamless integration of the software with minimal changes was enabled. System was officialy started in March 2016. Each user of the system has its own username and password, and thus certain authorizations and access.

Due to the integration of MEDIS.NET software into IZIS, it was necessary to retrieve outdated equipment. New computers and printers were purchased from its own funds for the needs of the Specialty Consulting Services. The speed of internet access in both the central facility and remote locations has been increased. Call Center work has been improved and IZIS adapted. Cooperation with the Clinical Center Niš has been improved with regard to scheduling appointments for examinations.

Since March 2019 paper prescriptions for prescribing medicines have been replaced by electronic ones. About 65 million paper recipes have been issued annually in Serbia. Thanks to this novelty, the number of patient visits to physicians due to prescribing therapy has decreased by more than 20%. Physicians now have more time to prevent, screen, and treat acute patients. Patient reactions are positive. It took a short period to adjust, both in prescribing therapy and in raising it. Digitization of the health care system has enabled acute and chronic therapy to be implemented electronically, only with the use of a health insurance card. The physician may prescribe therapy for a period of two to six months based on the

patient's medical condition, and the patient may, according to his or her medical condition, report to the chosen physician if he thinks that he needs a correction of the therapy.

The management of the Niš Health Center, as well as all employees, believe that the introduction of e-Prescription is a significant moment for the improvement of the health care system, contributes to greater satisfaction of employees and patients, and thus increase the quality of health care delivery.

Preparation of the Laboratory Information System (LIS) is underway to allow physicians to write analyzes through software-medis. The introduction of LIS will allow all the results to be electronically forwarded to the physician who has ordered an analysis. In this way physicians will be more familiar with the results of the required analyzes and making treatment and prescribing therapy timely. The material costs of printing laboratory instructions as well as a report printout should also not be neglected.

Conclusion

The application of information and communication technologies in the healthcare system represents a significant factor in the development and progress. Due to the continuous advancement of information technologies, the functioning of healthcare institutions has been considerably facilitated. The efficiency and quality of healthcare delivery, its organization and contact with patients are significant strengths and direction in which the healthcare system will move in the future.

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8. PREDICTIVE MODELS – PROCESS OF DEVELOPMENT AND VALIDATION

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Abstract

The model-based prediction relies on a combination of clinical characteristics and biomarkers. The most frequently used technique is multivariable regression modelling. The overall development and validation process of a predictive model is explained in a conceptual manner in this review. Predictors variables should be considered based on both clinical knowledge and statistical reasoning. The performance of the model should be assessed based on the calibration and discrimination ability. The calibration could be assessed by the Hosmer-Lemeshow test for a binary outcome or by the Num-D`Agostino test for survival data. The model performance should be assessed based on the following parameters: area under the ROC curve, net reclassification index and integrated discrimination improvement. External validation refers to generalizability of the final model, and its performance is important for to model to have clinical application. In the last decade, development and validation of, and reporting about predictive models have been thoroughly followed and supported with the development of the proper guidelines. Researchers should be familiar with the standards of the process of predictive modeling as well as its reporting.

Keywords: predictive model, development, reclassification, validation,

Introduction

Accurate predictions of medical outcomes are crucial in modern clinical practice, and are completely based on different predictive models. The scientific research to develop and validate predictive models has been very extensive and numerous particularly in the new millennium. Possibly, the best example of a predictive model routinely used is the Framingham risk score (FRS). FRS has been developed since 1948 and has successfully used more than 50 years for estimating the probability of the occurrence of cardiovascular events/disease within ten years. The estimation of the FRS is based on values of the traditional risk factors such as age, sex, smoking, total and high-density cholesterol levels, systolic blood pressure, hypertension treatment and diabetes [1]. Generally, in medical research, this is a combination of set of variables that predicts a value of outcome variable. Multivariable regression-type models (linear, binary logistic, survival) share a general form:

$$\text{Outcome} = \text{weight}_1 \times \text{predictor}_1 + \text{weight}_2 \times \text{predictor}_2 + \text{weight}_3 \times \text{predictor}_3 + \dots + \text{weight}_k \times \text{predictor}_k + \text{error}$$

Model development

Possible generalizability and the performance of predictive models depends on the study design and the quality of data gathered through research. Trough development and validation of specific models various study designs can be used. Those studies can be retrospective and prospective. The best option for prospective research is a cohort study [2]. Prospective longitudinal cohort studies allow optimal control and measurement of all predictors and outcomes, which minimizes the number of missing values and losses in the follow-up period. Retrospective cohort studies are commonly used, particularly, for datasets from hospital

records registries. The retrospective design allows a longer follow-up interval, but this design

Abstract

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leads to a selection bias. Randomized control studies, as a subtype of the prospective study, can also be used for the development of a predictive model. Selection of participants based on the pre-defined inclusion and exclusion criteria decrease the generalisability of the model.

Therefore, the first step to developing a predictive model is to define the endpoint (event or outcome)(Figure 1). The most common outcome in the survival analysis is death. The next step in the development of a predictive model is to define the population at risk. The population at risk should be defined by inclusion and exclusion criteria. The sample size should be considered in this step. Research simulation [3] has shown that the more predictors in the model, the more likely it is to get a significant relationship between the outcome and the predictors. There have been many rules of thumbs for the sample size in the regression-type model [4, 5]. Typically, regression analysis/the regression-type model includes 50 participants plus 8 additional participants per an independent variable. However, the sample size is not crucial for the logistic regression and particularly not for the survival analysis. For these types of analyses, the number of events per predictor (EPV) is the most crucial parameter. Simulation studies [4, 6] revealed that 10-15 EPV would produce a stable logistic

or survival model. If it is not possible to gather a sufficient sample size than the recommendation is to simplify the predictive model. The latest research [7] showed that problems in model development would be less prominent in studies with a dataset 20+EPV.

Beside the small sample size, there are other manipulations through data analysis that can potentiate overfitting. One of them is an automated selection of the model. Typically regression analysis would be conducted by using the backward, forward or stepwise selection. The simulation study [8] demonstrated that the stepwise selection creates the model with 30% to 70% of the predictors that were not related to the outcome in the population. The automated selection causes overfitting because of too many degrees of freedom that are used during the analysis that cannot be supported by the sample size. Several studies have recognized problematic modeling aspects [9-12]: a selection of predictor variables based on the statistical significance in univariate analysis, dichotomization of continuous variables and small sample size and small EPV in model development studies. Considerations in selecting predictors are mandatory step in the development of the predictive models. It is recommended to select predictors before modeling by considering clinical reasoning, theoretical background, relevant literature, and knowledge of experts in the specific research field.

A very common approach of selecting predictors variables is culling variables the univariate relationship between potential predictors and outcome. This univariate prescreening of variables, in the multivariable model, brings selection bias. Categorization of continuous variables, particularly dichotomization is very appealing to clinicians. However, this approach only brings a loss in information [13]. Although these abovementioned techniques have been widely criticized in theoretical as well as applied studies, they are still widespread in different research areas. Approaches to handling missing values have become very important issues in methodological researches and reviews. It is well-known that the complete-case analysis has caused biased results [14]. The best approach is using the multiple imputations technique.

Model performance

Model performance assessments include calibration and discriminative ability estimation. Perfectly calibrated models should lie on or around the 45° line of the plot. This metric reflects the agreement between the observed outcome and the predicted outcome.

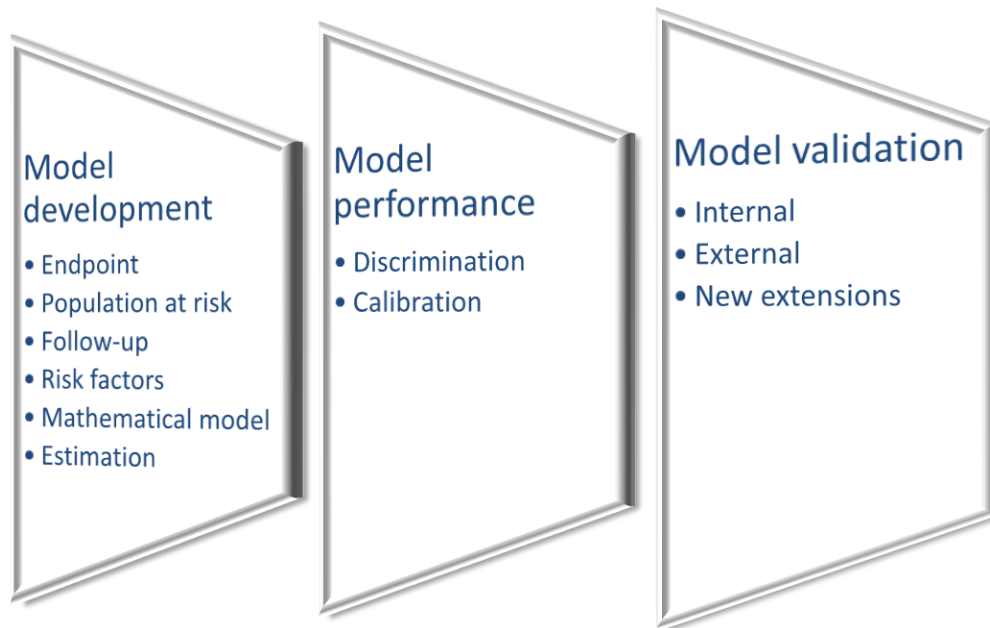


Figure 1. Steps in development, evaluation, and validation of multivariate predictive models

The Hosmer-Lemeshow test is commonly used for binary outcome [15]. The counterpart test in survival analysis is the Nam-D`Agostino test [16]. The acceptance of the null-hypothesis for these tests indicates poor calibration of the predictive model. The main drawback of the Hosmer-Lemeshow test is that it is often non-significant for small samples, indicating good calibration [17]. The discriminative ability is defined as the ability of a predictive model to differentiate two outcomes (event/non-event or fatal/non-fatal). The receiver operating characteristic (ROC) curve with the area under the ROC (AUC) and the concordance statistic (c-index) are the most widely used metrics in the estimation of the discriminative ability. The Harell`s c-statistic is the counterpart test for survival data. The value more closely to 1.0 indicates that the model has a perfect discrimination.

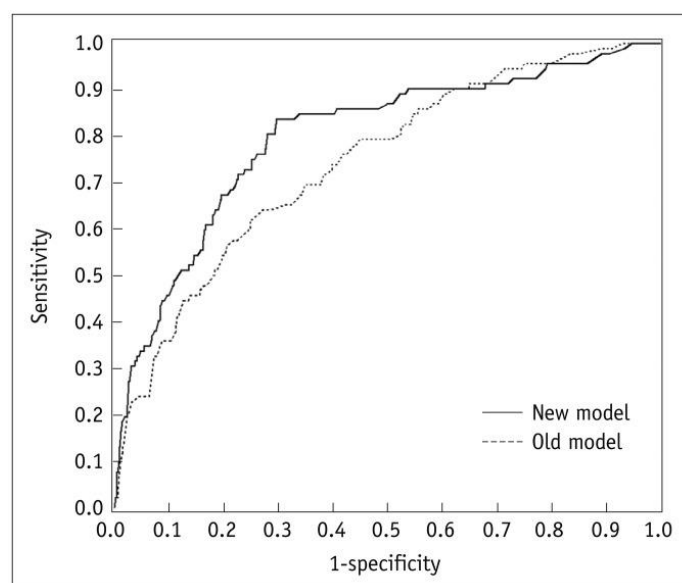


Figure 2. Discriminative ability of different predictive models

Figure 2 illustrates comparisons of the discriminative ability of two predictive models. This comparison can be made by the De Long test [18]. However, it has been established that it is very hard to achieve a significant increase in the model performance in the “good“ predictive model. The step beyond discriminative ability includes the estimation of risk reclassification. Pencina et al. [19] proposed two metrics: net reclassification improvement (NRI) and integrated discrimination improvement (IDI) to overcome the drawbacks of c-index. Those two indices quantify overall reclassification amount and also evaluate the incremental value of a set of predictors. The NRI is a combination of four proportions related to upward and downward movements of patients in a higher or lower pre-specified risk category. The NRI can have a range from -2 to 2. If E denotes the event status (Yes/No), the NRI is defined as:

$$NRI = (P[up|E=1] - P[down|E=1]) - (P[down|E=0] - P[up|E=0])$$

Up – refers to the upward movement to a higher risk category based on the new model,

Down – refers to the downward movement to a lower risk category based on the new model.

This metric has gained much traction in scientific papers in the last decade. However, it was established that there were a lot of misinterpretations [20]. The use of p-value of the NRI is considered completely inappropriate. The recommendation is to use only a confidence interval of the NRI. The second proposed statistical parameter is the IDI. This parameter is the difference in predicted probabilities in subjects with or without event as an outcome. It also shows some issues concerning the p-value, even in a large sample. Therefore, several statisticians recommended reporting of all three statistical parameters (AUC, NRI, IDI) as a measure of the performance of the final predictive model [21].

Validation of a predictive model is the process of assessment of its performance in a new dataset. Validation is an essential step in the process of modelling. Internal validation is a part of the model development, and it refers to the reproducibility of the model. Internal validation is usually performed by using resampling techniques such as cross-validation and bootstrapping. External validation is performed after the model development process, and it refers to the generalizability of the final model. External validation is performed on a different sample. It can be a validation on recent patients (temporal), in other health institution (geographical) or by other research teams (fully independent validation). Sample size calculation has not been well-established for this type of studies. The latest reports recommended that validation studies should have a minimum of 100 events per predictor variables, ideally over 250 EPV [22].

Further Considerations

In the last decade, development and validation of, and reporting about predictive models have been thoroughly followed and supported with the development of the guidelines. There are numerous guidelines for different research areas: **RiGoR** (2015) reporting guidelines to address common sources of bias in risk model development, **REMARK (2005)** - REporting recommendations for tumour MARKer prognostic studies, **GRIPS (2011)**- Strengthening the reporting of Genetic RIsK Prediction Studies, **STARD** (2015) - guidelines for reporting diagnostic accuracy studies: explanation and elaboration, **TRIPOD** (2015) - *transparent reporting of a multivariable prediction model for individual prognosis or diagnosis*. Those guidelines cover different aspects of predictive modeling and also the aspect of reporting about a predictive model. Each guideline has a checklist, accompanying explanations and corresponding examples. Researchers should be familiar with the standards of the process of predictive modelling as well as its reporting.

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SESSION: COMMUNITY IN FOCUS

1. DATA-DRIVEN DECISION MAKING AND STAKEHOLDERS INVOLVEMENT IN PUBLIC HEALTH. A FASCINATING CHALLENGE FOR A SUSTAINABLE DEVELOPMENT

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Over the last 200 years, life expectancy has more than doubled in Western countries, from 40 years at the beginning of the 19th century to about 80, with improvement in health and life quality. The widest gain in life expectancy was between 1880 and 1920, mostly thanks to public health improvements like foods safety, clean water, sanitation, the large production and distribution of vaccines and the study and delivery of important educational topics like personal hygiene, air quality, or healthy housing. From 1920 to today, an epidemiological transition occurred, gradually displacing the pandemics of infection by chronic diseases. This led to a disruptive change in facing public health characterized by an increasing use of epidemiological tools, data and a lot of information about population, to use to guide intervention. Globalization further complicated the picture, creating connections and interdependence among countries, increasingly related one another regardless of national borders, in a growing context of economic integration, communication, cultural and travel diffusion. This played an unexpected role in the burden and distribution of determinants of health. Health care systems all over the world need a right governance and a high resilience to promote the positive determinants of health and limit the negative ones: indeed, their unmanaged distribution among the population seriously undermines the sustainability of the system itself. A system is said to be sustainable if it meets the needs of the present without compromising the ability of future generations to meet their own needs. Long-term sustainability of healthcare systems is not only about finance and affordability, nor about efficiency and effectiveness; it also depends on different, cross-sectoral factors that can rapidly change or interfere with one another. In the complexity described above, Public Health challenge may be faced through two essential tools: data-driven decision-making and stakeholders' involvement. First, in the era of "Big Data", healthcare organizations and systems have to deal with the current growing amount of healthcare data. This means having a wider picture of populations based on a broad set of variables. Consequently, on one hand Evidence Based Public Health (EBPH) uses the data coming from the best available evidence in order to standardize the public health decision making process in the intervention context. On the other, personalized public health (PPH), uses data to stratify the population, in order to address the right public health interventions to the right targets. Second, the engagement of stakeholders is proved to contribute to resilience and flexibility, to learning opportunities and innovation, to the identification of new opportunities, and to the improvement of sustainable performance. The WHO Global Strategy for Women's, Children's and Adolescents' Health (2016- 2030) emphasizes the need to bring together many stakeholders as agents of change. Stakeholders' involvement can be fostered in 6 steps: first of all, there is the need to identify stakeholders, secondly defining roles and resources per each of them; third, it is necessary to detect dynamics among stakeholders; fourth, the optimal stakeholder group must be identified; fifth, a stakeholder engagement plan must be created and, finally, the level of engagement must be continuously monitored. This way of working requires the ability to interact with many people, matching together different values and perspectives to achieve a common goal. That's why public health experts' leadership plays a fundamental role in health programs planning: leaders should have a vision of what can be reached and must be able to communicate it to the others; they also should motivate people and manage the team

dynamics, being able to negotiate for support. Nowadays, it is proved that one of the most important stakeholders to involve in order to realize an effective public health intervention is the community itself. The importance of community participation was stated back in 1978 in the Alma Ata Declaration. Since then, it's clear that communities need to play an active role in driving decisions to improve the quality of health services, access and equity. People and their communities should be at the center of healthcare systems, because this increases the effectiveness, decreases the costs, improves health literacy and patient engagement.

Technology development must be considered, too. It changed the way human beings and data are connected. In fact, the current technological infrastructure allows for the storage and linkage of a huge amount of data: in the vision of EBPH, it means the smart access to the best available evidence on a specific topic; in the perspective of PPH, it means to integrate many population data to better tailor a health intervention on a specific population. It could be very helpful also to engage stakeholders: theoretically, there are no more physical barriers to isolate a possible partner, from an institutional organization to the most remote population. Community energies and knowledge is naturally on air, people who can access Information and Communication Technologies (ICT) share their opinion in every moment, without being asked about it. Today, engaged community using ICT, the so-called Smart Communities, are growing up in many places all over the world, supporting the implementation of numerous health promotion and prevention initiatives. The development of community programs can be a unique solution to address sustainability and innovation by generating a real community engagement. So, the two data clouds of EBPH and PPH become a trilogy: there is the cloud of community data related to lot of features such as population health data, community values, preferences, priorities and so on. In the portrait of this complex reality, Public Health should have an essential role in the regulation of light and shadow. There are available data, people, resources and ideas: public health professionals can be the enzyme which sparks the reaction among the chemicals.

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2. DEVELOPMENT OF PUBLIC HEALTH POLICIES AT THE LOCAL LEVEL IN SERBIA IN PERIOD 2010-2019

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Public health as public policy - a theoretical concept

In Serbian, the term "*policy*" has different meanings, and the translation of the term *public policy* in everyday speech is not completely clear to many. In English, the terms *politics* and *policy* denote two different terms. The term *politics* has a procedural meaning (politics as a political process) and encompasses concepts such as power, conflict, consensus and legitimacy and relates to the operation of political parties. The term *policy* has a functional meaning. It refers to the content of public decision-making and the way in which political decisions are implemented, processing and resolving problems through the administrative system. The result of this is obligatory decisions and their implementation. *Public policy* science has three basic characteristics: a *multidisciplinary approach*, a *multimethod approach*, and a *problem-oriented approach*.² The term *public policy* refers to the science of the decision-making process on issues of general or public interest. It is a process of identifying and defining a problem, considering, selecting and implementing a concrete solution that should involve all stakeholders.³ It consists of initiation (identifying and defining problems), formulation (making possible solutions, options, selecting a specific *policy* option), applying that option, evaluating the chosen and implemented public policy (evaluation), and correcting that chosen option (enhancement). Correction can also help redefine the problem itself⁴ - therefore the system has learned something. Public policy is applied in all areas of public interest: public health, health care and social care, education, environmental protection, justice, defense, etc. and competence for application can be allocated at central, regional and local level, or mixed.

The terms *policy networks* and *policy games* in public policy evolved in the late 20th century, drawing on Giddens' theory of structuring, on the basis of which a new definition of public policy was developed. *Public policy* is "*the result of a process of interaction between many actors, of which only a small number of state bodies will gradually become widely accepted*".⁵ The *policy* network, as a concept for describing and analyzing the environment in which public policy is developed and implemented, starts from the view that when a public policy actor tries to manage the public policy process, he/she must take into account the characteristics of that network. Networks are described as "*more or less stable patterns of social relations between interdependent actors formed around public-policy issues or resource clusters, which are formed, maintained and altered by a series of games*".⁶ The *policy* network is generally a stable context within which public policy decision-making games are played. *Policy game* means "*a continuous series of actions by different actors, conducted and guided by formal and informal rules, which address issues of interest to*

² Laswell, D.H. (1970): The Emerging Conception of the Policy Sciences, *Policy Sciences*: 3–14.

³ Lucic, S. (2001). The concept of public policy, *Evaluation of public policies - theory and practice*, SCTM, Belgrade: 10.

⁴ *The same*: 12–14

⁵ Klijn, E. H., Koppenjan, J., Termeer, K. (1995). Managing Networks in the Public Sector: A Theoretical Study of Management Strategies in Policy Networks; *Public Administration* Vol. 73: 437–454.

⁶ Klijn and Teisman (1991), according to: Klijn, E. H., Koppenjan, J., Termeer, K. (1995).

actors".⁷ The *Policy* network in public health in Serbia is comprised of the following most important *Policy players*: Ministry of Health, other relevant ministries (Ministry of Environmental Protection); Institute for Public Health "Milan Jovanovic Batut", a network of institutes, health institutions and in particular health centers, local self-governments, the Standing Conference of Towns and Municipalities, civil society organizations and the private sector. International Organizations - World Health Organization (WHO), UNICEF, European Union, EU Member States' development agencies as donors are also important actors in the Public Health *Policy network*. When it comes to local self-governments, with the relevant ministry, the Standing Conference of towns and Municipalities is a representative of all towns and municipalities.⁸

The characteristics of a *policy* network depend primarily on actors who, in order to achieve their goal, must interact with others through a successive series of interactions. Thus a pattern of interdependence relationships is established. The power of the individual in the game is a socio-political construct, as are the rules of the game. The outcomes of public policy (*policy*) are the public-policy measures and activities created in the *policy* games: adopted laws and by-laws, changed status of some institutions, introduced new measures, changed quotas, criteria, adopted contracts, etc. The power position of an individual player depends on the combination of resources they can potentially mobilize in combination with their own strategic abilities, but in fact it depends most on how others perceive the assumed power. In the traditional context of power among *policy* network actors, local self-governments are treated as outsiders, players who are attributed to a certain level of responsibility, but without the supposed power that responsibility brings. As a representative of the local self-governments, the Standing Conference of towns and Municipalities compensates for this lack of presumed power in systems that traditionally lean towards centralization through continuous cooperation and communication with the Ministry of Health, as well as with the network of institutes of public health. This co-operation was formalized by the co-operation protocols signed with the Ministry of Health back in 2009, and with the IFPH "Milan Jovanovic Batut" and the Institutes of Public Health in Nis, Kragujevac and the Autonomous Province of Vojvodina in 2016.

The *bureau-policy perspective* addresses the strategic dimensions of relationships within and between government agencies – by competition between different fragments of public administration.⁹ The main features of bureau-policy are the following: a multitude of actors in the policy-making scene; actors have different and conflicting interests; no actor has too much influence; decisions are compromise; the outcomes of decisions do not imply effective implementation. The scale of bureau-political influence on political decision-making ranges from limited competition; bureau-policy; and indicates the degree of compromise achieved. In *bureau-policy*, compromise is very difficult and there is a big difference between policy making and implementation, which makes it non-functional.¹⁰ Notwithstanding opposition from proponents of traditional public administration theories, bureau-policy does not necessarily have poor outcomes, especially in a crisis. An example is the position of public health institutes in Serbia that were brought to the brink of disappearance by the health care and system reforms. In the catastrophic floods of 2014 and 2016, this part of the health

⁷ Morgan (1986); Giddens (1984); Burns and Flam (1987), according to: Klijn, E. H., Koppenjan, J., Termeer, K. (1995).

⁸ The Union of All Local Self-Governments in Serbia, established in 1953. <http://skgo.org/strane/60>

⁹ Rosenthal, U., 't Hart, P., Kouzmin, A. (1991). The Bureau-Politics of Crisis Management, *Public Administration*, 69, 211–233.

¹⁰ Rosenthal (1988), according to: Rosenthal, U., 't Hart, P., Kouzmin, A. (1991).

system outlined much of the flood response and the mitigation of the consequences of the flood. In this way, their role was revitalized, and the new Law on Public Health further strengthened them in traditional jurisdictions, adding to them some new ones.¹¹

Increasing effectiveness and reducing costs in public administration led to the introduction of the new public management doctrine, which originated in the UK in the early 1990s. The market approach in the public sector has been applied. Public services were transferred to the private sector, calls for public procurement were introduced; they insist on the lowest cost of service; public-private partnerships were developing. It insists on reducing costs, manpower, measuring performance, competitiveness and customer service orientation. The goals of the new public management are directed towards a market economy, not democracy. As a kind of critique of this approach to public administration in Europe, a new administrative doctrine has emerged of the so-called *good public governance*. The emphasis is on the best possible process in decision making and implementation, not on the quality of the decision as such ("good" or "right"). Good public governance is responsible, predictable (strategically oriented), transparent, monitors the rule of law, sensitive to the needs of the local community, participatory; effective and efficient, fair and inclusive. The new public administration paradigm involves customer orientation and flexibility, which is a challenge for classic bureaucratic systems.¹² Public health in Serbia is an example of a mixture of these two public administration systems. The principles of new public management have been applied in the transformation of public health services from public to market ones, with the general interest shifted to the private sector and market. This has proven to be a problematic solution, especially in the area of social and environmental concern. as a representative of local self-governments. Therefore, with the new Law on Public Health, institutes were given exclusive competences in the provision of these services. On the other hand, the process of strategic public health planning at the local level is fully in line with the principles of good governance.

Public health as a public policy at local level in Serbia

Local self-government in Serbia is of a monotypic character - this means that all local self-governments have the same levels of authority, regardless of size. The functions it has are in the areas of public policy (creation, implementation, monitoring and evaluation); regulatory functions (adoption of regulations/individual acts based on general norms); administrative functions; provision of public services and inspection in specific areas. In the area of public policy, local self-government in Serbia has competencies for utilities, local transport and road network, water supply, environmental protection, housing policy, agriculture, local economic development, education (especially preschool and primary), primary health care (partially) and public health, social protection, culture, sport and youth policy, tourism, and protection against natural disasters and emergencies. Public health is "hidden" in many of these local public policies. The difference in the degree of development and size of towns and municipalities is problematic. Small, underdeveloped and devastated municipalities are in a more difficult position than others.

In order to create and implement a public policy, there must be elements that make up: a normative, institutional, strategic, operational and financial framework. **Normative framework** are laws and by-laws, both those enacted by the central level of government (regulations and ordinances), and those related to the local level (rules of procedure,

¹¹ Tanasic. J, (2018), Politics of crisis management in towns - examples of Serbia PhD, Belgrade, University of Belgrade, Faculty of Security Studies. Pg. 20-23;
<http://nardus.mpn.gov.rs/handle/123456789/9771;jsessionid=FFD916AD9226919125C3B1AF3D17F006>; Law on Public Health ("Official Gazette of the RS" No. 15/2016).

¹² Tanasic. J, (2018), Pg. 24-26.

decisions, programs, statutes, etc.). The Law on Public Health ¹³ is the umbrella document in this case, followed by the ordinances. The normative framework of public health policies at the local level consists of the rules of procedure of health councils, decisions on the establishment of councils, public health programs, decisions, etc. The **institutional framework** consists of parts of the system (bodies, institutions, councils, commissions, associations, networks...) in charge of the implementation of legally prescribed competencies. At the central level, it is primarily the Ministry of Health and the institutes for public health as the bearers of activities. At the local level, the institutional framework for the development of public health policies is represented by local health councils and local authorities. There are about 145 health councils in Serbia, and they have recently become mandatory for Belgrade's city municipalities. The **strategic framework** is one of the indicators of *good governance*, together with the financial framework: together, they make predictable public policy and affect the realization of the principles of legitimate expectations of citizens (every citizen has the same rights if they are prescribed by law). The strategic framework can be international, national and local and should be coherent with one another. Serbia has based its national public health strategy "Healthy People, Health in All Policies" ¹⁴ (2018-2026) on the European framework of the World Health Organization (WHO) "Health 2020 - Health in All Policies", adopted in 2012. From 2017 the process of strategic public health planning at the local level began with the development of public health plans. So far, about 30 towns and municipalities have adopted PH plans, which are long-term documents (8 years). The Public Health Program is an annual action document, enacted by the LSG and followed by the allocation of funds for one, with a projection to three years (following the logic of the LSG program budget). The **financial framework** is one of the most important conditions for the implementation of any public policy and depends to a large extent on the political will of the decision-maker. The condition for something to be compulsorily funded is to be included in the program budget scheme prescribed by the Ministry of Finance, whose structure and indicators are improved on an annual basis, in cooperation with the SCTM. Public health at the local level was first on the list of the local self-government program budget in Serbia after the adoption of the Law on Public Health, and is included in Program 13: Health, Program Activity PA 003: Public Care for Public Health. The **operational framework** consists of all actors involved in the implementation of public policies: employees of state bodies and local self-government units, institutions, etc. It is important that there is a job description of employees in public administration, based on legal obligation, who perform tasks to implement some of the responsibilities of a particular public policy. The Standing Conference of towns and Municipalities (SCTM), in cooperation with the Ministry of Public Administration and Local Self-Government (MPALSG) - Sector for Local Self-Government, has prepared models of the *Rulebook on the Organization and Systematization of Jobs in Town and Municipal Administration, Professional Services and Special Organizations* providing jobs with accurate job descriptions in the areas of health, public health and patient rights. At the local level in Serbia, these jobs are mostly performed by employees in the social services or health care sectors (which is less common and applies mainly to larger towns).

Development of public health policies at the local level in Serbia from 2009 to 2019

From 2009 onwards, the Republic of Serbia, with project support and on the basis of the *bottom up* principle, decentralized and fully established the legal, strategic and institutional framework of new competences of local self-government in the field of public health and

¹³ Law on Public Health, "Official Gazette of RS" No. 15/2016.

¹⁴ Public Health Strategy in the Republic of Serbia 2018-2026 - "Official Gazette of RS" No. 61/2018.

protection of patients' rights, which did not exist before. Changes were first established as optional in local self-governments and then assessed as useful and introduced into the legal and strategic framework. These are the following projects:

1. "Primary Health Care planning in the Balkans" (PHCPP), implemented by the *Canadian International Development Agency (CIDA)* (2006-2009)
2. "Provision of Improved Services at the Local Level" - (*DILS*), Government of the Republic of Serbia (2009-2013) from World Bank loan funds;
3. "Support to local self-governments in decentralization of social affairs" (SCTM, Association of Local and Regional Authorities of Norway - KS; Center for Liberal Democratic Studies - CLDS) (2011-2013), with the support of the Kingdom of Norway;
4. "Institutional support to SCTM - Phase I, II and III" in the period 2010-2019; with the support of the Government of the Swiss Confederation.

It should be noted that none of the projects listed had public health or the development of local public health policies as a major topic, but the changes that came as a product contributed to the establishment of public health policies at the local level. Through the three strategic cycles (2008-2021), the Standing Conference of Towns and Municipalities continuously plans, finances, implements, evaluates and promotes activities on the development of public health policies at the local level and strengthens the capacities of local self-governments to implement them. In the SCTM Strategic Plan (2017-2021), the development of a public health-responsible unit of local self-government is a set goal, and the expected indicator of this goal is 50% of towns and municipalities with adopted public health plan.

Chronological order of development of public health policies at local level - activities of the Standing Conference of Towns and Municipalities

I - Creating an institutional framework followed by the drafting of by-laws of the local level (2009-2013): Creating a model of partnership for health at the local level - local health council and introducing the LSG with the concept of partnership for health.

Main actors: MoH; SCTM; local self-governments; School of Public Health, World Health Organization.

SCTM activities: two analyzes to develop the health council model, its roles and functions; support for the establishment of councils as optional advisory working bodies in LSG (20 regional workshops and 2 conferences with international participation to promote public health at local level and model health councils).

Results: 2013 - 30 local health councils established; drafted rules of procedure, decisions on forming councils; developed a set of minimum indicators for public health monitoring at local level; informal SCTM Health Network is launched with the support of the MoH and the WHO.

II - Creating a legal framework (2013-16): Adopting the Law on Patients' Rights (2013) which obliges LSG to form health councils and expand the competencies of LSG and health councils in the Law on Public Health (2016).

Main actors: MoH; Institute for Public Health "Milan Jovanovic Batut", Network of Institutes of Public Health, SCTM, Local self-governments, World Health Organization.

SCTM activities: evaluation of the Law on Patients' Rights - analysis of the health councils and LSG capacities (2014); 21 regional workshops; 2 international conferences in cooperation with WHO; 4 Health Network meetings; forming a working group to make proposals for the drafting of the Law on Public Health and the National Strategy for the PH (2016); meeting of the Committee on Health and Social Policy dedicated to the PH (2016); over 60 visits to LSG in order to promote the concept of PH at the local level and to

strengthen the capacity of LSG to assume competencies in this field; Developed a curriculum for support to LSG in the area of PH.

Results of the process: Health councils formed in almost all LSG; SCTM Network for Health constituted (2015)¹⁵; during the catastrophic floods (2014 and 2016) on the recommendation of the MoH and the SCTM, health councils actively engaged in social care for health and emergency response; the proposals of the SCTM Working Group on the Law on Public Health and the National Public Health Strategy - introduction of new competences of public health services in the field of public health (2016); representatives of PH institutes became mandatory members of the council; signed co-operation agreements between the SCTM and 4 PH institutes; improved and harmonized models of local level by-laws with the new Law on Public Health and synchronization with other areas (introduction of public health into the program budget of LSG and recognition of tasks and competencies through the model Rulebook on organization and systematization of jobs in LSG.

Monitoring and Evaluation (2014): In the opinion of 80 health councils, the three basic prerequisites for strengthening the role of health councils in public health care at local level are: awareness and responsibility of council members on competencies, close cooperation with public health institutes and continuous education of council members. Percentage of health budgets average 1.15% of total LSG budget, of which 15% is for prevention and public health; on average, less than one employee (0.8%) works in health care services in LSG. Recommendations made to support LSG for improving public health at local level. Following the 2016 local elections, many LSG dissolved existing Health Councils and did not form new ones, which indicated the need for continued support to LSG in developing public health responsibility.

III - development and implementation of the strategic framework at national and local level (2017-2019): adoption of the National Public Health Strategy of the Republic of Serbia (2018 -2026), adopted by-laws, and started the process of developing and adopting public health plans of towns and municipalities.

Main actors: MoH, SCTM, LSG, Institute for Public Health “Milan Jovanovic Batut”, Network of Institutes of Public Health, WHO.

SCTM activities: development of a Handbook on Strategic Public Health Planning at the Local Level “Road Map”, development of public health promotional posters in the area of public health at local level; 3 Health Network meetings; completed 15 regional workshops during 2017-2018 with over 700 participants from 64 towns and municipalities in the process of developing public health plans. On the same occasion, in 2019, 34 workshops were organized for 28 towns and municipalities with a total of 425 attendees. The complete process was carried out in close cooperation with institutes for public health, especially with IFPH Batut, IFPH of AP Vojvodina, IZJZ Nis, IPH Uzice, IPH Sabac and IPH Timok-Zajecar).

Results of the process: developed model of the annual report on the implementation of the public health plan with the proposal of a set of minimum indicators related to the program budget of the LSG; by mid-2019, 30 public health plans were adopted at LSG assemblies; the City of Belgrade, by amending its Statute (2019), obliged the city municipalities to form health councils and to make plans for the PH.

Monitoring and Evaluation (2019): The implementation of the concept of public health and public health policies at the local level is significantly hampered for several reasons. The

¹⁵ The Network for Health is a body of the SCTM established to continuously monitor the implementation of regulations, the mutual exchange of knowledge and experience of all stakeholders in health policies at the local level, and is primarily intended for local health councils and patient rights advisers.

notion of public health and health care is equalized and prevention is placed largely in the system of health care institutions (often at the insistence of health system representatives) rather than in local public policies. Councils are often dysfunctional and exist formally. The PH strategic planning process enhances the capacities of the LSG and changes the situation for the better: councils are changed at the proposal of policy makers, working groups are formed for the preparation of plans, which include representatives of other sectors of the LSG: utilities, agriculture, inspection, environment, education, etc. Council members are often inert and uninterested in their work unless they have voluntarily consented to work in the council. Working on a PH plan is mostly unpaid employee activity, which further burdens them and is often avoided. Activation of the public health institutes, good cooperation and coordination with LSG are key success factors in both the strategic planning process and the implementation of LSG competencies. Directors of institutes who see this process as a strategic opportunity for their own institution are the drivers of the process and key to establishing public health partnerships at the local level. This applies not only to cooperation with LSG, but also to the motivation of their employees to actively participate in the work of the council. An aggravating circumstance for all is the recent rehabilitation of health centers and the obligation of LSG to repay the debts of the institutions they established. These debts are an extraordinary burden for towns and municipalities, which complicates the financing of public health obligations and further slows down the strategic planning process of PH at the local level.

Concluding remarks

Following the definition of *policy* games, local self-government units and health councils are in constant process of interacting with all other actors, in an effort to survive and be widely accepted in public health policies. Moreover, this interaction process also makes them functional and competent for the important task that is intended for them. The problem is not only that others do not recognize or accept them as equal partners, but also that often the councils themselves do not know what their task is. However, where the councils work properly, the results are visible to the local community and to all praise. A functional and competent health council influences the improvement of the quality of life of the residents of their local community. That is why cooperation, education, competence building of council members and exchange of experiences are of the utmost importance. The experiences of the meetings of the Health Network of the Standing Conference of towns and Municipalities prove this. The challenge is frequently change of council members. Given that responsibilities are high and remuneration for council work is generally non-existent, less influential representatives of the institutions are appointed as members. If the council becomes visible and important in the community with its activities, the composition of the council changes to more politically influential representatives, which often results in the extinguishing of the active council. The best results are situations where representatives are prominent persons, with some political support, leaders with the desire to make changes in the community and are visionaries. It is enough for the council to have one such member and the council will function. Constants are certainly local self-government employees in charge of this area, as well as representatives of public health institutes/institutions. Their mutual cooperation, frequent communication and shared vision of the public health of the town/municipality are the solution to the problem of possible changes in the composition of the council, but they must also be motivated to work. It is up to the directors/executives to identify and resolve this problem.

The process of accepting the concept of health councils from other public health actors, especially at the central level, is a lengthy and uncertain outcome. However, in the wave of centralization of LSG competencies in Serbia, public health is significantly decentralized, which is commendable. Almost all the necessary elements for the implementation of

competencies are fulfilled: normative, institutional, strategic, operational and financial. Of course, not all elements are equally developed. Weaknesses are the funding and the LSG employees in charge of this area. Establishing sustainability of public health policies through predictable funding is a particular challenge for all, and certainly one of the topics that will be addressed by the Standing Conference of Towns and Municipalities in the coming period.

The implementation of public health policy goals at the local level is clearly marked by a national strategy and there is high expectation from local self-governments. Given that there is a big difference between the creation and implementation of these policies, that processes are delayed and not implemented, that reaching compromise is difficult at all levels, the public health in Serbia has the characteristics of bureau-policy. Strengthening the capacity of local self-governments to develop and implement public health policies should be a common task of the first strategic order. The process of transformation of towns and municipalities in terms of public health awareness, literacy and accountability started 10 years ago and has been slow and uneven but it is systematically and continuously progressing.

As this is the year of the moon landing anniversary, the famous paraphrase fits the context of the theme: *This is a small step for public health, but a big one for Serbia.*

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ORAL PRESENTATIONS:

1. COMMUNITY-BASED PARTICIPATORY RESEARCH TO ENGAGE DISADVANTAGED COMMUNITIES: PRELIMINARY EVIDENCE FROM A SYSTEMATIC REVIEW

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Local Health Unit Rome

Community-based participatory research to engage disadvantaged communities: preliminary evidence from a Systematic review Pettinicchio V, Riccardi MT, Di Pumpo M, Damiani G.

Objectives Community-Based Participatory Research (CBPR) is an approach for Community Engagement with an intrinsic vocation to equity, particularly for disadvantaged communities. The primary aim of this systematic review was to evaluate the level of engagement reached in randomized controlled trials (RCT) using CBPR model to implement public health programs in vulnerable populations.

Methods Review was performed selecting articles in English, with an RCT design, explicitly stating the adherence to CBPR, or having CBPR in keywords. In order to evaluate the reached community engagement, the revised version of IAP2 spectrum elaborated in 2013 by five scientific societies was used.

Results Data from 10 articles were collected. Involved groups were ethnic minorities or low income communities or high-risk for chronic condition. The intervention aimed improving lifestyle in four cases and getting better self-management of chronic conditions in six ones. Only two papers reported outcome data. The studies showed, in most cases, to engage community “consulting” or “involving” it (five articles). Only in two cases it was possible to identify a level of “shared leadership”.

Conclusion These preliminary results show that, in CBPR model implementation, community is often involved in the phases of intervention planning and data collection. Nevertheless, there is a lot to do about other phases, such as outcomes management and data dissemination.

2. UNDERREPORTING OF EXTERNAL CAUSE IN MONTENEGRO HOSPITAL DISCHARGE DATABASE, DATA FOR 2018 YEAR

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Objectives: Hospital data discharges obtain the most information for injury prevention and control. The aim was to investigate volume of missing data on external cause on national level in Montenegro using discharges data. Proportion of underreporting was examined by institution.

Material and methods: Data on injury external cause and nature of injury were collected from Hospital in Montenegro (7 General, one special and one Clinical Centre) through Information Health System. The main fill-in form for obtaining information was the patient's statistical record sheet of the injured person.

Results: In 2018 was recorded 4827 discharges data due to injury. From this data we have reported 4707 like a nature of injury coded inside code S00-T99 and 120 like an external cause coded inside code V00-Y99 according to ICD-10. S00-T99 codes partly reported with both code, but more than 50% reported without code of external cause. The most underreporting was recorded for Clinical Centre, over than 70%.

Conclusion: Underreporting on external cause lead to missing information like leading causes of injury in Montenegro what further complicate injury control. Our results suggest more educational activities for medical doctors and medical workers responsible for filling injury data.

Keywords: injuries, external causes, underreporting

3. DEATH CERTIFICATION ERRORS AND THE EFFECT ON MORTALITY STATISTICS

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Objectives: Death certification (DC) represents an excellent source for mortality statistics and appropriate public health policy. Errors in reporting the cause of death (CD) prevent the development of national health strategies and, accordingly, distribution of resources. The aim of this study was to determine the frequency of errors in the cause of death and to identify factors that may be associated with inaccuracies in DC.

Methods: A cross-sectional study of death certifications in Nišava region was conducted over the period of May and June 2019. Specific criteria for major and minor errors were adopted for the evaluation of DC.

Results: Of the 415 death certificates reviewed, 108(26%) were completed correctly. Commonly encountered major errors were an improper sequencing 77(43%), diagnoses listed in no logical order 44(24.6%) and non-acceptable cause of death 42(23.5 %), while common minor errors were incomplete diagnosis 53(33.1%) and use of abbreviations and illegal writing 41(25.6%). Error rate significantly differ per manner of death ($p<0.001$).

Conclusions: Given the high rate of errors, there is an urgent need to design relevant training and educational programs beyond local and state efforts. Simplifying and standardizing underlying cause of death may improve accuracy, decrease coding errors, and improve national mortality statistics.

Keywords: Death certification, cause of death, errors, mortality statistics, health policy

Authors would like to acknowledge for financial support to the Ministry of Science and Technological Development of the Republic of Serbia (Projects 31060 and 41018).

4. RELATIONSHIPS AMONG SLEEP PROBLEMS, DEPRESSION, AND ANXIETY IN UNIVERSITY STUDENTS

Aleksandar Višnjić^{1,2}, Radulović O.^{1,2}, Marković R.^{1,2}, Jovanović T.^{1,2}, Bulatović K.²

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Objectives

Because sleep problems are very common among university students, this study explored the interplay between symptoms of depression, anxiety, quality of sleep, and insomnia.

Methods

The cross-sectional study was carried out at the University of Niš, Faculty of Medicine (Serbia) in 2016th and included 600 students of both genders. Students completed the questionnaire, which was compiled and developed from the Depression Anxiety Stress Scale, the Pittsburgh Sleep Quality Index, and the Insomnia Severity Index.

Results

Sleep problems are very frequent among university students: 432 (72%) and 258 (43%) of the students reported poor sleep quality or sub-threshold insomnia problems, respectively. Even 66 students (11%) reported moderate or severe insomnia. Above-threshold depression symptoms were reported by 168 students (28%) and anxiety symptoms by 180 of them (30%). Depression was strongly associated with poor sleep quality ($\chi^2=20.35$; $df=1$; $p<0.001$), and insomnia severity ($\chi^2=13.05$; $df=1$; $p<0.001$). Above-threshold anxiety was associated only with insomnia severity ($\chi^2=16.42$; $df=1$; $p<0.001$).

Conclusion

It has been found that an anxiety pathway was strongly associated with insomnia severity, while a depression was more relevant for worsening the quality of sleep.

Keywords: Depression, Anxiety, Sleep Problems

5. ELECTRONIC HEALTH RECORD AND INTEGRATED HEALTH INFORMATION SYSTEM IN THE FUNCTION OF IMPROVING THE QUALITY OF THE NOTIFICATION SYSTEM FOR INFECTIOUS DISEASES

Zoran Kokić

Primary health care centre “Voždovac”

Objectives: The purpose of this analysis was to examine the basic characteristics of reporting diseases from infectious diseases, and the impact of daily active monitoring of infectious disease reporting, using the EHR. The timeliness and efficiency of reporting are monitored, on the population of Belgrade, in the period from 2012 to 2018. In the paper we recommend the most optimal way of organization with increasing the efficiency of reporting infectious diseases.

Materials and methods: In this study a descriptive epidemiological method was used. The area covered by the research is the city of Belgrade in period from 2012 to 2018. Data on the number of infectious diseases reported by municipalities were collected from the published material of the City Bureau of Statistics. For the analysis of the disease, rates of illness were used on estimated numbers of inhabitants in Belgrade by age and sex, according to the 2002 census methodology

Results: In the observed period, the Primary health care center "Voždovac" reported each year with individual reports of diseases from infectious diseases, several times more illness, compared to the number of applications from other territory of the city of Belgrade.

The rate of illness from infectious diseases for Voždovac is significantly higher than for other municipalities of similar or higher number of inhabitants .

Conclusion Using the EHR and LAN intranet network in active surveillance of infectious disease reporting, information is obtained much faster, more precisely and most importantly in time

Recommendation An integrated health information system provides an opportunity to improve the quality of the reporting system for communicable diseases.

Keywords: Integrated health information system, registration of infectious diseases

POSTER PRESENTATIONS:

SESSION: PROMOTING HEALTH IN FAMILY AND SOCIETY

SESSION: PUBLIC HEALTH TODAY

SESSION: INFORMATICS IN THE HEALTH SYSTEM

1. FREQUENCY OF SMOKING AND ATTITUDES IN CONNECTION WITH QUITTING SMOKING OF MEDICAL STUDENTS

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Objectives: To determine the prevalence of smoking habits among medical students in Kosovska Mitrovica and the relationship with their main characteristics, and their attitudes about smoking quitting.

Methods: Research was conducted as a cross-sectional study on a representative sample of medical students in Kosovska Mitrovica, from 12 to 16 December 2018. The size of the sample was determined based on the number of students and the prevalence of cigarette smoking in the young population and amounted 273.. Questionnaire about frequency and attitudes about smoking quit was used.. From the statistical methods were used chi-square and Mc-Nemar tests, with significance of 0.05.

Results: Smoking was present among 25,9% of medical students in Kosovska Mitrovica. The most of smokers never tried to quit smoking, as the main reason for quit smoking state to high costs, considers that for quit smoking it is necessary more than a month, as situations or people who impede the quit smoking state a stres, as situations or persons who are able to help state sport; did not use or do not use pharmacological agencies or counseling services to quit smoking, and the most important measure for reducing number of smokers is considered to be a smoking ban in public places

Conclusion: Identification of groups who more often practice this habit, and the study of attitudes about smoking quitting is important for adaptation health promotion measures and activities.

Keywords: smoking, students, attitudes, quitting

2. THE IMPORTANCE OF SCREENING METHODS IN THE PREVENTION OF CERVICAL CANCER

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Objective: To point out the importance of informing women about the effectiveness of screening methods in the diagnosis of premalignant lesions, as prevention of cervical cancer.

Methods: The reserche was conducted from May 8 to May 9, 2019 in the territory of the Republic of Serbia anonymously, using a 15-questionnaire, which was active online. The questions related to women's knowledge of screening methods and their attendance at regular gynecological examinations. 573 women aged 20 to 65 participated by random selection. The questions were closed-ended, with the possibility of one answer from two to five.

Results: 78% of women were aged 20-35 years. 58% are college educated and 48% are employed. 87% of women are sexually active, and 32% use a condom all the time. 63% of women know that the cause of cervical cancer is HPV virus. 55% of women attend regular annual gynecological examinations, and 73% of women have had a PAPA test at least once in their lifetime. Only 2% participated in an organized screening program.

Conclusion: Organized decentralized screening programs make it possible to diagnose premalignant cervical lesions, reduce treatment costs, and improve the quality of a woman's health.

Keywords: cervical cancer, HPV, screening

3. COMMUNICATION WITH ANABOLIC STEROID USERS – NEW HEALTH CHALLENGES

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Introduction. The use of anabolic steroids became a critical issue in the mid-20th century, first by athletes, the effects of which led to their widespread use. It is estimated that the current prevalence is about 3-4% in the total population, with a further increase, firstly in bodybuilders to improve their physical appearance (both in men and more recently in women). The onset of steroid use usually begins at about 18 years of age with the development of addiction in at least a third of users after about 6 months. It takes place in 5-10 week cycles with different dosages adapted to users, with polypharmaceuticals being the most commonly used to enhance their effects. The consequences of steroid dependence are numerous and related to the length of their consumption in the field of fertility (decreased libido, erectile dysfunction, changes in hormonal status, testicular atrophy, sterility) and psychological (depression, anxiety, aggression, "roid rage" etc.).

This work aims to review the consequences of taking steroids in users from gyms in Niš and identify approaches in communication with them.

Methodology. Users were examined by a psychiatrist through a survey of their subjective sense of health (physical and psychological) in addition to controlling their fertility status with embryologists. Issues related to the use of anabolic steroids in male gym-goers and the association of those issues with their use have been investigated. Special attention has been paid to the specificity of communication with patients during their anamnesis, examination and counselling activities, given the complexity of the causes, types of anabolic steroids, knowledge of possible consequences for their current fertile and psychological status.

Results. The survey included 51 gym goers divided into 3 age categories: up to 20 years, 21-30 and 31 + years (average 28.3 years). Most frequently, the length of doing exercises was over a year (41.2%). Of all subjects, 68.6% used anabolic drugs, almost all of them with intermittent interruptions required by the treatment itself. Most of the subjects (58.8%) showed oligospermia or azoospermia (impaired or lost fertility) on examination of their sperm. The respondents with prolonged use of anabolic drugs (over a year) reported psychiatric disorders such as insomnia, irritability, excessive jealousy, disorders of thinking and feelings, which was observed in many when seen in direct contact with a psychiatrist (24 or 47.0%).

The conclusion was that anabolic steroid addiction treatment problems require activities of a multidisciplinary team, trained in accessing addicts, adopting and implementing various aspects of verbal and non-verbal communication and being prepared for their long-term use. The area under study has not been adequately explored, given the extensive network of actors involved: manufacturers, distributors, product controls, medical examinations before and during their consumption, insufficient awareness of not only practitioners but also their trainers about the effects of anabolic steroids to health. The authors advocate an approach that involves planning a unique program for the general population, but especially the young, requiring different types of communication: campaigns, use of mass media, the involvement of key personalities, encouraging steroid users to take steps towards a healthier life. Feeding information to the young (increasingly girls) about their own (often negative) experiences from more experienced athletes, preferably those who have developed a higher status in the field of bodybuilding, would be of particular help.

4. SELF-MEDICATION IN PREGNANT AND BREASTFEEDING WOMEN

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Introduction: Self-medication is defined as the selection and use of medicines by individuals to treat self-recognized conditions or symptoms. It involves obtaining medication without prescription called “over-the-counter medicines” (OTC) products.

Objectives: The aim was to evaluate the self-medication in pregnant and breastfeeding women and to analyze their attitudes toward self-medication and the medical professionals' role in the selection of OTC.

Methods: A prospective cross-sectional study included 70 pregnant and 76 breastfeeding women which were voluntarily answered on questionnaire with 16 closed-ended questions.

Results: The use of OTC was reported in 33% of the respondents. OTC were more prevalent in breastfeeding (56.52%) than pregnant women (9.09%; $p < 0.05$). The most common medical problems as the reason for self-medication were different kinds of pain (53%) and fever (23.52%). Paracetamol was reported as the drug of choice. Asked about their sources of advice for self-medication, 71.12% of the respondents consider that the pharmacist is a trustful person, who is easily accessible and provides advice aimed to the best self-medication options. Also, 80% respondents are aware of adverse effects and possible interactions of self-medication.

Conclusion: Our study clearly indicates that respondents are aware of the potential risk of self-medication during pregnancy and lactation. The pharmacists play a key role in providing information available, and may help patients in self-medication and choice of OTC.

Keywords: Self-medication, over the counter drugs, pregnant women, breastfeeding women, pharmacist

5. CHARACTERISTICS OF COMMUNICATION WITH ELDERLY PATIENTS AT THE LEVEL OF GENERAL MEDICINE

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Studying the tendencies of demographic changes, both globally and nationally, it is observed regularity in the movement towards an increasingly aging population. In the total population estimated for the year 2025, older persons are expected to account for 27,5 per cent in the most developed countries and 9.1-17,7 per cent in south Europe and 18.7 - 27.5 per cent in Serbia. Moreover, the 75-year-old segment of the elderly population will also increase in particular, with significant health, economic and social effects. The aim of our work was to point out the problems that exist at the level of communication of the elderly with healthcare professionals in the general practice., to the expectations of their future movements, as well as the need to take appropriate action. The methodology covered the findings of previous statistical and other public health surveys in various fields, as well as the results of own research on a sample of 1295 persons over 65 years of age. The results are as follows: the elderly are the health and socio-economically most vulnerable population category. The health of the elderly is characterized by polymorbidity, many disease complications and more frequent use of the health care service than the younger population. The mortality model is dominated by causes, most commonly unhealthy lifestyles (diet, smoking, physical inactivity, low levels of general and health culture). On average, every fifth elderly patient receives health lessons from selected physicians. The advice of healthcare professionals is often insufficiently clear, so most of elderly are oriented toward obtaining health information from non-medical sources (family members, friends, mass media, pharmacists, and others). The time they spend on examination is often evaluated as too short, that is generally true given the presence of hearing, movement, which slows down the preparation for examination. Some degree of drowsiness or dementia requires frequent repetition of advice, which is quickly forgotten if the visit is not made without the presence of a younger person. On the other hand, the doctor is still instructed to keep double records, which shortens the effective time for direct contact with patients. Finally, the physician does not have adequate printed health care resources, which the patient would take as a reminder and a constant source of advice for their own problems (about the importance of adequate nutrition, the importance of leaving tobacco, healthy eating, etc.). Conclusion. Poorer social support and increased pressure on the health service by geriatric patients, notably with regard to non communicable disease, the increasing need for home care services and the increasing need for various types of geriatric care. In such circumstances, given the current state of play in the field of observation, meeting the WHO's goals for active aging must be linked above all to a positive shift in communication, not only at the doctor-patient level, but also requiring a broader network of communications at the level of: family-family-community- health insurance funds-health policy.

Keywords: elderly people, health care, communications

6. PREDICTORS OF HEALTH PROFESSIONALS JOB SATISFACTION IN NISAVA DISTRICT HEALTH SECTOR

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Objective: Job satisfaction is a complex and multifactorial phenomenon, and has great influence on quality of performance and financial expenditure. The objective of this study was to define predictors of health professionals' job satisfaction in Nisava district health sector.

Methodology: A cross-sectional study was designed to identify factors that impact health professionals' job satisfaction in 15 health facilities in Nisava District. A 23-question self-administered survey covered 5.425 health professionals; 4.707 health professionals took the questioner and 3.899 completed it anonymously (response rate 82,8%). Univariate statistics were used to describe the study sample. χ^2 test was used for testing the statistical significance of the difference of absolute frequencies between samples. Multivariable analysis of variance was used to determine which variables contributed the most to job satisfaction.

Results: Total job satisfaction was $3,34 \pm 0,99$; the highest score was on the primary level of health. The group of communication factors of job satisfaction had the highest scores on all level of health. The organizational factors of job satisfaction had the strongest impact on the total job satisfaction, and could be recognized as predictors of job satisfaction.

Conclusion: Recognizing the predictors of job satisfaction enable defining the field that could be improved by strategic actions aiming to sustain and improve health professionals' job satisfaction.

Keywords: job satisfaction, health professionals

7. STRESS AS A PROFESSIONAL RISK TO THE HEALTH PROFESSION

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In health care, high stress and the effects of stress are exposed to those on which other people's lives depend.

A total of 815 health professionals were surveyed, of which 605 (74.2%) were women and 210 (25.8%) were men, 444 (54.5%) nurses and technicians were interviewed as well as 371 (45.5%) doctors.

Of the job characteristics and scores of COPSOQ questionnaires by domain, multivariate regression analysis extracted stress as a significant factor influencing IRS values. An increase in the score of 1 was associated with a significant decrease in the IRS, for stress 0.081 (0.018 to 0.144; $p = 0.012$).

When all factors that are singled out as significant in multivariate block analyzes are included in a single regression model, the final model confirms that stress in the group of the most significant factors is related to IRS values. An increase in the score of 1 was associated with a significant decrease in the IRS, for stress 0.082 (0.020 to 0.145; $p = 0.010$).

According to research, 22% of the working population in the EU is affected by occupational stress, making it the most important occupational health problem.

8. MEDICAL DEVICES INTENDED FOR SELF-MONITORING OF BLOOD GLUCOSE AVAILABLE IN SERBIA

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Objectives: The aim of this research was to identify blood glucose monitoring devices (glucometers) registered in Serbia and assess their selected properties.

Methods: Online search of the National Medical Devices Database was performed using “aparatus za određivanje glukoze u krvi” as a search string (under “generic name”). Detailed information on specific glucometers was found on manufacturers’ websites.

Results: A total of 20 glucometers for personal use from 12 different manufacturers were registered in Serbia according to the National Medical Devices Database. Countries of origin were China (4 manufacturers), Germany (2), Switzerland (2), South Korea (2), Taiwan (1), Austria (1). Measuring ranges varied slightly between different glucometers, most commonly being from 0.6 or 1.1 mmol/l to 33.3 mmol/l. Accuracy of all glucometers was declared to be in accordance with the ISO 15197 standard. Storage capacity was between 250 and 1000 test results (usually 300 or 500) with possibilities to display 1 to 90 days averages (most commonly 7, 14 or 30 days). Prices of different models varied from 20 to 80 EUR.

Conclusions: Considering the differences between glucometers registered in Serbia, possibly confusing for patients, healthcare professionals should be educated to help diabetics find glucometers that best fit their specific needs.

Keywords: medical devices; database; glucometers; blood glucose; Serbia

9. ASTHMA AS THE ROOT CAUSE OF HOSPITALIZATION AT THE KRAGUJEVAC CLINICAL CENTER

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Objectives: Asthma is a significant public health problem and a high burden disease for society and patients, whose prevention is partially possible and treatment can be effective.

Materials and methods: The study was designed as a retrospective descriptive epidemiological study. The hospitalization report was used as a research instrument. A total of 2.681 hospitalizations were diagnosed with bronchial asthma (J45) and asthmatic status (J46) at the Clinical Center Kragujevac in the period from 01.01.2007. until 31.12.2014. The results were processed at the Public Health Institute of Kragujevac.

Results: Among the patients hospitalized for asthma in childhood and adolescence, there were more boys than girls (59.5% vs. 40.5%), while in the adult population the ratio changed for the benefit of women (62.7% vs. 37.3%). In our study, the average hospitalization rate for bronchial asthma in children is significantly higher than in adults and is 265.9, while in adults it is 69.3. Respiratory tract diseases are the most common asthma comorbidity in childhood, while cardiovascular disease comorbidity is the most common in the adult population

Conclusions: Although the causes of the disease have not been fully elucidated, current medicine is able to help improve quality of life, control disease and avoid premature death.

Keywords: asthma, hospitalization report, public health problem.

10. EVALUATION OF THE BURDEN OF DIABETES IN SERBIA AND OTHER EUROPEAN COUNTRIES - COMPARISON OF SELECTED HEALTH INDICATORS

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Objectives: Diabetes mellitus is one of the most common chronic non-communicable diseases and represents a major public health problem. Despite the consistent advances in medical fields, diabetes continues to be a burning issue in terms of rising morbidity and mortality rates globally.

Methods: The research is presented as a descriptive epidemiological study. WHO, IDF and IHME data sources were used.

Results: Serbia is not only ranked in the top quarter of the list of world's countries with highest diabetes prevalence rate in 2017, it holds the second position in Europe with 13.3% of the diseased population (after Portugal with 13.9%), and the third in terms of prevalence growth from 2010 to 2017. after Turkey and Iceland. Mortality rates in Serbia are also among the highest in Europe and are constantly growing. Comparing the burden of disease measured by DALYs, Serbia is second in Central-European region with 1.578,7 DALYs per 100.000 persons (which represents 4,26% of total DALYs in the state), right after BiH which has by far the worst indicators when it comes to diabetes.

Conclusion: Serbia has very poor diabetes statistics and there are predictions that trends like this will continue. Investing in reducing this burden is justified and necessary.

Keywords: burden of disease, diabetes mellitus, Serbia, Europe

11. MORBILLI AS PUBLIC HEALTH PROBLEM

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Objectives: The objectives of this study were to determine demographic, social and epidemiological characteristics among measles affected, hospitalized children and their influence to severity of disease.

Methods: This descriptive cross-sectional study involved 55 measles affected, hospitalized children in Pediatric Department to General Hospital of Leskovac since the outbreak measles in Jablanica district, until December 2017 to July 2018. Data were collected from medical documentation and analyzed using descriptive statistics methods. Influence of factors on the severity of disease among affected children with and without complications was examined using χ^2 and t-test. Statistically significant was considered $p < 0,05$.

Results: During measles outbreaks were hospitalized 55 children (male gender 27 and female 28). It was 43 (78,18%) Roma children and 12 (21,82%) Serbian children. The highest number of affected children 25 (45,45 %) was age between 0-12 months. Most of affected children, 34 (61,81%) living in poor conditions, in multi-member family. In 30 (54,54%) cases family member were also measles affected. Unvaccinated was 46 (83,63%) and malnourished 12 (23,63%) affected children. The severity of disease was significantly in children who living in poor conditions ($p < 0,05$), under 1 year of age ($p < 0,05$) and infected during winter ($p < 0,05$).

Conclusion: Poor living conditions, low educational level, life in marginalized groups, unvaccinated were the most frequent factors among measles affected children. These are, also, the most significant interfering factors for low measles vaccination coverage and immunity gaps which makes measles a public health problem.

Keywords: measles, outbreak, children.

SESSION: MICROBIOLOGY TODAY

INVITED LECTURES

1. CLOSTRIDIUM DIFFICILE INFECTIONS IN THE NETHERLANDS AND EUROPE.

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Before 2005, CDI outbreaks were rarely reported in the Netherlands. In 2005, the *C. difficile* ribotype 027 strain (or NAP1/REA BI strain) was for the first time detected and rapidly spread within Netherlands while causing major outbreaks. Retrospectively, the rapid spread of the ribotype 027 strain across Northern-America and Europe has been attributed to its high level of fluoroquinolone resistance. A study by Collins et al. suggests that the rapid spread might also be attributed to a different trehalose metabolism in ribotype 027 strains, which causes the ability to metabolize low concentrations of trehalose. The implementation of trehalose as a food additive into the human diet, shortly before the emergence of ribotype 027, might have stimulated the spread of ribotype 027. CDI cases due to ribotype 027 were associated with unfavourable patient outcomes such as severe disease, mortality and recurrent CDI in comparison to other ribotypes, which may reflect type-specific host susceptibility and/or an increased virulence of the strain (Smits et al.). Since mid-2006, the occurrence of ribotype 027 in the Netherlands has decreased significantly. The CDI incidence rate has stabilised at 3 CDI cases per 10.000 patient-days. Interestingly, more ribotype 027-like strains are beginning to emerge, like ribotype 036, 198 and 181. They are mainly observed in Eastern-Europe, though in 2019 a cluster of four patients was found of Type 198

The Centre for Infectious Disease Control (CIb) of the National Institute for Public Health and the Environment (RIVM) started a National Reference Laboratory for *C. difficile* at the Leiden University Medical Center soon after recognition of *C. difficile* ribotype 027 outbreaks in 2005. Since then, this laboratory has offered ad hoc typing service for all microbiology laboratories in the Netherlands for typing of *C. difficile* isolates of patients with severe disease, or isolates from a suspected outbreak. Additionally, the National Reference Laboratory initiated a sentinel surveillance programme in May 2009 to monitor the incidence of CDI in an endemic situation. Furthermore, the programme aims to monitor (new) emerging strains of *C. difficile*. Each year, an annual report is published at the website of RIVM, publicable available.

In the period 2018-2019, a mean incidence rate of 3.06 CDI cases per 10.000 patient-days (varying from 0.95 to 5.88 CDI cases per 10.000 patient-days) was found through sentinel surveillance, similar to previous years. The disease severity was reported for 877 out of 900 patients included in the surveillance; 16.1% had severe CDI. The 30-day outcome was reported for 812 patients; 90.0% had an uncomplicated course, 0.2% were admitted to the ICU as a consequence of CDI, 0.4% needed surgery as a consequence of CDI and 9.3% of the patients died within 30 days (n=76). For 9 patients (1.1%) their death was known to be contributable to CDI. CDI-contributable mortality was decreased compared to last year. Other outcomes of CDI were comparable to previous years. However, a difference in severity of CDI is observed between the start of the surveillance in 2009-2010 with 27.9%, and 2018-2019 with 16.1%. This may be explained by the decrease in the proportion of ribotype 027. The proportion of community-onset cases has increased to 46% of all cases and will be topic for a surveillance in the general population in 2020. Similar as in 2017-2018, the most frequent encountered PCR ribotype was ribotype 014/020 (19.5%). Unlike 2017-2018, the second most encountered PCR

ribotype was 078/126 (11.7%). Ribotype 027 was found in 0.6% of samples (1.2% during May 2017-May 2018).



Currently, 24 hospitals participate in the sentinel surveillance. Five university hospitals (n=5) and primary or secondary care hospitals (n=19) are included, distributed all over the Netherlands. The geographical location of the participating hospitals is displayed in the figure.

The Netherlands is also participating in the European-wide CDI surveillance which is led by ECDC. Leiden is coordinating the microbiological support for this CDI surveillance program and revised a protocol for the surveillance of CDI (van Dorp et al, Eurosurveillance, 2016) which is now used in many European countries. The protocol, published in 2015, includes the description of the methodology and provides the data collection tools required to achieve the objectives of the

European surveillance of CDIs. ECDC initiated coordination of CDI surveillance using the ECDC protocol on 1 January 2016. The ECDC protocol specifies three options for surveillance in acute care hospitals (see table). In the ‘minimal’ option, hospitals collect aggregate numerator and denominator data. In the ‘light’ option, hospitals collect case-based data in addition to the same aggregate numerator and denominator data. In the ‘enhanced’ option, hospitals collect the same data as in the ‘light’ option, but they also collect microbiological data on at least the first five cases within a surveillance period. The minimum surveillance period is three months.

	Minimal surveillance	Light surveillance	Enhanced surveillance	Form
Collected information	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Form H (aggregated numerator and denominator data)
		<ul style="list-style-type: none"> • Information on each CDI case (case-based numerator data) 	<ul style="list-style-type: none"> • Information on each CDI case (case-based numerator data) 	<ul style="list-style-type: none"> • Form C (case-based numerator data)
			<ul style="list-style-type: none"> • Additional information on each CDI case (enhanced numerator data) 	<ul style="list-style-type: none"> • Form E (additional case-based numerator data; one form for each CDI case and <i>C. difficile</i> isolate)
			<ul style="list-style-type: none"> • Microbiological data (for the first 10 consecutively detected cases in each participating healthcare facility: characterisation, susceptibility testing and typing of each <i>C. difficile</i> isolate)) 	<ul style="list-style-type: none"> • Form M (one form for each <i>C. difficile</i> isolate)
Surveillance period	<p>Recommended: continuous surveillance for 12 months, starting on the first* day of the month.</p> <p>The recommended minimum surveillance period is three consecutive months, preferably from 1 October to 31 December, or from 1 January to 31 March.</p> <p>Note that on average, a 300-bed European hospital (with 100% bed occupancy) can expect seven CDI cases every three months, or 28 cases per year, for an incidence of three CDI cases per 10 000 patient-days.</p> <p><i>*The pilot study demonstrated that completion of Form H is made much easier by starting surveillance on the first day of a month.</i></p>			

In 2016, over 556 hospitals in 20 countries participated, of which 233 followed the ‘minimum’ surveillance option, 99 followed the ‘light’ option, and 261 followed the ‘enhanced’ option. A total of 7711 CDI cases were reported, 5 756 of which (74.6%) were healthcare-associated (HA) CDI. CDI contributed to a fatal outcome in 3.9% (207/5 248) cases with a known outcome. ESCMID-recommended diagnostic algorithms were used during 314/439 (71.5%) hospital surveillance periods, whereas less optimal algorithms were used during 125 (28.5%) periods. Metronidazole resistance was reported for 26/569 (4.6%) cases with data on susceptibility, and one case of resistance to vancomycin was reported. PCR ribotype (RT) data were available for 1 326/3 894 (34.1%) cases with enhanced case-based data. The most common RTs were the virulent strains RT027 (n=303, 22.9%), RT001 (n=99, 7.5%) and RT014 (n=89, 6.7%), demonstrating that virulent strains can become established in hospitals.

In 2019, the CDI surveillance program was extended. ECDC invited stakeholders from Western Balkan countries and Turkey to express interest and commitment to participate in a standardised surveillance of CDIs in Europe. Serbia responded very rapidly and a large collection of *C. difficile* isolates were received from Prof. Predrag Stojanovic, University of Niš, Faculty of Medicine. Other participating Balkan countries are Albania, Bosnia and Herzegovina, Montenegro, Kosovo and The former Yugoslav Republic of Macedonia.

An important task of the Leiden microbiology laboratory is to support typing and characterisation of *C. difficile* isolates. Important observations were made by recognizing new emerging types that are very much related to the hypervirulent 027 and belong to the same clade, such as types 176, 036, 181 and 191. Since 2018, a PCR had been applied to recognize the

plasmid-mediated metronidazole resistance (Boekhoud et al, submitted) and this form of resistance has been found in types 010, 014/020 and 027.

In summary, CDI surveillance is currently implemented in many European countries and already shows some interesting data, such as the emergence of new PCR ribotypes and the development of plasmid-mediated resistance to metronidazole. CDI in the community is also increasingly recognized and should be surveyed too.

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2. MICROBIOLOGICAL DIAGNOSIS OF INFECTIONS CAUSED BY CLOSTRIDIUM DIFFICILE

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Clostridium difficile (*C. difficile*) is the leading cause of infectious diarrhea in hospitalized patients (*C. difficile* associated disease - CDAD; *C. difficile* infection - CDI is more commonly used today). Diagnosis of CDI is set by various clinical and microbiological methods whose reliability has variations in sensitivity and specificity (molecular methods, immunochromatographic tests, toxins A and B immunoassays, cytotoxicity test on cell culture, etc.) (1, 2).

Cytotoxicity testing on cell culture is a "gold standard" for the detection of toxin B *C. difficile* in stool samples due to good sensitivity (<1 pg of toxin B) and specificity (neutralization of cytopathogenic effect by specific antiserum to *C. sordelli* toxins). The sensitivity of the gold standard can be increased to 98% if combined with cultivation and determination of toxin production in the liquid culture of the isolates, resulting in higher costs and a longer time interval (24 h to 4 days) to finally diagnosed CDI (3, 4). Researchers point out that the PCR method can also provide a greater number of accurate positive findings than a cytotoxicity test, which shows that different PCR methods successfully replace cultivation and the gold standard in CDI diagnostics. The characteristics of individual PCR tests often show individual high values (up to 100%) of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) (5, 6).

Microbiological laboratories in everyday work, use different tests, protocols - CDI diagnostic algorithms. Most of these techniques and methods (GDH, metabolic products (isocaproic acid, etc.), gas liquid chromatography, etc.) are not specific because non-toxic strains of *C. difficile*, as well as some residents of the normal flora of the digestive tract, have identical identification products (2, 3).

Glutamate dehydrogenase (GDH) is a highly specific enzyme for all *C. difficile* isolates, and in most studies it has high sensitivity and even better specificity. Results of meta-analysis of Shetty et al. (7) show a high association between GDH findings and the presence of *C. difficile* in patient samples. The sensitivity and specificity rate was > 90%, which is very close to the results obtained by cultivating on selective substrates. However, it should be kept in mind that this test has a high rate of false positive findings (up to 20%) because it detects both non-toxic isolates and a large number of other bacterial species that produce this enzyme. All researchers agree that high sensitivity values, even more negative predictive rule values, low cost, short time and simple performance, GDH tests provide a powerful reagent especially when combined with another toxin test within two or three steps of the CDI diagnosis algorithm (3, 7, 8).

Evidence of produced toxins in patient samples is a key procedure in CDI diagnosis. A large number of tests that detect individual or both toxins at the same time. In general, the results obtained indicate that the detection of both toxins by one test takes precedence over tests that only detect toxin A (the performance values (above all the specificity) of the tests were over 90%) (3, 5).

The reasons for the unreliability of the toxin detection tests should be sought in the event of a poor design of the test. It is less likely that the crossed reaction is due to contamination during ELISA testing - a step of washing the pool or another step, which depends on the type of ELISA test. A false negative finding of toxin can be due to instability of the strain in the amount of toxin produced, inactivation of toxins due to temperature change, activation of toxin-disrupting proteases, the presence of inhibitors in the sample, and inadequate laboratory procedures (5). In the study of Shin et al. (4) it has been confirmed that a false negative toxin finding may be associated with a small number of *C. difficile* isolates (semi-quantitative diagnosis), which reflects a smaller amount of the produced toxin that is broken by proteases or is blocked by inhibitors. Freezing of the sample can also influence the reliability of the findings. According to some studies (5), freezing has little effect on immunoblot methods and latex agglutination but can therefore affect the sensitivity of the PCR method and its decrease from 100% to 74%.

In practice, two, three or more step algorithms are used. Most researchers agree that due to high sensitivity, specificity and NPV values, the GDH test is the best first step (3, 4).

The use of GDH in a two-step algorithm, together with a confirmatory test (for produced toxins or PCR for gene toxins) is an acceptable strategy. A negative finding by the GDH test confirms the CDI negative diagnosis but a positive GDH finding requires a confirmatory test of the produced toxin or toxin-encoding genes. It is best to confirm with the PCR method in the stool and isolate. In research by Fenner et al. (9) of 187 GDH positive stool samples, 69 (37%) were positive for toxins. In the group of GDH negative, 10 patients had a toxin positive result, of which in five, the PCR method confirmed a positive finding. In 52.9% of GDH and toxin-positive patients, the rise of *C. difficile* colonies was determined.

In the research Brown and Sar. (5) using the diagnostic algorithm, test performance (GDH EIA-Wampole C. DIFF CHEK-60 Assay, Iver Med, Princeton, NJ; *C. difficile* Toxin AB EIA -Remel prospect; *C. difficile* toxin AB, Microplate, Lenexa, KS) were better than their individual testing. Using algorithms, the reliability of the CDI diagnostics is improved by 10%, as part of false positive and false negative results is excluded (83% sensitivity, 100% specificity, PPV 100%, NPV 98.2%). Using the three-step algorithm (GDH → toxin EIA tox AB → PCR), even better results are obtained (sensitivity 92%, specificity 100%, PPV 100%, NPV 99.1%). If PCR is used as a third step then it should work with fresh samples, in which case the sensitivity is 100%.

In the diagnosis of CDI, the relationship between laboratory findings and clinical diagnosis is not always completely clear. Several pre-analytical factors (eg chamber sampling conditions, sample time before testing and arrival in the laboratory, etc.) can significantly influence the diagnosis (10). Finally, to set the diagnosis of CDI, but not less important, is the attitude of a clinician in the individual examination of patients. Also, CDI empirical therapy usually begins prior to laboratory confirmation and even some doctors continue despite negative results. It should be noted that a significant number of moderate CDI cases go on after the suspension of the use of antibiotics that preceded the CDI and consequent reduction in *dietary-carbohydrate*. A positive finding of rapid tests on *C. difficile* toxins can lead to therapy without providing the possibility that the symptoms will spontaneously withdraw. Despite the disadvantages, the possibility of obtaining the findings of the same day, successful screening of negative results and use in each laboratory makes fast tests necessary in everyday work.

Keywords: *Clostridium difficile*, toxin, glutamate dehydrogenase (GDH), microbiological diagnosis

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3. CLINICAL INTERVENTION USING PROBIOTIC BIFIDOBACTERIUM STRAINS IN CELIAC DISEASE CHILDREN

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Introduction

Celiac disease (CD) is a common immune-mediated pathology diagnosed by intolerance to gluten. Gluten is found in wheat and other gluten containing cereals. Ingestion of gluten in affected individuals damages intestinal mucosa, that leads to gastrointestinal upset, chronic fatigue, nutrient malabsorption and poor growth (1). Currently, the only available treatment involves life-long gluten free-diet. Although genetic background is a well known predisposing factor for CD, the role of intestinal microbiota is still not understood. In principle, microbiota could play a role in the pathogenesis of CD, since patients generally have a reduced ratio of potentially beneficial to pathogenic microbes. However, it is not clear if dysbiosis is the consequence of the disease, a simple concomitant association or a concurring causative factor (2). Nevertheless, extensive evidence suggests that microbiota interacts with the host through multiple pathways, also through the production of various metabolites. Short chain fatty acids are well known microbial metabolites, which have been identified to have multiple roles in human physiology. To name a few, butyrate serves as a primary metabolic fuel for colonocytes, acetate is supposed to have a pro-inflammatory while propionate and butyrate an anti-inflammatory role (3).

Probiotics have become a popular way to alleviate symptoms related to various gut disorders. They have been shown to be beneficial due to their modulation of immune function, production of organic acids and antimicrobial compounds, modulation of resident microbiota, interfacing with the host, improving gut barrier integrity and enzyme formation (4).

Methods

Our aim was to study the effects of *Bifidobacterium breve* (*B. breve*) BR03 and B632 administration on children with CD. For this purpose, a double-blind placebo-controlled study enrolled 40 children with CD (CD) and 16 healthy children (HC). CD children were randomly allocated into two groups, of which 20 belonged to the placebo (PL) group and 20 to the probiotic (PR) group. The PR group received a probiotic formulation containing a mixture of 2 strains, *B. breve* BR03 (DSM 16604) and *B. breve* B632 (DSM 24706) in 1:1 ratio for 3 months. Blood and fecal samples from CD children (on enrolment - T0 and after 3

months, at the end of intervention with probiotic / placebo - T1) and HC children were collected. The HC group was sampled only once (T0). Patients' blood was analyzed for serum TNF α by ELISA. Feecal samples were analyzed for SCFA levels (acetate, propionate, butyrate) using HPLC. In addition, DNA was extracted from feecal samples and microbiome composition was analyzed by 16S RNA gene sequencing using next generation sequencing methods. Statistical correlations between feecal microbiota composition analyzed by next generation sequencing, serum TNF- α and feecal SCFA levels were examined.

Results

B. breve administration significantly decreased serum TNF α in CD patients after receiving probiotic for 3 months. Levels of TNF α increased again after 3 months of follow up (5). Interestingly, administration of probiotic affected presence of various microbial phyla. *Enterobacteriaceae* family might not be directly addressed to pathogenesis of CD. *Verrucomicrobia*, *Parcubacteria* and some yet unknown phyla of *Bacteria* and *Archaea* may be involved in the disease, indicated by a strong correlation to pro-inflammatory TNF- α . Likewise, *Proteobacteria* strongly correlated with feecal SCFAs concentration. The effect of probiotic administration has disclosed a negative correlation between *Verrucomicrobia*, some unknown phyla of *Bacteria*, *Synergistetes*, *Euryarchaeota* and some SCFAs, turning them into an important target in microbiome restoration process. *Synergistetes* and *Euryarcheota* may have a role in the anti-inflammatory process in healthy human gut (6).

Conclusions

Our results indicate that probiotics could be an effective complementary therapy for CD patients. Its beneficial role has been reflected in decresed inflammatory markers, as well as changes in SCFA levels and microbiota composition. In addition, new phyla have been indicated, which may have an important relation to disease-related parameters, CD itself and health.

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4. NEW FEMS INITIATIVES-CHALLENGES AND OPPORTUNITIES FOR MOST TALENTED MICROBIOLOGISTS

Vaso Taleski

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FEMS (Federation of European Microbiological Societies) established in 1974, is a federation of 54-member societies from 38 countries, an active and diverse network of around 30,000 professionals, early and senior career scientists committed to advance microbiology.

FEMS publish five highly regarded journals, hold biennial European congresses, promote education and professional development, provides support for various microbiology meetings in Europe.

Early career scientists are one of the main focus of FEMS providing every year grants for Research and Training at a European prestige institutions (exceptionally outside Europe) on their own choice, in a country other than their own country of residence.

In 1987, the available FEMS funds permitted the award of ten fellowships for ten-member societies, each nominated one candidate in the years 1988, 1989 and 1990. However, the constantly improving FEMS resources permitted an increase to 12 and 14 fellowships respectively in 1989 and 1990.

Great success of five FEMS journals provided larger budget for various FEMS grants.

Last 15 years FEMS developed several different types of grants for early career scientists, senior scientists (as visiting scientists) and meeting grants. FEMS is supporting microbiology with grants amount of 400.000 to 500.000 EUR each year.

The noble idea appears, to organize serial of FEMS postdocs summer schools, for excellent European and non-European postdocs, in organization by worldwide scientifically recognized and distinguish professors, lecturers, researchers and scientists. It would be a new landmark of FEMS, a place for connection of young and senior scientists, knowledge exchange, and production of ideas for new scientific projects.

With great help of Croatian Microbiological Society (HMD) and acceptance with delight from prof. Miroslav Radman, founder of MedILS (Mediterranean Institute of Life Sciences), FEMS Board of Directors selected MedILS as a venue and made agreement with MedILS to organize postdocs summer schools in following five years, starting in 2019.

MedILS, is situated in Split, Croatia, and founded in 2003 as a nonprofit research institute, a leading international center of excellence in the field of natural sciences. Institute is located in pine forest in the heart of hill Marjan (178 m), in a beautiful completely renovated building, comprises on ground floor conference room for 170 people, several smaller classrooms for smaller groups, and complete audiovisual equipment. In the basement, several excellently equipped labs on disposal for experiments for postdocs, depending on the school program.

Director and co-director of the First FEMS – MedILS postdocs summer school are prof. Miroslav Radman and prof. Graham Walker. A dozen of distinguish scientists are mentors and speakers. Excellent program attracted about 40 young scientists to apply for summer school.

Scientific board selected 24, but unfortunately due various, serious personal reason 7 canceled, and 17 postdocs, 13 from 11 European and four from three non- European countries, will attend the first FEMS summer school taking place from 28 August to 7 of September 2019.

In addition, another new initiative, very important for young scientists, is organization serial of FEMS biennial conference on microbiology, between FEMS Congresses. Conference will have limited number of topics, but always one topic will be included: FEMS grants – Influence on scientific career of Early career Scientists.

First FEMS conference on microbiology will be organized in association of Serbian Society for Microbiology (SSM), 2-4 July 2020, in hotel Hilton, Belgrade, Serbia.

ORAL PRESENTATIONS

1. ANTIMICROBIAL SUSCEPTIBILITIES OF HAEMOPHILUS INFLUENZAE ISOLATES IN NORTH MACEDONIA IN 2017-2019.

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Center for Public Health – Bitola, Republic of North Macedonia

Objective: The objective of this study was to determine antibiotic susceptibility of Haemophilus influenzae(Hi) strains isolated from respiratory tract, specifying the mechanisms of beta- lactam resistance.

Materials and methods: This study, which take place from January,2017 to May, 2019, made use of 457 Haemophilus influenzae strains isolated from tracheal aspirate, sputum, eye and ear swab at Microbiology laboratory at Center for public health Bitola. Haemophilus influenzae strains were isolated on Haemophilus Chocolate 2 agar, Biomerieux and were confirmed on VITEC 2, NH cards. Susceptibilities of Hi to specific antibiotics were determined using Kirby- Bauer method according EUCAST criteria. Mechanisms of beta-lactam resistance were determined by E-test for ampicillin and amoxicillin-clavulanic acid and Nitrocefin disk,Mast Group, Ltd., Marseyside.

Results: The isolates were found to be antibiotic non-susceptible in the following order: trimethoprim-sulfamethoxazole (40.2%), ampicillin (32.6%), ciprofloxacin (7.8%), amoxicillin-clavulanic acid (6.5%), and we didn't detect any isolate that was resistant to chloramphenicol and tetracycline. The prevalences of each resistance class to beta-lactams were 72.5% for beta-lactamase-negative ampicillin-susceptible (BLNAS) strains; 4.8% for the beta-lactamase-negative ampicillin-resistant (BLNAR) strains; and 1.5% for beta-lactamase-positive amoxicillin-clavulanate resistant (BLPACR) strains, which showed both resistance mechanisms.

Conclusion: In summary, the susceptibility testing of Haemophilus influenzae strains, showed the increasing of resistance to tested antibiotics. Therefore, continued monitoring of the susceptibility trends will be needed to guide the appropriate antimicrobial chemotherapy.

Keywords: Haemophilus influenzae, antimicrobial susceptibility, b-lactamase production

2. ANTIMICROBIAL SUSCEPTIBILITY OF MULTIREsISTANT GRAM-NEGATIVE BACILLI TO CARBAPENEMS AND PHENOTYPIC DETECTION OF CARBAPENEMASES IN ISOLATES FROM PATIENTS AT THE CLINICAL CENTER NIŠ IN 2017-2018.

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OBJECTIVE: To investigate the antimicrobial susceptibility of multiresistant strains of Gram-negative bacilli to carbapenems and phenotypic detection of carbapenemases in hospital isolates from patients at the Clinical Center Niš. **MATERIAL AND METHODS:** The study included 4996 Gram-negative bacilli from the *fam. Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter spp.* from different clinical samples, taken from patients hospitalized at the Clinical Center Niš in 2017-2018. and processed at the Microbiology Center of the Institute of Public Health in Niš. **METHODS:** Isolation and identification were performed using standard bacteriological methods. Antibiotic susceptibility was determined by Kirby-Bauer disc diffusion method, Bio Rad tablets, according to the EUCAST protocol with control strains *E.coli* ATCC 2922, *Pseudomonas aeruginosa* ATCC 27853 and *K.pneumoniae* NCTC 13438. For all multiresistant isolates resistant to carbapenems, detection of carbapenemase was performed by a combined disk test- KPC, MBL and OXA-48 Confirm Kit: Carbapenemases (Rosco Diagnostica, Denmark). Multidrug-resistant isolates (MDRs) are those that are resistant to at least one representative from each of at least three groups of antimicrobials (AMLs), and extended-resistance isolates (XDR) isolates resistant to all but one or two groups of AMLs recommended for the testing of enterobacteria and species of *P. aeruginosa* and *Acinetobacter spp.* **RESULTS:** 3587 enterobacterial isolates were processed, of which 54.9% were MDR and 3.1% XDR. *E.coli*, with 1271 isolates, was the most common bacterial species. Of this number, 36.08% were MDRs and 0.3% were XDRs. *Klebsiella spp.* was represented by 976 isolates, of which 76.4% were MDR and 7.3% were XDR. Of the 663 isolates of *Pseudomonas aeruginosa*, 49.1% were MDR and 18.8% were XDR. There were 746 *Acinetobacter spp.* isolates, 84.45% MDR, and 17.6% XDR. Carbapenem resistance was highest in MDR *Acinetobacter spp.*, 97.5%, while in MDR isolates of *Pseudomonas aeruginosa* it was 92%. For all MDR enterobacteria, carbapenem resistance (imipenem and meropenem) was 10.6% and ertapenem 20.4% and for MDR *E. coli* carbapenem (imipenem and meropenem) 3.0 and ertapenem 5.3%. In isolates of *Klebsiella spp.* carbapenem resistance (imipenem and meropenem) was 13.95 and ertapenem 36.7%. In routine work, carbapenemases were phenotypically determined for all carbapenem resistant isolates. In enterobacteria, 7.41% of potential producers of carbapenemases were detected, most often being potential producers of metallo-beta lactamases and OXA-48, while *Pseudomonas aeruginosa* isolates were most often potential producers of metallo-beta lactamases (7.99%). **CONCLUSION:** The highest percentage of MDR isolates was in enterobacteria and *Acinetobacter spp.*, And XDR isolates were in *Pseudomonas aeruginosa* isolates. Class A, B and D carbapenemases were phenotypically detected in carbapenem-resistant XDR isolates.

Keywords: enterobacteria, *Pseudomonas aeruginosa*, *Acinetobacter spp.*, multiresistance, phenotypic detection of carbapenemases

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3. ROC ANALYSIS OF SERUM IGA AND IGG ANTIBODY LEVELS ON THE CHLAMYDIAL MOMP ANTIGEN

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OBJECTIVE: Improving the diagnostic efficacy of the immunoassay test (ELISA) by ROC analysis of the serum level of IgA and IgG antibodies to the chlamydial MOMP antigen.

MATERIAL: The study included 225 sexually active respondents of both sexes who tested for chlamydial infection in Institute of Public Health Kragujevac.

METHODS: For the detection of an acute chlamydial infection among other tests, an immunoenzyme test (ELISA) was used to detect the serum IgA and IgG antibody levels on the chlamydial MOMP antigen (Euroimun, Lubeck, Germany). Diagnostic efficiency of the test was determined in relation to the results obtained by the gold standard RT-PCR method (Sacace Biotechnologies, Como, Italy).

RESULTS: Based on the *cut-off* values recommended by the manufacturers, IgA (sen: 44,4%; spec: 94,2%; PPV: 26,7%; NPV: 97,3%) and IgG (sen: 66,6%; spec: 85,4%; PPV: 18,1% NPV: 98,2%) show low diagnostic efficacy. Based on the characteristics of the ROC curve (IgA: AUC = 0.952; IgG: AUC = 0.930), cut-off values were defined (IgA: S / Co \geq 0.87; IgG: Ru / ml \geq 17.57). Using new *cut-off* values, we have shown that with a sensitivity 100% and satisfactory specificity (84%) it is possible to correct the diagnostic efficiency of the IgG test, which is the case with the IgA test, with a sensitivity of 77.8% and a specificity of 90.2% .

CONCLUSION: ROC analysis of the serum level of IgA and IgG antibodies to the chlamydial MOMP antigen and the definition of new *cut-off* values has significantly improved the diagnostic efficacy of these tests.

Keywords: *C. trachomatis*, diagnostic efficacy, ROC analysis

4. MULTIPLEX QUANTITATIVE RT PCR TEST FOR DIAGNOSTIC OF BACTERIAL VAGINOSIS

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Bacterial vaginosis (BV) is the most common dysbiosis characterized with replacement of predominant lactobacillus microflora by numerous anaerobic bacteria. BV is associated with various gynecological and obstetric complications as well as increased risk of HIV and other STI's.

Objectives: demonstrate that multiplex RT-PCR is a highly specific and sensitive method for rapid and reliable simultaneous detection of different microbial genomes using a single swab and determine the quantitative relationships of bacteria commonly associated with BV - Lactobacillus spp, Gardnerella vaginalis and Atopobium vaginae and the total bacterial concentration in the vaginal flora.

Methods: the vaginal swabs of 50 women in reproductive age, with or without specific symptoms, were analyzed using RT-PCR method.

Results: the identification and quantification of anaerobic bacterial DNA as well as the total bacterial concentration and their relative relationship showed the following: BV was detected in 19 samples, BV was not present in 28 samples, intermediate flora was detected in 2 and nonspecific vaginal flora was detected in 1 sample.

Conclusion: using the RT-PCR method, it was found that the qualitative and quantitative diversity of the vaginal microbiome is far more complex compared to microscopic and clinical analyzes and has a great diagnostic value and preventive-medical significance.

Keywords: multiplex quantitative RT PCR, bacterial vaginosis, anaerobic bacteria

5. THE CYTOKINE MILIEU IN PATIENT WITH SEROLOGICAL EVIDENCE OF PERSISTENT CHLAMYDIAL INFECTION

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Objectives Immune response to genital *Chlamydia trachomatis* infection has been implicated in the disease outcome, either in resolution or severe sequelae such as tubal factor infertility (TFI) or spontaneous miscarriage (SM) and the cytokine profile during infection has been implicated in the disease outcome. Main goal of our study was to determine differences in serum cytokine profiles between healthy and women of different clinical and serological status of *C. trachomatis* infection.

Methods Firstly, serum samples were tested for antibodies against *C. trachomatis* MOMP and HSP60 using commercial ELISA test. According to serological status of *C. trachomatis* infection, women were divided into three groups: seronegative, seropositive and women with serological evidence of persistent infection. Secondly, using flow cytometry we quantified serum cytokine levels in 38 patients with TFI, 59 patients with SM and 20 healthy controls women.

Results Majority of measured cytokines were higher in group of healthy women. Contrary to that, we found that patient with serological evidence of persistent chlamydial infection, have lowest cytokine levels. We also found that these patients, not only to have lowest levels of measured cytokines, but also display unique cytokine pattern characterized by virtually complete absence of Th1 cytokines, accompanied by significant predominance of pro-inflammatory Th17 and anti-inflammatory IL-10 and Th2 cytokines.

Conclusion In conclusion, our study showed that chlamydial infection not only silencing cytokine immune response, but also modified cytokine pattern in patients with persistent infection.

Keywords: *Chlamydia trachomatis*, persistent infection, serum, cytokines

6. THE SIGNIFICANCE OF DERMOSCOPY IN DIAGNOSING OF ACRAL MELANOMA

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Acral lentiginous melanoma (ALM) is the form of cutaneous malignant melanoma (CMM), which occurs predominantly on the nailbeds, palms and soles. Among all types of melanoma it appears of about 2-3%, predominantly in darker-skin individuals. ALM located on the foot may be misdiagnosed or diagnosed with delays which leads to poor prognosis. We present a 63-year-old man with asymptomatic multicolored pigmentation on plantar region of left feet. He noticed the lesion a year ago and reported to primary health care where a general practitioner treated him with a bandage. Since the lesion persisted, the patient was referred to a dermatologist. Dermoscopic examination revealed many melanoma criteria: asymmetry of colors and structures, as well as parallel ridge pattern. Diagnosis of ALM was confirmed by pathohistological examination. In conclusion, early detection of ALM by using dermoscopy is a simple and inexpensive procedure, but essential to improve the prognosis and survival.

Keywords: Acral lentiginous melanoma (ALM), Melanoma, Dermoscopy

POSTER PRESENTATIONS

1. THE ANTIMICROBIAL SUSCEPTIBILITY OF BACTERIA ISOLATED FROM BLOOD CULTURES OF PATIENTS HOSPITALIZED IN CLINICAL CENTER NIŠ

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The gold standard for diagnosis bacteriemia and sepsis is the blood culture. High rate of mortality in patients with these infections requires rapid empirical treatment. The data about common isolated microorganisms and their susceptibility to antimicrobial agents could be important for ensuring appropriate therapy. Objective: to determine susceptibility of the most common bacteria isolated from blood cultures. Methods: in the Center for microbiology, Public Health Institute Niš, during the period from January 2017 to December 2018, we processed 3167 blood cultures obtained from patients hospitalized in Clinical center Niš. Isolated bacteria were identified using VITEK2 System (bioMerieux, France) and BBL Crystal system (Becton Dickinson Microbiology Systems). Susceptibility testing was performed according to EUCAST standard. Results: a total 667 non-duplicate facultative and anaerobic bacterial isolates were obtained from examined blood cultures. The most isolates originated from patients hospitalized in Nephrology Clinic (4,53%). Out of all isolates, 67,62% were Gram positive and 32,38% Gram negative bacteria. *S.epidermidis* was the most common isolate (35,38%) followed by *S.aureus* (8,1%), *E.faecalis* (6%), *E.coli* (5,1%), *K.pneumoniae* (4,5%), *A.baumannii* (3,74%), *P.aeruginosa* (2,54%). All staphylococci were sensitive to vancomycin and linezolid, 25,93% were MRSA. Isolates of *E.coli* were sensitive to ceftriaxone, carbapenems and ciprofloxacin in 58,82%, 97,05% and 47,05% respectively. Isolates of *K.pneumoniae* sensitive to ceftriaxone, ertapenem, imipenem, meropenem and ciprofloxacin in 13,3%, 70%, 86,7%, 83,3% and 50% respectively. Isolates of *A.baumannii* and *P.aeruginosa* were sensitive to carbapenems in 4% and 47,05% respectively, and all were sensitive to colistin. Conclusion: the data about susceptibility pattern in local clinical settings are important for optimal initial and causative treatment of bloodstream infection.

Keywords: blood culture, susceptibility pattern

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2. MULTIDRUG RESISTANT NONFERMENTIG GRAM-NEGATIVE BACILLI AS CAUSATIVE AGENTS OF HOSPITAL-ACQUIRED PNEUMONIA IN THE INTENSIVE CARE UNIT

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Objectives: Hospital-acquired pneumonia (HAP) show the highest incidence rate in intensive care units (ICU). The common causes include nonfermentative Gram-negative bacilli, which are today largely multidrug resistant (MDR). The aim of the study was to investigate the incidence of MDR nonfermentative Gram-negative bacilli isolated from patients with HAP in ICU in order to establish a basis for empirical therapy.

Methods: Prospective cohort study was conducted in ICU of Clinical Centre in Kragujevac, Serbia, from January 2009 to December 2018. Diagnosis of HAP was performed according to CDC (*Center for Disease Control, Atlanta, USA*) diagnostic criteria. The samples were obtained from: sputum, bronchoalveolar lavage and endotracheal aspirate. Isolation and identification of strains were based on standard microbiological methods. Antibiotic susceptibility was tested by disk diffusion method according to EUCAST recommendations.

Results: Of a total of 1499 isolates, nonfermentative Gram-negative agents represented 61.1% (n=916). Generally, the most common among them was *Acinetobacter spp* (65.1%, n=596), *Pseudomonas aeruginosa* (30.2%, n=277) and *Stenotrophomonas maltophilia* (4.7%, n=43). MDR isolates of *Acinetobacter spp* were 92.4%, *P. aeruginosa* 71.5%, and *Stenotrophomonas maltophilia* 93.0%. Sensitivity to colistin was found in 93.8% of *Acinetobacter spp*, while in *P. aeruginosa* it was 98.7%.

Conclusion: Each ICU should collect similar data to establish its own “best empirical therapy regimen,” in accordance with antibiotic susceptibility patterns of the local flora. This paper highlights the urgency of introducing a custom-modified guideline to ICU.

Keywords: hospital-acquired pneumonia, non-fermenting Gram-negative bacilli, antimicrobial resistance

3. ANTIMICROBIAL RESISTANCE OF PSEUDOMONAS AERUGINOSA CAUSATIVE AGENTS OF HOSPITAL-ACQUIRED INFECTIONS IN THE TERTIARY HEALTHCARE FACILITY

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Objective: The aim of this study was to evaluate the antimicrobial resistance profile of *Pseudomonas aeruginosa* as an important causes of hospital-acquired infections (HAI).

Methods: A retrospective study was conducted, during the 2009 to 2018 in Clinical Centre in Kragujevac. Classification and localization HAI was determined using diagnostic criterion the CDC (*Center for Disease Control*, Atlanta, USA). The susceptibility testing was performed in institutional Microbiology laboratory, by using disk diffusion method and results were interpreted according to the guidelines issued by EUCAST recommendations.

Results: During the 10-year period in 736 patients (mean age: 61.9±16.2) registered 757 HAI caused by *P. aeruginosa*. The most common types of HAI were pneumonia (50.5%), surgical site infection (25.2%), followed by urinary tract infection (17.7%), pressure sores (4.2%) and blood stream infection (2.4%). Isolates obtained from the respiratory tract, surgical wounds and urinary tract showed a higher rate of resistance to carbapenems (65-75% vs. 60-65% vs. 50-60%, respectively). Most of these strains were multi-drug resistant. Resistance to third generation cephalosporins was high in the examined groups of isolates (90-95%), as well as aminoglycosides and fluoroquinolones (70-90% vs. 85-95%), while for fourth generation cephalosporin (cefepime) was slightly lower (70-75%). The highest level of sensitivity from all groups was retained toward piperacilin- tazobactam (70-85%). All isolates were sensitive to colistin - MIC range from 0,5µg/ml to 2,0µg/ml.

Conclusion: A good knowledge of the susceptibility patterns of *P. aeruginosa* at the local level should be used by physicians to select the most appropriate antibiotic in empirical therapy, and a proper management policy for antibiotic use may have the effect of reducing resistance.

Keywords: hospital-acquired infection, *Pseudomonas aeruginosa*, antimicrobial resistance

4.DERMOSCOPY AS EFFECTIVE AND NON-INVASIVE METHOD IN THE DIAGNOSIS OF INFLAMMATED MOLLUSCUM CONTAGIOSUM

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Molluscum contagiosum (MC) is the skin infection caused by the Molluscum contagiosum virus. Clinically, MC is characterized by translucent, most often multiple, umbilicated, pink papules. Diagnosis is usually straightforward. However, lesions that lack umbilication or display strong inflammatory response may pose diagnostic challenge. In that cases, dermoscopy is the fastest, non-invasive diagnostic method that can facilitate the diagnosis. We report a 56-year-old female patient with itchy, multiple, solid and pinkish papules, mostly covered with yellowish crusts involving the erythematous and oedematous skin of the right breast. In addition, solitary pinkish papules with umbilicated centre were noticed on the abdomen and right thigh. Dermoscopic examination revealed whitish and yellowish multilobulated structures in the centre, while serpiginous telangiectasias that do not cross the centre of the lesions were noticed at the periphery which all corresponds to the diagnosis of MC. Treatment with general and topical antibiotic therapy with placement of antiseptic solutions in the form of dressings and topical corticosteroids has been started. After the inflammation was restored, electrodesection of the lesions were successfully carried out.

Keywords: molluscum contagiosum, dermoscopy

5. BACTERIOLOGICAL PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF BACTERIA ISOLATED FROM URINE SAMPLES OBTAINED FROM PATIENTS AT THE CLINIC FOR ENDOCRINOLOGY, DIABETES AND METABOLISM DISEASES OF THE CLINICAL CENTER NIŠ

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Objectives: To determine the most common types of bacteria from urine samples in patients with Diabetes mellitus hospitalized at the Clinic for Endocrinology at the Clinical Center Niš and to examine their susceptibility to antimicrobials. **Material and methods:** The study included 413 urine isolates which were processed by standard microbiological methods at the Microbiology Center of the Institute of Public Health in Niš in the period from 1.1.2017 to 31.7.2019. Antimicrobial susceptibility testing was performed according to EUCAST recommendations and methods. **Results:** *E. coli* was the most commonly isolated bacterium with 35.3% isolates, followed by *Staphylococcus spp.* with 15%, *E. faecalis* with 10.6% and *Klebsiella spp.* and *Acinetobacter spp.* with 9.73% isolates. There were also 6 isolates of *Enterobacter sp.*, 4 isolates of *Proteus mirabilis*, 3 *Serratia marcescens*, 2 isolates of *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* and *Citrobacter spp.* and *Streptococcus β haemolyticus group B*, and one *Morganella morganii* isolate. Of all enterobacteria, represented by 61%, there were 82 non-multidrug resistant isolates, with the highest resistance observed for ampicillin (62.5%), ciprofloxacin (19.4%) and amoxicillin-clavulanate (18.8%), and the lowest for cefixime (4.2%), cefotaxime (4%), gentamicin (3.2%) and cotrimoxazole (0%). Multiresistant enterobacterial isolates- 15 (13.2%) had resistance to ampicillin (100%), ciprofloxacin (93.3%) and amoxicillin clavulanate (92.9%), cefotaxime (83.3%) and gentamicin (78.6%), and the lowest resistance was colistin (0%), imipenem and meropenem (15.4%), and amikacin (23%). Ertapenem resistance was 46.2%. In *Staphylococcus spp.* isolates, high rates of sensitivity was reported for all beta lactam antibiotics except penicillin and aminopenicillines (96.2%), gentamicin (78%), ciprofloxacin (86%) and cotrimoxazole (95%). *E. faecalis* was most resistant to high doses of gentamicin (54%) and ciprofloxacin (33%), while the highest sensitivity was observed with linezolid (100%), vancomycin (98%) and ampicillin (91.7%). In *Acinetobacter spp.* sensitivity was recorded on colistin alone (100%). **Conclusion:** Our data indicate that the third-generation cephalosporins, cotrimoxazole and gentamicin may be the first choice in the management of acute urinary tract infections caused by enterobacteria and staphylococcus, while ampicillin would be the drug of choice for enterococcal infections. A particular problem is represented by multidrug isolates of enterobacteria, where imipenem, meropenem and amikacin are first-line drugs and in *Acinetobacter spp.* the therapeutic option is colistin

Keywords: Diabetes mellitus, urinary infections, antimicrobial resistance

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6. PREVALENCE OF ANTIMICROBIAL USE IN SURGICAL CLINICS OF THE UNIVERSITY CLINICAL CENTRE OF THE REPUBLIC OF SRPSKA

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Objective

The objective of this study was to analyze antimicrobial use at surgical clinics of the University Clinical Centre of the Republic of Srpska (UCC RS), using data obtained through the point prevalence survey.

Material and methods

In this study, we used standardized methodology for the point prevalence survey of hospital-acquired infections and antimicrobial use, established by the European Centre for Disease Control (ECDC). The study was conducted in October 2015 in surgical clinics of the UCC RS, and it included a total of 196 patients.

Results

Prevalence of antimicrobial use among 196 patients included in point prevalence survey at surgical clinics of UCC RS was 74% and was statistically higher comparing to surgical clinics/departments of other hospitals in Banja Luka region.

The main purpose of antimicrobial use was surgical prophylaxis (72,5% of total antimicrobial use), mostly surgical prophylaxis that lasts longer than 24h (70% of total antimicrobial use). Of all antimicrobials 23,5% was used for infections treatment and 4% for medical prophylaxis.

The most frequently used antimicrobials were cefazolin (32.5%), gentamicin (15.5%) and parenteral metronidazole (9.5%). The highest prevalence of antimicrobial use was observed in the Maxillofacial surgery clinic (100%), Surgical ICU (92.3%) and Urology clinic (91.9%), and the lowest was in Orthopaedic clinic (41.4%).

Conclusion

The data obtained in our study show a high prevalence of antimicrobial use at most surgery clinics, very frequent use of long-term surgical prophylaxis, significant differences between clinics in prevalence of antimicrobial use and prevalence of prescribing surgical prophylaxis that lasts more than 24 hours etc. We can conclude that there is a need for further research as well as for adapting antimicrobial use to the principles of rational use of antibiotics.

Keywords: prevalence of antimicrobial use, hospital acquired infections, surgical prophylaxis

7. MONITORING OF WEST NILE VIRUS IN MOSQUITOES DURING THE PERIOD MAY - AUGUST 2019, VOJVODINA, SERBIA

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Objectives: West Nile virus (WNV) is a mosquito-borne RNA flavivirus. This emerging zoonotic arbovirus has become endemic in many countries all around the world and has a considerable impact on public and animal health. In this study the activity of West Nile virus in mosquitoes collected in Vojvodina, Serbia was investigated.

Materials and methods: From May to August 2019 mosquitoes were sampled in selected sites in Vojvodina, counted, identified to the genus level and pooled into 234 groups by Ciklonizacija d.o.o. The majority of mosquitoes belonged to the genus *Culex* (213 pools). There were 17 pools of *Aedes sp.* and 4 pools of *Anopheles sp.* mosquitoes. Molecular testing of mosquito pools for WNV was done at the Department of Virology, Institute of Public Health of Vojvodina. Viral RNA was detected using real-time RT-PCR assay ("Sacace", Italy) and genotyping was conducted using the protocol described by Fall and al. (2016) at Applied Biosystems 7500 thermocycler.

Results: Four pools of *Culex sp.* were positive for WNV RNA Lineage 2. Three investigated sites yielded WNV infected mosquitoes: city of Vrbas and two sites in city of Novi Sad: Klisa and Detelinara.

Conclusion: These results confirmed WNV circulation in Vojvodina from May until August 2019 and highlight the risk of infection for humans, birds and horses.

Keywords: West Nile virus, mosquitoes, real-time RT-PCR

This study was funded by City of Novi Sad, City Administration for Utilities and the Ministry of Education and Science of the Republic of Serbia as a part of the projects TR 31084 and III 43007

8. SIGNIFICANCE OF WEST NILE VIRUS IN PERSISTENT KIDNEY INFECTION

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West Nile virus (WNV) has the capacity too invade the CNS and to cause neuroinvasive disease in humans, equines and birds. On animal models renal tropism of WNV was demonstrated. Studies conducted in Italy, Hungary, Greece and USA have shown that virus may be excreted with urine during acute WNV infection in humans. Examination of urine sample enlarge the window period, in molecular diagnosis of WNV infection, because of longer duration of viremia than viremia. The presence of WNV in human urine was proven by the detection of genome using PCR. Infective WNV in human urine was also demonstrated by isolation on cell culture. Experimental studies on animals point to ability of WNV to establish the persistent infection in spleen, kidney, lung and brain for various periods. Despite the clinical recovery and immune response, animals inoculated with WNV develop a persistent renal infection with chronic viruria. Recent study discovered WNV in the human urine sediment by electron microscopy many years after laboratory confirmed infection. Although a prospective study on a cohort of 139 WNV patients from Houston suggested that WNV infection is associated with chronic kidney disease (CKD) the association of WNV infections with CKD remains unclear.

Keywords: West Nile virus, kidney

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9. CUTANEUS LARVA MIGRANS: A CASE REPORT

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Cutaneous larva migrans (LCM) is a clinical term for a cutaneous eruption caused by nematode larvae, mainly *Ancylostoma braziliense* and *Ancylostoma caninum*. Adult hookworms live in the intestines of dogs and cats, and their ova are deposited in the feces. Under favourable conditions, the ova hatch into infective larvae. Infestation is often acquired by children playing in the sandpits, plumbers under houses, gardeners and farm-workers. The larvae penetrate through intact skin causing characteristic erythematous linear or serpiginous lesions, usually accompanied by sensation of itch. Commonly affected sites include hands, feet and buttocks but any part of the body can be involved. LMC is self-limiting disease. Although most of the lesions resolve after 1-3 months, treatment is often required, since the lesions are extremely itchy. Treatment options include: topical thiabendazole as well as oral albendazole or ivermectin. Herein, we report a 10-year-old girl with typical, severe itching LCM lesions on the gluteal area, successfully treated with single dose of ivermectin. In conclusion, ivermectin is the preferred treatment option for LCM.

Keywords: Larva cutaneous migrans, infestation, therapy

SESSION: CURRENT PARASITOSIS AND FUNGAL INFECTIONS

INVITED LECTURES

1. *GIARDIA LAMBLIA*: HAS ANYTHING CHANGED?

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Abstract

Giardia lamblia (GL) is an intestinal protozoan present throughout the world. It most commonly causes an intestinal infection, especially in children below five years of age. The epidemiology of this parasitosis is rather complex and involves both direct and indirect transmission routes. Due to significant genetic variations of the parasite, molecular characterization is necessary in the assessment of zoonotic transmission of the infection. Clinical manifestations of the disease may vary, and asymptomatic infections frequently occur as well, and some recent studies suggest that they may afford protection against other diarrheal diseases. Although it does not lead to invasive infections, the disease pathogenesis is still insufficiently elucidated. Current diagnostic approaches require the use of new diagnostic tools to demonstrate the presence of GL not only in biological materials, but in food and water. As for the treatment, metronidazole and/or nitroimidazole preparations have long been the mainstay of therapy, against which the parasite is currently developing resistance, so that an increasing number of chronic and refractory cases of giardiasis are being reported.

Keywords: giardiasis, epidemiology, diagnosis, therapy

Introduction

Giardia sp. is one of the most prevalent intestinal parasites in humans; it is also a very common parasite in domestic animals, including cattle, dogs and cats [1], but wild animals are also frequently affected [2]. GL species causes giardiasis in humans and in most mammals.

Giardiasis has a significant impact on public health due to its high prevalence rates, especially in developed countries, its ability to cause epidemics if larger groups of people are exposed, and its impact on the growth and cognitive functions in infected children [3]. Being a zoonosis as well, it is also important in veterinary medicine [4].

Contaminated water is the principal transmission route for giardiasis, but the Food and Agriculture Organization (FAO) of the United Nations (UN) has ranked *Giardia* as the eleventh most important parasite worldwide transmitted by food [5, 6].

Infection rates are especially high in younger children, people working in children daycare facilities, but also in closed institutions (psychiatric care, prisons, etc.) [7, 8]. Other high risk population groups involve homosexuals, international travellers, immigrants/refugees, immunodeficient individuals, family members of the infected [9, 10].

Nomenclature

The taxonomy of the *Giardia* species has been controversial, resulting in a rather confusing nomenclature with different names for the same species [11]. So far, six species have been recognized to belong to the *Giardia* genus, one in amphibians (*G. agilis*), two in birds (*G. ardeae* and *G. psittaci*), two in rodents (*G. muris* and *G. microti*), and one in mammals (*G. duodenalis*). In the case of *G. duodenalis*, due to historic reasons, there are two synonyms, *Lamblia intestinalis* and *Giardia lamblia*. The latter term for the species is usually used in medicine in connection with human infections [11]. In addition to morphological variations

of cysts and trophozoites, which is the basis of their taxonomy, there are considerable genetic variations between and within each of the species, as shown by protein [12] and DNA polymorphism studies [13]. There have been eight identified groups of genetically related strains (assemblages or genotypes, A-H) within the complex of *G. lamblia* species, out of which two (A and B) may infect humans [14].

The Giardia life cycle

There are two phases in the Giardia life cycle: proliferative (trophozoite) and cystic (infective). A Giardia infection is initiated by the ingestion of infectious cysts, which in the acidic environment in the stomach and bile and trypsin in the duodenum, transform into trophozoites, which further adhere to the cells of the intestinal epithelium with their adhesive disk (an essential structure of the cytoskeleton and the main virulence factor) [15].

In unfavorable conditions, the process of encystation is initiated and transit of the parasite into the small intestine, and afterwards via feces into the external environment. Proteomic and transcriptomic analyses have shown that encystation is a highly coded cascade gene expression, with changes at both the RNA and protein levels. Regulation factors are here the transcription factors specific for encystation, enzymes for chromatin remodeling and post-translational modifications. Encystation-specific vesicles (ESVs, vesicles that transport cyst-wall proteins to the parasite surface) appear at the beginning of encystation, and expression of variant-specific surface proteins (VSPs) and high cysteine membrane proteins (HCMPs) is altered during encystation, demonstrating the association between encystation and antigen variation on the parasite surface. The greatest changes in gene expression have been observed at the end of encystation [16].

Epidemiology

Some epidemiological studies have reported the importance of zoonotic transmission in the appearance of human giardiasis, while others have denied the accuracy of these findings [4]. Any interpretation of the results of numerous studies concerning the source of human Giardia infection can be done only in combination with the data on the distribution of species and genotypes of Giardia in potential sources of contamination [1].

Numerous Giardia isolates collected from various host types in various geographical regions have been genotyped, and the presence of the same species/genotype in both humans and animals has been adequately demonstrated. Such information indicate a zoonotic potential, especially of GL species, and particularly the assemblages A and B. However, the use of genotyping and subtyping tools, especially the new ones, in well designed epidemiological studies is required for us to be able to assess the disease onset in humans caused by zoonotic giardiasis [13]. The finding of the same genotypes in humans and animals does not constitute sufficient evidence that zoonotic transmission has in fact occurred. A better assessment of zoonotic transmission can be obtained only from the studies focusing on the dynamics of transmission of Giardia between humans and animals living in common households or localized endemic foci [1].

Giardia pathogenesis

Giardiasis is thought to be a multifactorial disease, since it presents a complex host-parasite interaction. Giardia induces pathophysiological intestinal effect in the host via cellular binding and excretory-secretory products, causing structural damage which disturbs the integrity of intestinal epithelium, as well as the function of enzymes, inducing cellular apoptosis, disturbing the balance of electrolytes with increased bowel permeability, which ultimately leads to diarrhea. Pathological outcomes depend on parasite virulence and therefore cannot be seen with all Giardia infections. Further research should provide the answers related to Giardia virulence factors, which would contribute to better understanding of the infection caused by this parasite [17].

After the period of incubation (7-12 days), the most common clinical signs of infection are diarrhoea (with or without malabsorption syndrome), nausea, vomiting and weight loss. Some of the affected have milder, self-limited symptoms; others may experience a prolonged, severe disease, refractory to commonly prescribed treatments. Nevertheless, most patients are situated in between these extremes. Chronic *Giardia* infections may lead to complications such as irritable bowel syndrome (IBS), food allergies, arthritis or chronic fatigue syndrome [18].

There is no statistical evidence regarding the association of acute diarrhoea with *Giardia* infection in children over 5 years of age in developing countries, but an association has been found instead for children aged up to one year. A strong association has been also found with persistent diarrhoea lasting for more than 14 days in children in developing countries. Evidence has been found that the inhabitants of industrialized countries coming in contact with the parasite in the water or travelling to endemic regions are prone to the development of acute diarrheal disease [19]. Differences related to diets, immune status, coinfections and composition of normal bowel flora can contribute to the differences in disease outcomes observed in inhabitants of developing countries, compared to those in developed countries. It is possible that the observed protective effect of *Giardia* against other agents causing diarrhoea can be the consequence of recently demonstrated antiinflammatory action of *Giardia*, since numerous organisms causing diarrhoea induce a high degree of inflammation [20].

The roles of normal intestinal flora and host co-infection during an infection with *Giardia* are still unknown. *Helicobacter pylori* and *Giardia* coinfections have been identified in asymptomatic children (age group 1-5) in Uganda [21], while the use of probiotics in mouse models, before or during a *Giardia* infection, leads to milder clinical manifestations and shorter infections [22].

The differences in the outcome of infection may be the result of the parasite itself since there are eight *Giardia* assemblages or genotypes. Worldwide, human infections are caused by the assemblages A and B, with B much more frequently than A (58% vs 37%); the ratio does not change when the data from the developing are compared to those from developed countries, while the prevalence of mixed infections is higher in developing countries. A large number of publications deal with *Giardia* genotyping, but the association between different genotypes and disease outcomes has not been demonstrated [23]. Future research and genomic studies in combination with adequate patient data can reveal whether and how genotype influences disease outcome during giardiasis [17].

Giardia diagnosis

The standard procedure to demonstrate trophozoites and/or cysts in collected samples (feces, duodenum, tissues, water) is light microscopy of native and/or stained preparations, with/without concentration methods [17]. As the consequence of intermittent parasite excretion or their low counts, it is often necessary to examine even more than three stool samples during 1-2 weeks [24]. Electron microscopy can be useful in the identification of some species, but it is not routinely applicable [25].

The need for better sensitivity and specificity of the method has necessitated the development and routine use of immune tests. Demonstration of the presence of antigens in feces is possible using enzyme immunoabsorption assays, non-enzyme-based immunoassays or fluorescein-labelled monoclonal antibodies [26]. In the cases of negative findings with conventional microscopy and immunodiagnosis, endoscopy can be undertaken, with sampling of the duodenal fluid and biopsy of the duodenal or gastric mucosa [24].

Various enzyme-linked immunoassays (including ELISAs) and immunochromatography (IC) tests have been used to detect *Giardia* antigens in feces samples (coproantigens), reaching different sensitivity and specificity levels, depending on the study in question [26]. Although

the variations in immunodiagnostic performance are significant, the main advantages compared to microscopy is the detection of infection before cyst excretion in the host feces and cost-effective and rapid screening of a large number of samples. However, the assays do not provide either reliable identification of the *Giardia* species, or its genotype [26].

The methods to recover or concentrate *Giardia* cysts from water samples, feces or the environment provide for subsequent microscopic, immunologic or genetic examination. The current methods for water can be associated with immunofluorescent microscopy. These techniques rely on filtration, immunomagnetic separation (IMS) and complementary detection by direct fluorescent antibody (DFA) and/or Nomarski differential interference contrast (DIC) microscopy. Flow cytometry (FC) is another approach for the recovery of *Giardia* cysts and is not used routinely [27].

Some methods rely on the assessment of cyst vitality and/or infectivity in mice. However, not all *Giardia* species and genotypes are equally infective in rodents, and these approaches have been considered too expensive, strenuous and time-consuming for routine use and usually require a large number of cysts for analysis. Further, vital staining techniques have been used, although without much success. The focus is nowadays on the development of methods to assess cyst vitality by specific amplification of messenger RNA from *Giardia* cysts by enzymatic amplification of the betagiardin or heat shock protein-70 (hsp-70) gene. The amplification method is used too, which simultaneously assess cyst vitality and discern *G. duodenalis* assemblages A and B using *bg* [27].

The advances have been made in the development of specific and sensitive molecular tools for identification and genetic characterization of *Giardia* and diagnosis of giardiasis. Identification and classification of *Giardia* species and assemblages using genes (*bg*, *C4*, *ef1a*, *gdh*, *tpi* and/or *vsp*), in combination with more or less variable loci in ribosomal DNA, have helped in the elucidation of systematics, population genetics and epidemiology of *Giardia*, and in the confirmation and surveillance of epidemics occurring in both humans and animals [26].

Modern diagnostic nucleic-acid based methods used for specific identification of *Giardia* or diagnosis of giardiasis involve the following approaches: (A) Fluorescent in situ hybridization (FISH); (B) Polymerase chain reaction (PCR) approaches, including one-step, nested and random amplification of polymorphic DNA (RAPD) methods; (C) Gel-based single-strand conformation polymorphism (SSCP), (D) Restriction fragment length polymorphism (RFLP) or (E) Capillary electrophoresis (CE) analysis of PCR products; (F) Real-time PCR combined with high resolution meltingcurve analysis (HRM); (G) Sanger sequencing of PCR products [26].

Integrated use of advanced technologies, molecular and bioinformatic, opens new horizons in designing diagnostic approaches.

Treatment of giardiasis

The agents most commonly used are the members of the 5-nitroimidazole (5-NI) family, metronidazole and tinidazole. Therapeutic failure has been observed in 20% of cases, cross-resistance has been reported between different agents [28], as well as the resistance to all major anti*giardial* drugs [29]. Albendazole is also effective in the treatment of giardiasis [28], although its effectivity markedly varies (25-90%), depending on the dosage regimen [30]. It has been shown that nitazoxanide reduces symptom duration in those affected with giardiasis [31], and quinacrine, an old antimalarial drug, allegedly has a 90% effectiveness against giardiasis [32], but has potentially serious side effects [30].

During anti*giardial* therapy, there may exist numerous reasons for treatment failure, one of them being GL resistance to drugs. Clinically, refractory giardiasis occurs when stool samples remain positive one week after treatment completion, if other reasons for failure are excluded and if the risk for reinfection is very low [33].

Although the need for new drugs is not urgent at the time being, some recently discovered compounds may represent the future of anti-giardial pharmacotherapy. The issues related to their mechanisms of action, effectivity with isolates refractory to well established agents, their safety and tolerability, have to be completely resolved, i.e. they have to be tested in clinical trials. Probiotics or their released peptides should be investigated as a potential alternative or supportive therapy for strains resistant to anti-giardial agents and in the surveillance of treatment for refractory cases [33].

Conclusion

Although it is one of the oldest eucaryotic organisms, GL is still a parasite able to intrigue the scientific and general public. Numerous questions related to its pathogenesis, epidemiology, zoonotic potential, diagnosis and therapy, do not have as yet a complete and precise answer. Nevertheless, rapidly advancing science and current technologies and an integrative approach to these problems definitely hold promise, and will hopefully provide the much sought answers and the resolution of GL enigma.

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- 34.

ORAL AND POSTER PRESENTATIONS

1. SURFACE WATERS AS A POTENTIAL SOURCE OF GIARDIA AND CRYPTOSPORIDIUM IN SERBIA

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Objectives: Giardiasis and cryptosporidiosis are recognized as important emerging diseases of the 21st century. Symptoms are similar and include diarrhea and vomiting, and may be particularly severe, even life-threatening, in the immunocompromised population and children under five. In Serbia, drinking water is not routinely tested for protozoa; however, between 2013 and 2017 there have been several water-borne epidemics of unconfirmed cause. Using a newly implemented methodology for detection of waterborne protozoa, we analyzed surface water samples from four major rivers and their tributaries.

Materials and methods: The samples (10 L each) were concentrated by filtration and the (oo)cysts purified using immunomagnetic separation and detected by commercial immunofluorescence kits. The positive samples were further submitted to PCR analysis. For detection and assemblage identification of *Giardia*, the β -giardin gene was used, while COWP and TRAP-C2 were used for *Cryptosporidium*.

Results: *Giardia* was detected in 10 out of 31 samples by IFA, *Cryptosporidium* in five, while two were positive for both. *Giardia* DNA was detected in eight samples of which two and one, respectively, were identified as belonging to the zoonotic assemblages B and A. Amplification of *Cryptosporidium* genes was unsuccessful.

Conclusion: These results show a significant level of contamination with enteric protozoa making water a potential source of infection in Serbia.

Keywords: *Cryptosporidium*, *Giardia*, waterborne, protozoa, rivers

2. OCCURRENCE OF GIARDIA LAMBLIA IN SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

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Objective: Lambliasis is zoonoses caused by Giardia lamblia. Lambliasis can be asymptomatic and symptomatic. The aim of this study was to determine the lambliasis occurrence during the period from 2014-2018 in symptomatic and asymptomatic patients whose samples were examined at IPHS.

Methods: Asymptomatic persons were examined in the context of law obligatory epidemiological surveillance, while symptomatic patients were mostly from Belgrade PHCs. Stool samples were examined by microscopy and rapid immunochromatography tests were used as an auxiliary diagnosis. Retrospective analysis of the results was done.

Results: The total number of positive findings in symptomatic patients stool samples was 169 (1,76%) out of 9610 samples examined, while the total number of positive findings in asymptomatic patients was 58 (0.05%) out of 119178 samples examined. The highest number of positive findings was in 2017, while the highest number of requests for parasitological examination was in 2018, both for asymptomatic patients. During this period, the total number of positive findings is 227 (0.19%) out of 119 178 samples.

Conclusion: Epidemiological studies on lambliasis and surveillance are needed. Conventional microscopy is still the indispensable standard in the diagnosis of lambliasis, which does not diminish the need for the other diagnostic methods.

Keywords: lambliasis, microscopy, immunochromatography tests

3. TROPICAL RAT MITE DERMATITIS IN HUMANS TRANSMITTED FROM INFESTED PET RODENTS

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University of Novi Sad, Faculty of Agriculture, Department of Veterinary Medicine, Serbia

Objective: To report dermatitis in humans caused by Tropical rat mites transmitted from infested pet rodents in Novi Sad, Serbia.

Materials and methods: In January 2019, a woman brought package of live mites collected from the environment of pet guinea pig to our Veterinary clinic. Week before arrival, the woman cleared scratching guinea pig from severe mite infestation by daily showering. Other pet rodent (a rat) was healthy. She reported the finding of itchy red papules on herself and her daughter corresponding to onset of clinical signs on guinea pig. Four of brought mites were mounted in Berlese solution and identified according to morphological features.

Results: Based on morphology of relevant structures, the mites were identified as *Ornithonyssus bacoti* (Acari: Mesostigmata: Macronyssidae). There were three adult females and one protonymph. Pets were treated with topical selamectin, all clothes washed and environment cleaned. The dermatitis in humans resolved and didn't occur further.

Conclusion: This is the first finding of *O. bacoti* in Serbia. These mites cause nonspecific dermatitis in humans; therefore definitive diagnosis is not easy unless the parasites are found. Physicians in Serbia should consider *O. bacoti* in patients with pruritic dermatoses, especially in those with close contact with pet rodents.

Keywords: Tropical rat mite, pet rodents, *Ornithonyssus bacoti*, human, dermatitis

POSTER PRESENTATIONS

1. HUMAN ECTOPARASITOSIS ON THE CAPILLITIUM- THE UNUSUAL ZOONOSIS

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Objectives: Epidemiological, clinical, histopathological and immunological data on ectoparasites with zoonotic potential, that can be threat to human health, are limited. Additional problem is the lack of diagnostic tools which often lead to misdiagnosis. The goal of this case report was to describe a very unusual zoonosis on the capillitium caused by ectoparasite.

Materials and methods: Seventeen-year-old male patient with suspected superficial fungal infection of scalp was referred to microbiological laboratory for mycological examination. Clinically it presented as alopecia areata (approximately 4cm in diameter) with several distinct pustules. The surrounding skin and hair remained intact.

Microscopic examination of the patient's material revealed various evolving forms of arthropod. Adult, mite-like parasite, 193,81µm by 360,90µm in size, with four pairs of legs was detected together with an egg. Moreover, three successive parasitological analysis also confirmed presence of larval form of mite-like parasite. The patient's personal history was without any particularities. He is a student living in the urban area of the City of Nis, healthy, immunocompetent, who does not keep pets. No history of traveling abroad or prolonged outdoor activities was recorded.

Results: Based on clinical examination and microscopic finding of only one adult form of mite-like parasite, it can be concluded that this arthropod belong to subclass *Acari*, which morphology implies that it could be *Otodectes cynotis* – very common ear mite of dogs and cats.

Conclusion: Monitoring and knowledge of bio-epidemiological and clinical significance of ectoparasites are of great importance for correct management of infestation in humans as well as for the establishment of preventive measures.

Key word: Ectoparasites, mite, *Otodectes cynotis*, human

SESSION: NUTRITION AND HEALTH

INVITED LECTURES

1. THE DIET OF SPORTSMAN

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Introduction: Nutrition of athletes represents one of the key factors of success in sport. It primarily depends on the specific sport branch, category in which an athlete competes (junior or senior), the rank (lower rank or upper rank), as well as the age of an athlete. The duration of training activities should be taken into serious consideration since in certain sports and in top athletes training lasts for up to eight hours per day. In addition, special attention should be paid to the gender and individual preferences of certain types of food.

Fluid intake is significant in its own way. It is important because the loss of body fluids is evident in sport either through perspiration or urinary tract. We mention some of the activities that lead to an excessive liquid loss (marathon, football and a series of sport branches and disciplines).

There is no unique nutrition program for athletes because the time when certain training sessions and competitions take place varies (closed space- sport hall, open space-stadium, track and field paths). Weather conditions, as well as differences in temperature, have influence on nutrition (spring, summer and winter).

Calorie expenditure

Physical activity in sport can compare to the most demanding activities in certain professions. Daily calorie expenditure goes from 4500 to 5000 calories for 24 hours. Therefore, daily calorie intake should be divided into three, or maximum five meals. The number of consumed calories should be in proportion to burned calories. Special attention should be paid to the fact that 2 to 2.5 hours should pass from the last meal to the training or competition of an athlete.

Optimal nutrition means optimal consumption of all types of food with the aim of achieving optimal functioning of the body. We can conclude that with proper nutrition in athletes we achieve good body composition as well as protective and energetic function.

Nutrition of athletes during the preparation period includes optimal fat, carbohydrate, protein as well as vitamin consumption. This includes nutrition rich in carbohydrates (55 to 60% of calorie intake), low in fat (less than 30% of calorie intake), with an appropriate amount of proteins (10-15% of calorie intake).

The research conducted so far have confirmed that food rich in cereal, vegetables and fruit (or in other words carbohydrates) helps in prevention of diseases, in maintaining body weight, and increases competitive abilities. The popularity of modern nutrition has not been scientifically confirmed yet.

The recommendation for macronutrient consumption includes carbohydrates, namely 50 – 60% of the total calorie intake, fat 30% of the total calorie intake and proteins 10-15% of the total calorie intake. One gram of carbohydrates releases 4 kJ of energy. During the physical activity, body mostly relies on carbohydrates as the source of energy, therefore the amount of deposited carbohydrates has a direct influence on strength and endurance of an athlete. Carbohydrates are stored in muscles and liver in the form of glycogen. Glycogen is energetic fuel in muscles, while glycogen in liver maintains the level of blood sugar necessary for the brain function.

Daily calorie intake can be based on "the food pyramid" of the American Department of Agriculture. If we want to understand the concept of the pyramid we should take into consideration the fact that within daily intake of 2400 calories, athletes should consume the following amount of food from each category: 12 portions from the group of cereals, rice and pasta, 4 portions of fruit, 4 portions from the group of milk and dairy products and 9 portions from the group of fat, fish, beans and group of nuts.

The size of each portion does not have the aim of indicating the amount that the person should consume during a meal or snack. It has the purpose of providing a scheme for comparison of the amount consumed.

One portion of cereals, rice or pasta for an adult person equals to a slice of bread, or two thin slices of diet bread, one half of an English donut or one half of the hamburger bun, a small roll, a half a cup of starchy vegetables, a half a cup of mashed or baked potatoes, a half a cup of boiled cereals, 4 to 6 crackers, three cups of baked popcorns, 2 rice cakes or 5 small cookies.

One portion of fruit for an adult person corresponds to a medium sized fruit portion of fresh fruit such as an orange, an apple, a banana, two big spoons of grapes, one quarter of a cup of dried fruit, one half a cup of boiled or canned fruit or half a cup of fruit juice.

One portion of vegetables for an adult person corresponds to a cup of leafy fresh vegetables, a half a cup of boiled or chopped vegetables or three to four cups of vegetable juice.

If we want to consume one smaller meat meal of an adult person it would correspond to a cup of skim milk or milk containing 1.6% of fat, one quarter of a cup of milk with 2% of fat, one cup of fat free yoghurt, or a half of a cup of low fat yoghurt, 30 to 50 grams of low fat cheese or one half of a cup of fat free or young cheese with 1,0% of fat.

One regular portion for an adult corresponds to one cup of full fat milk or yoghurt, three quarters of a cup of frit yoghurt, 25 grams of regular or one half a cup of young cheese.

If we include meat, poultry, fish or beans and nuts in our diet, one portion for an adult corresponds to 75 grams of cooked low fat meat, fish or poultry. 25gr 'low fat' meat correspond to one half of a cup of cooked beans, one egg or two spoons of peanut butter

3 to 5 days before the competition, athletes start to decrease the intensity of training. With the given diet they can duplicate the amount of glycogen in their muscles.

Proper nutrition before a physical activity has the aim to prevent a low level of sugar in blood during the activity, provide energy using stored glycogen in muscles, calm down the stomach, absorb gastric juices and prevent hunger as well as improve confidence of an athlete in his or her physical abilities.

A meal before any physical activity during the training or competition has to contain a high level of carbohydrates, low level of fat for faster and easier digestion. However, the consumption of carbohydrates with high glycemic index one hour before a certain physical activity can have a negative influence on competitive abilities because faster increase in blood glucose levels causes increased insulin production which further leads to relative hypoglycemia and prevents mobilization of fat in fat tissue, which leads to faster use of carbohydrate supplies. On the other hand, the increases supplies of glycogen in muscles and those with low glycemic index will not cause such an effect, furthermore it will provide steady flow of glucose from the digestive tract during the physical activity.

Glycemic index represents the speed at which glucose in blood increases by the consumption of certain type of food. This is a parameter of hyperglycemic potential of food rich in carbohydrates.

Glycemic index

Classification	Glycemic index	Examples
Low GI	≤ 55	Fruit and vegetables (apart from potatoes and water lemon), whole meal bread, pasta, pasta, legumes, milk, meat, oils, brownrice
Medium GI	56-59	Products made of whole grain wheat, white rice, orange juice
High GI	≥ 70	Corn flakes, boiled potatoes, watermelon, croissant. White bread, pure glucose

A meal eaten 4 hours before a competition helps increase glycogen supplies in muscles and liver (especially during morning hours), keeps the balance of liquids in body, and prevents hunger and gastrointestinal problems.

Daily protein needs

A healthy person needs 0.8 g of proteins per kilogram of body weight, during adolescence 0.9 g per kilogram of body weight. In endurance sports from 1,2 to 1,4 g per one kilogram of body weight, in sports that require strength and speed from 1,2 to 1,8 g per one kilogram of body fat, bodybuilding from 2 to 3 g per one kilogram of body weight.

Fats primarily provide energy: they meet up to 70% energetic needs at rest and around 50% of mild or high intensity. When a physical activity lasts more than three hours (e.g. a marathon) the role of fat storage becomes more important because it can provide more than 80% of energy.

Fats have a lot of other functions which are indirectly linked to physical activity. Fats are a component of cell membrane and nervous tissue; they circle and protect vital organs. All steroid hormones are produced by cholesterol. Fat soluble vitamins are stored in and transported through fat. Subcutaneous tissue helps preserve body heat.

Vitamins and minerals play an important role in energetic metabolism. Their intake is exactly proportional to the intake of energetic substances, and a deficit in one or more microelements decreases competitive ability. Vitamins and minerals can be found in a wide range of foods and they rarely lack in people with well-balanced diet.

Antioxidants

Many vitamins and minerals have antioxidant ability: Vitamin E, beta-carotene, ascorbic acid (vitamin C) and minerals, such as selenium, iron, zinc, copper and magnesium. Antioxidants can be found in different types of food or are produced in the body in order for it to be able to fight against oxidative stress. The consequences of oxidative stress are premature aging, atherosclerosis, cancer, diabetes mellitus, muscular dystrophy, rheumatoid arthritis, Alzheimer's disease, Parkinson's disease, muscular fatigue and injury.

Antioxidants help in decreasing the damage caused by free radicals by preventing their development, they neutralize free radicals and transform them into less reactive molecules. They improve tissue regeneration and together with other agents help create healthy environment.

Important minerals for athletes

Minerals that are necessary for the human body and the amounts of which exceed 100 mg per day are called macro elements, whereas those necessary in smaller amounts microelements. On average 4% of body mass is composed of different minerals. They are needed for

numerous physiological processes including muscle contraction, oxygen transport, balance of liquids and production of energy.

Anemia – iron status. Iron is a component of hemoglobin responsible for oxygen transport in blood and myoglobin which represents storage of oxygen in muscles.

Some women have greater need for iron because of intensive blood loss during their period. Even a small deficit of iron has a negative effect on sport performance

Calcium status. Calcium is necessary for the formation and maintenance of bones. Even though moderate physical activity is necessary for formation of bones, intensive training can change menstrual cycle and bring to hormonal imbalance which has an impact on the health of bones. It is very important that nutrition of athletes, especially female athletes, contains appropriate amounts of calcium.

Supplements. It is generally accepted that optimal nutritive status is not only important for the maintenance of competitive abilities but also for the decrease of health risks, especially muscle stress and inflammatory reactions after an intensive physical activity.

Competitors need larger amounts of minerals and vitamins which go together with greater energetic needs. It is necessary to stress out the importance of well-balanced diet during the training process, competition and recovery period. Despite the fact that there is no irrefutable evidence that supplements together with various vitamins and minerals improve competitive abilities and shorten recovery period, athletes often consume them.

Supplements are divided into following groups: vitamins, minerals, amino acids, combined supplements, metabolites and herbal supplements.

There are certain risks linked to supplement consumption such as: unfamiliarity with the expected effects, contamination of supplements with unpermitted substances, the coach or the doctor may not be appropriately acquainted with the effects of a certain supplement, distribution of supplements via mail or gyms.

The importance of water in nutrition lies in the appropriate amount of liquid intake before, during and after the competition. There are three phases of liquid intake into the body: prehydration, hydration, dehydration and rehydration.

Prehydration is very important for the maintenance of body temperature during competition and for prevention of weight loss. Two days before the competition one should drink excessive amounts of liquids (water). The success of prehydration is directly linked to some supplements to liquids that contain 7% of carbohydrates and consist smaller amounts of potassium, magnesium, phosphate, and sodium and for which it has been proven that stimulate liquid absorption. In order to start competing an athlete should intake 1000-1200 ml of water 1-4 hours before the competition (some authors consider that the ideal amount is 600-800 ml).

Hydration is conducted when we drink water during and after the physical activity. It can be said that we should consume fluids constantly. If the body is not hydrated enough before the competition, this can be compensated by drinking water during the training or competition. The main point is that during physical activity body should be fully hydrated.

Research conducted so far have shown that 3-4% loss of fluids in the body leads to the loss of contractive muscle power up to 30%, and speed and explosive muscle power up to 8%. In addition, there is increased production and decreased emission of heat which leads to overheating of the body. Such conditions have a negative effect on muscle work, and sport achievements are nonexistent.

During the competition, it is important to consume water as often as possible in small amounts 100-200ml every 15-20 minutes (UEFA has considered the possibility of introducing a timeout for drinking fluids during the competition). Under these conditions a coach and doctor have an assignment to give fluids to as many athletes as they can.

Rehydration represents the most important phase in preservation of glycogen in muscles (2.7gr of water binds 1gr of glycogen). In order to preserve glycogen in muscles the best thing to do after physical activity in the first phase is to consume 10% of carbohydrates in the form of beverage and in the second phase after 90-120 minutes, 4-8% of carbohydrates (according to body weight), and later energetic fat and minerals Na, Mg, K, Ca. Potassium is especially important for the resynthesis of glycogen (500-700mg). The recommended water temperature for athletes in winter and summer is +4C to +10C. It is considered that the greatest water loss occurs when the intake is the highest.

After a long and intensive physical activity, rehydration is a nutritive priority. After rehydration one should restore supplies of carbohydrates. In order to stimulate resynthesis of glycogen in muscles and liver within the first two hours after physical activity, the recommended consumption of carbohydrates is 0.7 to 1.5 g/kg of body weight per hour.

Rest is mandatory for an athlete, namely 9-10 hours of night rest and one to two hours during the day which would represent optimal time for an athlete exposed to great physical exertion.

We give an example of how a meal containing 5000 calories per 24 hours would look like for an athlete: 300gr of white bread 300gr, 300gr of whole meal bread, 300-400gr meat, 150gr of fish 300gr of milk, 90gr of fat-butter-oil, 2 eggs, 100gr of different types of cheese, 150gr of pasta, 300gr of potato, 300gr vegetables, 150gr of sugar, fruit-cooked fruit-chocolate, 250gr of honey 10gr of coffee, milk, tea, 100gr of cookies. Other types of food may be used.

On the day of competition the habits of an athlete should be respected. The recommended amount of carbohydrates should be consumed in order to avoid early loss of glycogen supplies in liver and hypoglycemia with decreased motoric function and failure. The diet should include moderate amount of easily digestible proteins in order for the gluconeogenesis to slow down the use of glycogen supplies in liver. It should not contain food with high glycemic index, but should contain certain amount of pectin in order to slow down the resorption of carbohydrates.

The last meal 2.5-3.0 hours before the competition should contain around 500 to 550 calories. Such a meal is usually called 'light meal'. It contains 100 of spaghetti with tomato sauce, 60gr of cooked fish or chicken, 2 cooked potatoes of medium size (covered with lemon and parsley); 100gr of orange juice (or some other fresh juice).

If the last meal is taken 3.5-4.0 hours before the competition, an athlete should intake 700-750 Cal. Such a meal is called 'medium pre competition meal' and it is recommended to eat: 150gr of carrots with tomato sauce, 60gr of boiled fish or chicken, two potatoes of medium size, cooked (covered with lemon and parsley), 200gr of orange juice (or some other fresh juice).

If the last meal is taken 4.5-5.0 hours before the competition, an athlete should consume 1000-1100 Cal. Such a meal is considered a 'heavy meal' by nutritionists. Today a lot of nutritionists do not recommend it. This meal includes: 150 gr of carrots with tomato sauce, 60gr of cooked fish or chicken, 2 medium size boiled potatoes (covered with lemon and parsley), 20gr of butter, 20gr of marmalade or jam, 1 slice of bread, 200 gr of orange juice (or some other fresh juice).

How would an ideal nutrient intake of cadets and seniors look like based on our experience: ideal carbohydrate intake for cadets is 6 gr per 1k/bw; young athletes 1.8gr per 1kg/bw, senior athletes 10-12gr per 1 kg/bw .

Ideal fat intake: cadets 0,6gr per 1kg/bw; young athletes 0,8gr per 1kg/bw senior athletes 1,0gr per 1kg/bw;

Ideal protein intake: cadets 1,5gr per 1kg/bw; young athletes 1,8gr per 1kg/bw; senior athletes 2,0gr per 1kg/bw.

Table 1. Nutritive needs of athletes

Daily nutritive needs of athletes per 1kg per body weight (Volgarev)			
Sport	Proteins	Fat	Carbohydrates
Track and field: running, short, long	2,3-2,5	1,8-1,2	9,0-9,8
Long track, marathon, walking, 20, 50 km	2,3-2,5	1,8-1,2	9,0-9,8
Jumps	2,3-2,5	1,8-1,2	9,0-9,8
Gymnastics, figure skating	2,2-2,5	1,7-1,9	8,6-8,7
Swimming and water polo	2,3-2,5	2,2-2,4	9,5-10,0
Weight lifting, throwing	2,5-2,9	1,8-1,0	10,0-11,8
Wrestling, box	2,4-2,8	1,8-2,0	9,0-11,8
Rowing	2,5-2,7	2,0-2,3	10,05- 11,3
Football, hockey	2,4-2,6	2,0-2,2	9,6-10,4
Basketball, volleyball	2,4-2,4	1,8-2,0	9,5-10,8
Cycling	2,5-2,7	2,0-2,1	12,2-14,3
Equestrian sport	2,1-2,3	1,7-1,9	8,9-10,0
Sailing	2,2-2,4	2,1-2,2	8,5-9,7
Shooting	2,2-2,4	2,0-2,1	8,3- 9,5
Skiing, short slopes	2,3-2,5	1,9-2,2	10,2-11,0
Skiing, long slopes	2,4-2,6	2,0-2,4	11,5-12,6
Fast ice skating	2,5-2,7	2,0-2,3	10,0-10,9

Table 2. Needs for minerals

THE MOST IMPORTANT MINERALS IN HUMAN BODY, RECOMMENDED DAILY DOSES FOR REGULAR PEOPLE, WHERE TO FIND THEM IN FOOS AND THEIR ROLES IN THE BODY				
MINERAL	The amount in the human body (g)	Average daily need of an adult (mg)	Food	Basic function
CALCIUM	1500	1200	Milk, cheese, eggs, dark green vegetables	Bone and teeth growth, neuromuscular irritability, nerve transmissions
PHOSPHORUS	86	1200	Milk, cheese, meat, legumes	Bone and teeth growth, acid-base balance
SODIUM	64	1100-3300	Kitchen sault	Acid-base balance, osmotic pressure
MAGNESIUM	25	280-350	Grain food, dark green vegetables	Activates enzymes in the process of protein synthesis
IRON	4,5	10-15	Eggs, meat, legumes, wheat, dark green vegetables	Increases hemoglobin myoglobin and enzymes involved in energy metabolism
FLUORINE	2,6	1,5-4,0	Water, sea food	Construction of tooth enamel, correct bone structure
ZINK	2	12-15	Can be widely found in food	Production of digestive enzymes

Table 3. Average energetic needs– endurance sports

AVERAGE ENERGETIC NEEDS IN ENDURANCE SPORTS					
Sport	Daily needs		Body weight	Daily needs	
	KJ	Cal		KJ/kg	Kcal/kg
Middle-distance running	20934	5000	70	299	71
Long distance running	22609	5400	65	348	83
Marathon running	20934	5000	60	349	83
Walking 20 and 50 km	25539	6100	70	365	87
Cross country skiing	23865	5700	65	367	88
Swimming (200-1500M)	22609	5400	70	323	77

Table 4. Average energetic needs – combat sports

AVERAGE ENERGETIC NEEDS IN COMBAT SPORTS					
Sport	Daily needs		Body weight	Daily needs	
	KJ	Cal		KJ/kg	Kcal/kg
Wrestling	24283	5800	75	324	77
Box	24283	5800	75	324	77
Judo	24283	5800	75	324	77

Table 5. Average energetic needs- sport games

AVERAGE ENERGETIC NEEDS IN SPORT GAMES					
Sport	Daily needs		Body weight	Daily needs	
	KJ	Cal		KJ/kg	Kcal/kg
Basketball	23027	5500	75	307	73
Hockey	22609	5400	70	323	77
Football	23027	5500	70	329	78
Handball	24283	5800	75	324	77
Rugby	23027	5500	75	307	73
Tennis	21771	5200	70	311	74
Water polo	24283	5800	75	324	77

Table 6. Average energetic needs

AVERAGE ENERGETIC NEEDS					
Sport	Daily needs		Body weight	Daily needs	
	KJ	Cal		KJ/kg	Kcal/kg
Figure skating	20515	4900	70	293	70
Fencing	21771	5200	70	311	74
Gymnastics	17585	4200	60	293	56
Skiing	23027	5500	75	307	73
Bowling	21353	5100	75	285	68
Sprint	20934	5000	70	299	71
Track and field multidiscipline	25958	6200	80	324	77
Contemporary multidisciplinary sports	24283	6800	75	324	77
Track cycling	20934	5000	70	299	71
Jumping (bob)	23027	5500	75	307	73
Swimming	23037	5500	70	329	78
Sailing	21353	5100	75	285	68
Alpine skiing	22609	5400	70	323	77
Ski jumps	24283	5800	75	324	77
Jumping disciplines	22609	5400	75	301	72
Table tennis	19259	4600	70	275	66
Diving	20097	4800	70	287	68
Volleyball	22190	5300	75	296	71
Fast ice skating	22609	5400	70	323	77

Instead of the conclusion

12. The importance of positive influence of good nutrition on athletes was noticed even in the sixth century BC.
- Excessive calorie intake as well as the intake of certain types of food in athletes is still present (the menu of an antique wrestler Milo of Croton contained 9 kg of meat, 9 kg of bread and 8,5 l of wine)
 - We should be aware of the fact that there is no diet that would create a champion without an optimal training.
 - Optimal results in sport can be achieved by optimal daily intake of 59 different substances.

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2. ASSOCIATION BETWEEN MEDITERRANEAN DIET AND ACUTE CORONARY SYNDROME RISK FACTORS

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Introduction: The Mediterranean diet (MD) represents specific eating habits of the population of Greece, Southern Italy and Spain during period of the 1940s and 1950s. The main aspects of MD include high consumption of olive oil, legumes, unrefined cereals, fruits and vegetables, moderate to high consumption of fish, moderate consumption of dairy products, mainly cheese and fermented dairy products, moderate consumption of wine and limited consumption of meat (1). MD has been a subject of interest since the middle of 20th century and became widely known for the first time through The Seven Countries Study (1). Since then, numerous studies suggest that adherence to the MD is associated with a reduction in the risk of developing cardiovascular disease (CVD), a reduction in cancer rates of various localities, and even overall mortality among the population of the Mediterranean region, such as Greece and Italy, compared to the population of northern Europe or the United States, which is most likely attributable to different eating habits (2,3). Cardioprotective effects of MD, especially in the field of primary prevention, have been well documented (4,5). Still, far less studies address secondary prevention of CVD and the possibility of alleviating the course and consequences of disease in a population fed according to MD principles (6). According to data from the National Institute of Public Health of Serbia "Dr Milan Jovanovic Batut" from 2014, more than half (53.3%) of all deaths in Serbia were due to CVD (7). In our country, the rates of the disease are twice higher in men. The highest age-specific incidence rates were observed in the population over 75 years of age (7). It is believed that the greatest increase in life expectancy at birth in our country would occur if the elimination of premature mortality due to the consequences of ischemic heart diseases in men (2.4 years) and premature mortality due to the consequences of CVB in women (2.1 years) (8).

A survey on the eating habits of the population in the Republic of Serbia, based on the number of elements of the MD that are present in our country, was conducted within the research of the national institute of public health.

Study showed that at least one cup of milk and/or dairy products was consumed daily by about half of our population (51.7%), a significant increase compared to 2006 survey when it was 43.5% (9). Survey results showed that white bread is still predominantly consumed (60.1%), while only 8.2% of the population used "whole grain" bread, which is about 6% less than in the previous survey in 2006. (9). The use of animal fat in meal preparation has been reduced compared to a previous study, and it is concluded that the prevalence of this habit among the population is declining with an increase in educational attainment and population well-being index (9). Only 12.5% of the population of the Republic of Serbia consumes fish at least twice a week. It was more often done by residents of urban areas and higher education. An increase in fish consumption has been observed with an increase in the well-being index (9). The results of the study show that every other resident does not consume fruit. It was observed that fruits are more commonly consumed by women as well as the elderly population aged 65-74 (9). Higher educated women also consumed vegetables more frequently (60.2%).

Motive for choosing this topic for our research, where subjects with ACS and subjects at increased risk of developing CVD are in focus, was attempting to answer whether MD can be a key protective factor in the occurrence and severity of ACS manifestations in already ill patients and in subjects with an increased risk of developing CVD.

Aim: The aim of this study was to determine the degree of adherence to the MD in patients with acute coronary syndrome (ACS) and in individuals at risk for developing CVD, using a validated Mediterranean diet score - MedDiet score.

Material and method: The study was conducted as an analytical cross-sectional study on the sample of 294 subjects (146 women and 148 men), aged 30 to 82 years. The survey was conducted in the period from February 2016 until March 2017. The first group consisted of subjects diagnosed with acute coronary syndrome, who were hospitalized at the Institute of Cardiovascular Diseases in Vojvodina in Sremska Kamenica, while the second group comprised of those with established at least one risk factor for CVD, without clinically manifested coronary artery disease, which were reported to the Counseling Center for Proper Nutrition, Institute of Public Health of Vojvodina in Novi Sad. All subjects in the study underwent: anthropometric measurements, blood pressure measurements, appropriate biochemical analyzes, ECGs and application of specially prepared questionnaire, which included a MedDiet score - a validated score system for assessing the level of compliance with MD in an individual.

Results: The mean MedDiet score of subjects without ACS was 27.48 ± 6.59 , the minimum established MedDiet score was 12, and the maximum was 43. The mean MedDiet score of ACS subjects was 20.53 ± 4.01 . the minimum determined value was 13 and the maximum value was 36. The difference between the mean MedDiet scores between subjects with ACS and subjects without ACS was statistically significant ($p = 0.029$). subjects without ACS had an average of 25% higher MedDiet score.

The study results show a statistically significant inverse association between the consumption of unrefined cereals and the occurrence of ACS ($p < 0.0005$). The lowest incidence of ACS (11.6%) was in the category of subjects who brought in the most unrefined cereals (more than 18 servings per week, "Category 5" according to the MedDiet score). The study results do not show a statistically significant association between potato consumption and the occurrence of ACS ($p = 0.0586$). Fruit intake and ACS onset showed statistically significant inverse correlation ($p < 0.0005$). In the category of respondents who stated that they did not consume a single serving of fruit on a weekly basis, 60% had a developed clinical picture of ACS. Among those who indicated that they consumed 1 to 4 servings of fruit on a weekly basis, 100% had a developed clinical picture of ACS. Respondents who indicated that they consumed 5-8 or 9-12 servings on a weekly basis had 75.4% and 64.6% respectively of the developed clinical picture of ACS. On the other hand, respondents who indicated that they consumed 13-18 and > 18 servings of fruits on a weekly basis showed a significantly lower percentage of the developed clinical picture of ACS, 17.3%, respectively. 8.3% respectively, indicating an inverse relationship between fruit consumption and ACS development (the more fruit consumed, the occurrence of ACS is less frequent). Weekly intake of vegetables showed an inverse association with the development of ACS in the study subjects. A statistically significant association was found between vegetable intake and ACS development ($p < 0.0005$). The highest incidence of ACS was reported in the category of subjects who stated that they consumed vegetables on a weekly basis in the amount of 5-8 servings (93.2%), followed by 1-4 servings (83.3%) and 9-12 servings (61.9%). Respondents who indicated that they consumed vegetables in quantities of 13-18 and > 18 servings per week had a significantly lower percentage of ACS clinical presentation (9.1% and 6.7%, respectively). The results of the study indicate that there is a statistically significant inverse association between legume consumption and the development of clinical signs of ACS ($p < 0.0005$). The most common occurrence of ACS was observed in respondents who indicated that they did not consume legumes (83.3%) and those who indicated that they consumed legumes in the amount of 1-4 servings per week (56.7%). The developed clinical picture of

ACS was the least frequently observed (31.6%) in the category of subjects who consumed legumes in the amount of 5-8 servings per week (category "2 points" according to MedDiet score).

The results of the study of the association between fish consumption and the occurrence of ACS were statistically significantly correlated ($p < 0.0005$). The occurrence of clinically expressed ACS is most commonly seen in the category of subjects stating that they never consume fish (73%). In subjects who indicated that they consumed fish in the amount of 13-18 and >18 servings per week, clinically expressed ACS (11.8% and 0% respectively) was significantly less frequently reported. There was an association between consuming red meat and meat products and the development of clinically pronounced ACS symptoms ($p = 0.001$). The most common occurrence of clinically pronounced ACS symptoms was observed in the category of subjects who consumed 5-8 servings of red meat and meat products per week (60.4%). The most frequent symptoms of severe ACS clinical picture were observed among the respondents who stated that they did not consume this category of foods (9.1%). However, a small number of respondents in the study ($n = 11$) stated that they did not consume this category of foods, which according to the MedDiet Score is defined as "5 points". The study results show a statistically significant correlation between poultry meat consumption and the occurrence of ACS ($p < 0.0005$). Most commonly, the occurrence of clinically severe ACS symptoms is seen in subjects who consume poultry meat in the amount of 13-18 servings per week (category "1 point" according to the MedDiet score). The rarest occurrence of ACS was observed in subjects who reported that they consumed 1-4 servings per week (37.5%) of poultry meat (category "4 points" according to the MedDiet score).

There was a statistically significant correlation between the intake of whole milk dairy products and the occurrence of ACS in subjects ($p < 0.0005$). The most frequent occurrence of ACS S (70.4%) was recorded in the category of respondents who stated that they consumed whole-fat dairy products in the amount of 1-4 servings per week (category "4 points" according to MedDiet score). The lowest incidence of severe clinical symptoms of ACS (18.4%) was observed in subjects who consumed full fat dairy products in the amount of 13-18 servings per week (category "1 point" according to the MedDiet score).

The results of the study indicate that there is a statistically significant inverse association between the consumption of olive oil and the onset of clinically pronounced symptoms of ACS ($p < 0.0005$). The most common symptoms of ACS were present in the category of respondents who stated that they never used olive oil in their diet (73.7%), (the "0 points" category according to the MedDiet score). The least frequent symptoms of ACS were present in the category of respondents who stated that they consumed olive oil daily (8.8%) (category "5 points" according to the MedDiet score). The study results showed a statistically significant association between alcohol consumption and the onset of clinically pronounced ACS symptoms ($p < 0.0005$). The incidence of ACS in subjects who consumed alcohol daily in the amount of 100-300ml (category "5 points" according to the MedDiet score) was 19% ($n = 8$). The most commonly reported pronounced symptoms of ACS were present in subjects who indicated that they consumed alcohol in quantities of 300ml and 400ml (100%). Symptoms of ACS in subjects who indicated that they did not consume alcohol at all or consumed it in an amount > 600 ml during the day was (50%, $n = 113$). The results obtained, however, should be taken with caution, since they do not satisfy the condition, because the percentage of frequencies in the categories less than 5 (categories 1 to 4) according to the MedDiet score is less than 20%.

Conclusion: The onset of ACS shows a strong statistically significant negative correlation with the following food categories defined by MedDiet score: unrefined cereals, fruits and vegetables, legumes, poultry, fish, olive oil and alcohol. In other words, frequent

consumption of these food groups is associated with a reduction in the risk of acute coronary syndrome. Contrary, onset of acute coronary syndrome shows a strong statistically significant positive correlation with the following food categories defined by MedDiet score: red meat and meat products and whole milk products. In other words, frequent consumption of these food groups is associated with an increased risk of acute coronary syndrome. This research may provide a framework for developing a local nutritional scoring system appropriate for the non-Mediterranean area, as well as a model for assessing the risk of acute coronary syndrome, which in addition to known cardiovascular disease risk factors, will include elements of the individual's diet.

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3. MEDICINAL PLANTS AND FUNCTIONAL FOOD

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INTRODUCTION

Food can be considered functional if it is scientifically confirmed that it has a positive effect on certain functions in the body, in addition to its usual nutritional effect, in terms of promoting health and reducing the risk of illness. Functional food must always be in the form of food, and a positive effect on health must be consumed by consuming the usual amount. Adding nutrients to basic foods can increase its intake at the level of the entire population (iodine can be considered one of the "first-generation" functional products). The second generation of "functional products" emerged as a reaction to the over-saturation of saturated fat and sugar in food (products with reduced fat, cholesterol and sugar content compared to equivalent products of the same category). During the seventies and eighties of the last century, a number of physiologically active substances of plant origin were identified with potentially beneficial action in the prevention and treatment of many chronic diseases. These discoveries have enabled the development of the third generation of "functional products". In herbal products, herbal supplements are incorporated in powder form (dried herbs), extracts (liquid, thick or dried), cut juices, waxes, vegetable oils, lipids, essential oils, as well as purified components: vitamins, antioxidants and other biologically active substances (Mišan et al., 2013).

Wild apple fruit is a good source of a large number of natural biologically active substances (including polyphenolic compounds as antioxidant substances), which have a therapeutic effect on many diseases caused by oxidative stress. Investigated wild apple (*Malussylvestris*(L.) Mill., Rosaceae) represents a biomarker of territory of Serbia and a plant used in Serbian folk medicine for prevention and/or treatment of various diseases. Their extracts can be potentially used in herbal products for prevention and/or treatment of many oxidative stress related-diseases (cardiovascular or degenerative diseases, atherosclerosis, diabetes, osteoporosis, cancer, contact dermatitis, phototoxicity, photoaging, cancer)(Nešić et al., 2019; Sarić, 1989; Stojiljković et al., 2014; 2016a; 2018; Šavikin et al., 2014; Žugić et al., 2014).

Therefore, the aim of our study was characterization of extracts of wild apple fruit, obtained using different solvents and different extraction methods, determination of their *in vitro* antioxidant effects and stability estimation of investigated characteristics and effects, in order for potential use in production of functional food (containing herbal supplements- plant extracts).

MATERIALS AND METHODS

Plant material and reagents

Investigated wild apple fruit (*Malussylvestrisfructus* (L.) Mill., Rosaceae) was collected on Kopaonik Mountain, southern Serbia. It was fragmented at fragmentation degree of 5mm and dried for three weeks at temperature of $22 \pm 2^{\circ}\text{C}$ (evidenced number 3709HFF, Department of Botany, Faculty of Pharmacy, University of Belgrade, Serbia).

For this study followed reagents were used: 70% ethanol were purchased from Hemos (Serbia) and purified water from Medical faculty of Niš (Serbia). HPLC standards were purchased from Sigma–Aldrich (USA) or from Extrasynthese, Cedex (France). DPPH radical

(1,1-diphenyl-2-picryl-hydrazyl) and linoleic acid were purchased from Sigma-Aldrich (USA).

Methods

Preparation of extracts of wild apple fruit: Before extraction, wild apple fruit was pulverized two minutes at degree of 1mm using a mill (IKA - Werke, Staufen, Germany) (Ph. Yug.V). Liquid extracts of wild apple fruit were prepared in drug:extract ratio D:E = 1:5 (w:V - weight:Volume) using 70% ethanol (V:V) and purified water as solvents and by maceration and percolation as extraction methods (Ph. Yug.IV, Stojiljković et al. 2016a). All extracts were made, stored and used for further investigation as liquid extracts.

Organoleptic and physico-chemical analysis: Characterization of wild apple fruit extracts included organoleptic analysis (observing the color, odor and clearness) and physico-chemical analysis (pH values, the refraction index and density), 7 and 180 days after preparation (Stojiljković et al., 2016a).

HPLC analysis of bioactive substances: HPLC analysis of polyphenolic compounds in investigated extracts was achieved by “*fingerprinting*” applying the method described by Pereira et al. (2010), with necessary modification, 7 days and two years after preparation, and expressed as percentage content (%). Preparation of samples was carried out using procedure used in our previous studies (Nešić et al., 2019; Stojiljković et al., 2018).

Antioxidant activity analysis: Antioxidant activity of wild apple fruit extracts was assessed *in vitro* by DPPH method (Brand-Williams et al., 1995) and by thiocyanate method (Gordon and Maisuthisakul, 2009), with minor modification (explained in our previous studies (Stojiljković et al., 2016a, 2016b), and expressed as %RSC (Radical Scavenging Capacity) and %AOA (AntiOxidant Activity), respectively. Measurements were taken 7 and 180 days after preparation.

Statistical analysis

Results were presented as arithmetic mean \pm standard variation (SD). The obtained results were analyzed using the software package SPSS 16.0, by ANOVA followed by Tukey test (with statistical significance of $P < 0.05$), while the change at time was tested by Student-t test.

RESULTS AND DISCUSSION

Organoleptic and physico-chemical analysis

Type of used solvents and extraction methods had important influence on organoleptic characteristics of investigated extracts. After 7 days of storage, obtained extracts were bright-yellow to brown color, due to the red-brown color of used drug (wild apple fruit). The water extracts were darker brown color compared to ethanol extracts, and the extracts obtained by percolation were darker than the extracts obtained by maceration. The odor of extracts was the odor of used drug, while the ethanol extracts had partly a odor of used solvent (odor of ethanol). The ethanol extracts were clear after the preparation, without visible particles, while the water extracts were slightly blurred.

Type of used solvent showed important influence on pH values and refraction index, while type of used extraction methods didn't have influence on physico-chemical characteristics. Water extracts had significant lower pH values 7 days after preparation (3.17 for E3 and 3.30 for E4) compared to ethanol extracts (4.44 for E1 and 4.37 for E2) (Table 1) (Stojiljković et al., 2016). The values of refraction index and density of the investigated

extracts were consistent with reference values of the refraction index and density for the appropriate extraction solvent (Nikolić and Mitić, 2007). Water extracts had lower refraction index (about 1.34), which was also showed by Arsić et al. (2014), compared to ethanol extracts (1.37). Values of density were similar for all extracts (Table 1).

Organoleptic and physico-chemical characteristics of investigated extracts were constant during storage of 180 days at temperature of $22\pm 2^\circ\text{C}$, under normal storage conditions (except pH values, which were slightly lower, probably due to the presence of acidic substances from acidic wild apple fruit), which might be an indicator of the potential physico-chemical stability of extracts.

Table 1. Organoleptic and physico-chemical characteristics of investigated extracts of wild apple fruit 7 and 180 days after preparation

Characteristics	Time	E1 extract ethanol- maceration	E2 extract ethanol- percolation	E3 extract water - maceration	E4 extract water - percolation
pH values	7 days	4.44±0.12	4.37±0.19	3.17±0.11 ^{a)}	3.30±0.07 ^{b)}
	180 days ^{c)}	4.29±0.09	4.28±0.21	3.01±0.14	3.21±0.15
Refraction index	7 days	1.371±0.001	1.369±0.001	1.345±0.003 ^{d)}	1.342±0.000 ^{e)}
	180 days	1.370±0.001	1.368±0.002	1.341±0.002	1.339±0.001
Density (g/cm ³)	7 days	0.961±0.000	0.982±0.001	1.008±0.003	0.952±0.002
	180 days	0.963±0.001	0.983±0.001	1.000±0.001	0.955±0.001

^{a)} E3 vs E1 and E2, $P < 0.05$; ^{b)} E4 vs E1 and E2, $P < 0.05$; ^{c)} 7 days vs 180 days, $P < 0.05$

^{d)} E3 vs E1 and E2, $P < 0.05$; ^{e)} E4 vs E1 and E2, $P < 0.05$

HPLC analysis of bioactive substances

Content of polyphenolic compounds, as a good antioxidant substances, 7 days after preparation was significantly better in ethanol extracts compared to water extracts (Table 2). Ethanol extracts had about six times higher content (8.99% for E1 and 9.68% for E2) than water extracts (1.40% for E3 and 1.67% for E4) (Table 2). Type of used solvents showed important influence on polyphenolic content, while extraction method didn't have significant influence.

Content of polyphenolic compounds was generally decreased in the investigated extracts during storage for a period of two years, at temperature of $22\pm 2^\circ\text{C}$ in relation to the content determined 7 days after preparation (especially E2 and E3 - more than two/three times lower content) (Table 2). Stable content was shown for E4 extract, but still lower compared to ethanol extracts.

The obtained results indicated that extracts with standardized and stable concentrations of polyphenolic compounds might be used as a potential antioxidant active substances, from plant origin, in production of functional products.

Table 2. Polyphenolic content after 7 days and two years and antioxidant activity of investigated extracts, 7 and 180 days after preparation

Characteristics	Time	E1 extract ethanol- maceration	E2 extract ethanol- percolation	E3 extract water - maceration	E4 extract water - percolation
Content of polyphenols (%)	7 days	8.99 ^{a)}	9.68 ^{b)}	1.40	1.67
	two years ^{c)}	6.31	4.07	0.44	1.67
Antioxidant	7 days	70.96	73.39	47.90	53.50

activity (%RSC)	180 days	50.46	55.76	35.56	52.87
Antioxidant activity (%AOA)	7 days	69.08	77.30	72.20	75.60
	180 days ^{d)}	49.98	55.23	48.28	66.96

^{a)} E1 vs E3 and E4, $P < 0.05$; ^{b)} E2 vs E3 and E4, $P < 0.05$; ^{c)} 7days vs 2years for E1 and E2, $P < 0.05$

^{d)} 7 days vs 180 days for E1 and E2, $P < 0.05$

Antioxidant activity analysis

Antioxidant activity of extracts of wild apple fruit was analyzed in order to assess the possibilities of their use as antioxidant active substances in production of functional food, taking into account that the antioxidant food supplement and functional products can be used in the prevention and/or treatment of many diseases caused by oxidative stress (Lesjak et al., 2011). Type of used solvents showed important influence on antioxidant activity, while extraction methods didn't show, but it can be said that extracts obtained by percolation as extraction method showed better antioxidant activity, compared to maceration. Better radical scavenging capacity, 7 days after preparation, was shown for ethanol extracts (the best for E2 - 73.39 %RSC) compared to water extracts (Table 2), while ability for inhibition of lipid peroxidation was similar for all extracts (slightly better for water extracts) (Stojiljković et al., 2016). Generally, the best antioxidant activity (%RSC and %AOA) was shown for E2 extract (extract obtained by ethanol and percolation), probably due to the presence of polyphenolic compounds, which content was the best for this extract.

There wasn't significant differences in antioxidant activity after 180 days of storage between investigated extracts in relation to the used solvents and extraction methods. Antioxidant activity was lower after 180 days compared to after 7 days (significantly for %AOA), but still satisfactory (Table 2).

The obtained results indicated that extracts of wild apple fruit with good and stable content of polyphenolic compounds have good antioxidant activity and might be used in production of functional food.

CONCLUSIONS

Functional food, containing medicinal plants (including herbal extracts), might be considered functional if it is scientifically confirmed that it has a positive effect on certain functions in the body, in terms of promoting health and reducing the risk of illness, as well as for prevention and/or treatment of many diseases. Wild apple fruit represents a good source of bioactive antioxidant polyphenolic compounds, and their extracts might be used in production of functional products. Type of used extraction solvents (70% ethanol and purified water) and extraction methods (maceration and percolation) had shown important influence on organoleptic and physico-chemical characteristics of extracts (which were stable during investigated period), as well as on content of polyphenolic compounds and antioxidant activity. Ethanol was better solvent for extraction of polyphenolic compounds and gave extracts with better antioxidant activity compared to purified water, while percolation as extraction method was better compared to maceration. The best antioxidant activity was shown for extract obtained using ethanol as solvent and percolation as extraction method, probably due to the presence of polyphenolic compounds (which content was the best for this extract). Due to these results, wild apple fruit extracts might represent a valuable source of natural antioxidant substances (including polyphenolic compounds), with potentially beneficial action in the prevention and/or treatment of many chronic diseases, and thus may be considered as a great potential for application in production of functional food.

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Keywords: functional food, medicinal plant, wild apple fruit extracts, polyphenolic compounds, antioxidant activity

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ORAL PRESENTATIONS

1. ORGANIC FOOD - HUMAN HEALTH IMPACT

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Introduction: In the last two decades, the consumption of organic food is increasing steadily worldwide. Today 181 countries produce organic food on more than 69,8 million hectares of organic farmland. People are mostly motivated to eat organic food because they believe it's healthier than the conventional one.

Objectives: A literature review focusing on studies investigating impact of organic food on human health.

Materials and methods: A search strategy was implemented in the following bibliographic databases: Scopus, Since Direct and PubMed. The search algorithm comprised a targeted combination of food production-related terms (organic food, conventional food), risk-related terms (pesticide residues, contaminants, antibiotics, health impact) and food-related terms (nutrients).

Results: Many studies that investigated nutritional value of organic compared to conventional food, showed that organic food contains a significantly more polyphenols, vitamin C, and some mineral components. Also, because of the way of production, organic food contains less pesticides residues, antibiotics, and nitrates. Organic food and food products of animal origin have a higher content of omega-3 fatty acid, α -linolenic acid, and conjugated linoleic acid. However, both, organic and conventional food, can be contaminated with environmental contaminants such as OCPs, PCBs, lead, and cadmium.

Conclusion: People eating organic food are healthier and with better body shape. They have lower incidence of some metabolic diseases, cardiovascular disease, allergies, and overweight or obesity. However that is also in high correlation with their healthier lifestyle and healthier dietary patterns in general. That's why new long-term studies should be carried on to determine whether organic food compared to the conventional one significantly contributes to the overall health status of an individual or population.

Keywords: Organic food, Human health, Nutrients, Pesticide residues, Contaminants

2. DIETARY SUPPLEMENTATION AMONG STUDENTS OF THE FACULTY OF SPORT AND PHYSICAL EDUCATION, UNIVERSITY OF NIŠ

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Objectives: Supplements are products widely used among athletes to improve sports performance and reduce fatigue symptoms. The aim of the study was to assess the diet supplement use and attitudes to it among students of the Faculty of Sports and Physical Education in Niš.

Materials and methods: The survey was conducted on a sample of 201 students of both genders, all four years of Undergraduate Studies, aged 19 to 23 years old. The respondents completed questionnaire containing questions related to dietary supplementation, physical activity and the existence of symptoms of fatigue.

Results: Survey results show that 40.8% of respondents use supplements. The male students more often than female ones used diet supplementation. Students most commonly take vitamins (68.3%), proteins and amino acids (15.1%) whereas 5.6% of them use minerals. The results show that with the increase of the year of study, the number of students taking supplements decreases significantly ($p = 0.02$). The analysis of the results by gender shows that male students are more likely to take amino acid supplements ($p = 0.006$). Students who use supplements are less likely to report symptoms and signs of fatigue. No correlation was found between the duration and frequency of physical activity and the use of supplements.

Conclusion: With the increase of the year of study, we note positive changes in students' attitudes to the use of supplements, which can be explained by the acquisition of knowledge in the field of sports nutrition and supplementation through the curriculum contents of the study program.

Keywords: supplementation, students, attitudes

POSTER PRESENTATIONS

1. ANTIOXIDANT ACTIVITY OF STANDARDIZED WILD APPLE FRUIT EXTRACTS: A COMPARISON OF POLAR AND NON-POLAR SOLVENTS

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Objectives: Wild apple fruit (*Malus sylvestris* (L.) Mill., Rosaceae) have been used as a good bioactive antioxidants in phytopreparations and dermocosmetic products for prevention and/or treatment of oxidative stress-related diseases. The aim of present study was preparation of different extracts of wild apple fruit, originated from Serbia, and estimation and comparison of antioxidant activity of obtained extracts.

Materials and methods: The liquid extracts were prepared in drug:extract ratio - 1:5, by maceration as extraction method and using purified water as polar solvent-PE and virgine olive oil as non-polar solvent-NPE. Antioxidant activity was determined by three methods: DPPH, FRAP and thiocyanate method and expressed as %RSC, mM Fe²⁺ and %AOA, respectively.

Results: The antioxidant activity od extracts depended on polarity of used solvents. PE showed better antioxidant activity than NPE: about three-times better radical scavenging capacity (%RSC was 47.90%RSC and 14.94%RSC, respectively) and ferric reducing antioxidant power (FRAP was 7.16mM Fe²⁺ and 2.25mM Fe²⁺) and 15% better ability to prevent lipid peroxidation (%AOA was 72.20%AOA and 62.20%AOA).

Conclusion: The results of our study indicated that wild apple fruit extracts (especially extract obtained by polar solvent) might be taken into consideration for use in food and dermocosmetic industry as a good bioactive antioxidant substances.

Keywords: wild apple fruit extracts, antioxidant activity, polar and non-polar solvents

Acknowledgements: Serbian Ministry of education, science and technological development supported this study (Project No III 45017) and Internal Scientific Project No 2 (11-14629-4/2).

2. DIETARY SUPPLEMENT USE IN THE CITY OF NOVI SAD, SERBIA: THE “WHOS”, “WHAT’S” AND “WHYS”

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Objectives: The aim of this research was to identify the most commonly used dietary supplements (DS) in Novi Sad, Serbia and the reasons for their use.

Methods: A random sample of adults from Novi Sad (N=435) completed a pre-tested online survey on their demographics and use of DS.

Results: In total, 42.8 % of participants used DS. Users were mostly women, seniors and people with lower socioeconomic status. The most commonly used DS were minerals, vitamins or their combinations (68.8 % of DS users), omega-3 fatty acids (19.3 %), propolis-based DS (12.4 %). Iron, aminoacids, ginkgo, weight loss DS, collagen and probiotics were used by less than 10 % of DS users. Respondents usually used only 1 DS (43.0%) but 5.3 % of participants reported concomitant use of 5 or more DS. The main reasons cited for dietary supplement use was maintenance of general health and disease prevention and treatment/control.

Conclusions: Similar to global trends, dietary supplement users from Novi Sad most commonly use vitamins and/or minerals. Propolis-based DS are ranked unexpectedly high. Users expectations from dietary supplements are sometimes unrealistic (“disease prevention and control”). Surprisingly high proportion of DS users with lower socioeconomic status needs further investigation.

Keywords: dietary supplements; nutritional supplements; food supplements; Novi Sad; Serbia

3. THE DIETARY PATTERN OF PATIENTS WITH SCHIZOPHEIA: GENDER DIFFERENCES

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Objectives: Several epidemiological studies have suggested a cardioprotective role of the Mediterranean Diet. The aim was to investigate the quality of food habits (and gender differences) in the population of patients diagnosed with schizophrenia

Methods: Ninety-five patients diagnosed with schizophrenia (51 male, mean age 46.11±11.61) were included. A Short Mediterranean-diet questionnaire was used.

Results: 67.4% had one meal with vegetables, and 80% one meal with fruit daily. 58.9% did not drink soda, while almost none of the subjects (2.1%) drank wine. Only 5.4% ate more than 3 meals with legumes per week. 40% of participants did not eat any fish at all. 64.8% male and 56.8% female were tobacco smokers. 7.8% male and 18.2% female used olive oil in their diet. Men had statistically significant more portions of meat than women (F=8.1; p<0.05). Regarding the intake of fruit, vegetables, legumes, soda, wine, fish, nuts and concentrated sugar, there was no statistically significant difference.

Conclusion: Our results found that people suffering from schizophrenia had bad dietary habits, which is in line with findings of the prior research. Interestingly, we did not find significant differences consider gender regarding this population food intake.

Keywords: Mediterranean Diet, schizophrenia

4. DIETARY SUPPLEMENTS FOR JOINT AND BONE HEALTH IN SERBIA

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Objectives: The aim of this research was to identify the most commonly used dietary supplements (DS) in Novi Sad, Serbia and the reasons for their use.

Methods: A random sample of adults from Novi Sad (N=435) completed a pre-tested online survey on their demographics and use of DS.

Results: In total, 42.8 % of participants used DS. Users were mostly women, seniors and people with lower socioeconomic status. The most commonly used DS were minerals, vitamins or their combinations (68.8 % of DS users), omega-3 fatty acids (19.3 %), propolis-based DS (12.4 %). Iron, aminoacids, ginkgo, weight loss DS, collagen and probiotics were used by less than 10 % of DS users. Respondents usually used only 1 DS (43.0%) but 5.3 % of participants reported concomitant use of 5 or more DS. The main reasons cited for dietary supplement use was maintenance of general health and disease prevention and treatment/control.

Conclusions: Similar to global trends, dietary supplement users from Novi Sad most commonly use vitamins and/or minerals. Propolis-based DS are ranked unexpectedly high. Users expectations from dietary supplements are sometimes unrealistic (“disease prevention and control”). Surprisingly high proportion of DS users with lower socioeconomic status needs further investigation.

Keywords: dietary supplements; nutritional supplements; food supplements; Novi Sad; Serbia

5. COMPATIBILITY OF IDENTIFIED AMOUNTS OF MINERALS IN DIETARY SUPPLEMENTS WITH THEIR LABELED VALUES

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Objectives: Modern diet is the main reason why some individuals are deficient of minerals or other substances with nutritive effect. Dietary supplements are additional sources of minerals that are presented on the market in a variety of pharmaceutical forms (powder, pill, liquor). EFSA guiding document for competent authorities for the control of compliance with the EU legislation is demanding that the product must meet labeled value of minerals of +45%/-20%. Our aim was to assess content of minerals in dietary supplements.

Methods: We analyzed 4 types of mineral supplements, or a total of 80 samples (zinc, calcium, magnesium and selenium). The metals were analyzed by atomic absorption spectrometry and inductively coupled plasma – optical emission spectrometry.

Results: Analyzed metals in supplements showed compliance with the EFSA criterion regarding calcium, zinc, magnesium and selenium content (100%; 95.6%; 91.2%; 81.2%; respectively).

Conclusion: Fact that minerals have significant roles in biochemical and physiological processes, the need for control of their concentrations in dietary supplements is essential for preventing misleading consumers, and possible disruption of consumers health.

Keywords: Dietary supplements, consumer safety, nutrition, ICP-OES, AAS

6. STUDY ON ANTIOXIDANT ACTIVITY OF EXTRACTS OF LEMON BALM LEAVES

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Objectives: The leaves of lemon balm, *Melissa officinalis* L (*Lamiaceae*), are used in folk medicine for their digestive, antispasmodic, sedative, antimicrobial and antioxidant properties. We estimated the antioxidant activity of lemon balm extracts obtained using conventional and supercritical fluid extraction (SFE) with carbon dioxide (CO₂) as the extracting solvent.

Materials and methods: Hydrodistillation was carried out using **Clevenger** method. The first step SFE extraction was performed is at 40°C and 10 MPa. The second step of the extraction is realized at 30 MPa and at different temperature (25°C, 40°C and 100°C). The obtained extracts were studied for antioxidant activity using FRAP, β-Carotene bleaching assays and **total phenolic** content (TPC).

Results: The TPC ranged from 10.01 mg GAE/g in extract 10 Mpa/40 °C to 23.63 mg GAE/g in extract 30 Mpa/40 °C. Extract obtained at a pressure of 30 MPa and a temperature of 100 °C expressed the greatest activity (0.24 mmol Fe²⁺/g of dry extract in FRAP assay and IC₅₀ = 0.96 mg/mL in β-carotene bleaching assay).

Conclusion: *Melissa officinalis* L leaves extracts obtained by SFE are a is a rich source of components which may have the potential to prevent oxidative stress.

Keywords: Lemon balm, leaves, supercritical fluid extraction, antioxidant activity, **total phenolic** content.

Acknowledgement: This research was financially supported by the **Ministry of Education, Science and Technological Development of the Republic of Serbia** (Project No. III 45017 and TR 31060) and by the Faculty of Medicine University of Niš Internal Scientific Project No. 2 (11-14629-4/2).

7. DETERMINATION OF SORBIC AND BENZOIC ACID IN FOODS

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Objectives: Sorbic and benzoic acid are intentionally added during manufacture, processing, preparation, treatment, packaging or storage of foods, in order to keep the quality as well as ensure food security. Consumption of foods who contains sorbic and benzoic acid, in humans, and above all in sensitive people, can lead to irritation or allergic reaction. The objective of this paper was to determine presence and content of sorbic and benzoic acid in food who used in everyday nutrition.

Methods: Fifty samples of commercial products (non-alcoholic beverage, syrup, pickled products and ketchup) were analyzed by HPLC (High-performance liquid chromatography) for their contents of benzoic and sorbic acids. The HPLC operating mode was isocratic. The mobile phase consisted of 20 mM phosphate buffer (pH 3.8) and acetonitrile 90:10 (% v/v).

Results: All samples contained benzoic acid with levels ranging between 20.5 and 975 mg/kg and 17 samples contained in addition sorbic acid amounts in the range of 30.4 and 386 mg/kg.

Conclusion: Information of quantity of sorbic and/or benzoic acid in different foods are necessary to properly combine and avoid excessive intake and adverse effects.

Keywords: benzoic and sorbic acid in foods; nutrition, HPLC

8. COMPATIBILITY OF IDENTIFIED AMOUNTS OF VITAMINS IN DIETARY SUPPLEMENTS WITH THEIR LABELED VALUES

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Objectives: Popularity of the use of dietary supplements in our country is increasing. Due to enhancement of different types of the products every day, significance of control of dietary supplement labels is enormous. EFSA guiding document for competent authorities for the control of compliance with the EU legislation is demanding that the product must meet labeled value of vitamins with a minimum of -20% and maximum +50%. Our aim was to assess compatibility between labeled and identified amounts of vitamins using HPLC-DAD.

Methods: We analyzed 166 samples of dietary supplements submitted, for the laboratory control in the period from January 2018. to June 2019., on the content of hydrosoluble vitamins.

Results: Quantification was carried out on Agilent 1200 chromatograph with diode array detector. Gradient elution was employed using water/acetonitrile, with addition of 0.1% TFA as a mobile phase. Of the total number of analyzed samples, 15% did not meet EFSA criterions. Below -20% and over +50% of labeled concentration were found in 13.8% and 1.2% of total samples respectively.

Conclusion: Vitamins are physiology active compounds, and necessity for the control of their concentration is present. Products that do not satisfy EFSA guidelines lead to deception of consumers, and eventually can cause health issues.

Keywords: Dietary supplements, vitamins, nutrition, HPLC-DAD

9. THE IMPORTANCE OF RECOGNITION OF VITAMIN D DEFICIT IN THE POPULATION OF WOMEN IN ORDINATION OF GENERAL PRACTICE

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Objectives: Vitamin D determination or screening isn't foreseen at the primary health care. Optimal level of vitamin D is 50-75 nmol / L. The aim of the study was to examine whether we fit into the global trend of vitamin D deficiency.

Methods: Random sample of 57 subjects from Novi Sad territory 20-69 years measured serum 25 (OH) D and body weight, without osteoporosis and additional vitamin D. Data were collected by examination, 01-30. 04. 2019 at the Health Center Novi Sad, occupational medicine.

Results: We identified three groups: first group of 34 subjects (59.65%) has a deficit below 50 nmol / L, second group of 16 subjects (28.07%) has an optimal level of 50-75 nmol / L, third group of 7 subjects (12.28%) had a neat level above 75 nmol / L. Statistically significant difference was found between the groups (χ^2 -test = 19,895; DF = 2; p = 0.000). A small negative correlation between 25 (OH) D and years of age (r = -0.10) and body weight (r = -0.09) was also obtained.

Conclusion: It's important to recognize vitamin D deficiency in women. We're in line with the global trend of deficits.

Keywords: vitamin D, hormone, deficiency, general practice

10. STUDENTS EATING HABITS AND HEALTH SELF-ASSESSMENT AT THE UNIVERSITY IN KOSOVSKA MITROVICA

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Introduction: Qualitative and quantitative needs for a well-balanced diet during studying are higher than in any other period of a lifetime.

Aim: The aim was to determine the frequency of certain eating habits among students of the University of Pristina with a temporary headquarters in Kosovska Mitrovica, and to examine the connection of these habits with self-assessment of the health of the respondents.

Methods: This research was a cross-sectional study of a representative sample of students at the University of Pristina with a temporary headquarters in Kosovska Mitrovica in March and April 2011. It was surveyed by 567 students. The research instrument was *The Behavior and Health Questionnaire*. The frequency differences were tested by the hi-square test. The criterion for statistical significance was $p < 0.05$.

Results: More than a quarter of students, who declare that they never have breakfast (26.3%), assess their health as "Middling", while among the students who have breakfast on a daily basis most of them are those (63.6%) who assess their health as "Very Good" ($\chi^2 = 22.668$; $df = 12$; $p = 0.031$). There is a statistically significant difference between our students in terms of consuming dinner. Among the respondents who "Never" have dinner the largest share (16.7%) of students are those who assess their health as "Bad", while four fifths (78.0%) of respondents, who assess their health as "Very Good", have dinner "Everyday" ($\chi^2 = 21.348$; $df = 12$; $p = 0.046$). Three quarters of students who evaluate their health as "Very Bad" (75.0%) eat fruits only "2 to 3 times a week", while more than three-fifths of students (67.7%), who evaluate their health as "Very Good", have fruits "Repeatedly" or "Once a day" ($\chi^2 = 35.410$; $df = 16$; $p = 0.003$). Among the students who evaluate their health as "Very Bad" the highest proportion (75%) of students are those who "Never" use cooked vegetables in the diet. On the other hand, most of the respondents, half of them (49.2%), who evaluate their health as "Very Good", use cooked vegetables in their diet "Repeatedly" or "Once a day" ($\chi^2 = 34.878$; $df = 16$; $p = 0.004$). Students (100%) who consider their health as "Very Bad" have soda drinks and sweets "Repeatedly", while less than a third of students (30.1%), who evaluate their health as "Very Good", do that ($\chi^2 = 42.209$; $df = 16$; $p = 0.000$). Students (100%) who evaluate their health as "Very Bad" have coffee "Repeatedly" or "Once a day", while more than a fifth of students (22.5%), who evaluate their health as "Very Good", "Never" drink coffee ($\chi^2 = 37.125$; $df = 16$; $p = 0.002$).

Conclusion: The fact that acquiring healthy habits in youth contributes to better health and a better quality of life over a longer period requires the initiation of activities in terms of developing responsibility for one's own health.

Keywords: eating habits, self-assessment of health, students.

11. INFLUENCE OF PHYSICAL ACTIVITY ON THE QUALITY OF CHILD'S LIFE

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Introduction: Physical activity is a significant factor in the quality of life of all age groups, especially children who are in the process of constant growth and development. Insufficient physical exercise contributes significantly to the onset of obesity.

Objective: The purpose of our research was precisely to determine the extent to which children of the test age are practicing physical activity.

Material and Method: A total of 100 students, ages 6 to 8, were tested. A survey was used.

Results: The results show that the largest number of respondents (53.0%) practice sports occasionally. Daily sports activities are practiced by 30.8% of respondents, and 16.2% of them do not practice sports at all. More frequent exercise of sports activities acts as a protective factor when it comes to preventing obesity. Sports children are 12% less likely to become obese compared to children who do not.

Conclusion: It is necessary to take measures to improve the quality of life of school children in terms of establishing and maintaining healthy life habits, Minimal exercise of physical activities that lead to positive effects and which are desirable in the prevention of illness means thirty minutes daily moderate physical activity, adapted to individual health and fitness. Children are advised to use the "Pyramid of Physical Activity" as the proper way of life.

Keywords: physical activity, children, obesitas, prevention

12. SALT CONTENT IN BELGRADE PUBLIC PRESCHOOL MEALS

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Objective: Estimation of salt intake in preschool-aged children by exploring the salt content in daily meals (consisting of: breakfast, lunch and a snack) sampled in public preschools in Belgrade.

Methods: Analysis of the results of salt content in sampled daily meals during 2016/2017. The samples were taken by the Institute of public health Belgrade from every public preschool in Belgrade (280 objects). The SPSS 22.0 software package was used for statistical analysis of obtained results.

Results: Average salt concentration ($3,97 \pm 0,96$ g) was higher than normatives set by current legislation in both age groups (1 to 3 and 4 to 7). Most of sampled meals (>90%) had higher salt content relative to legislation. No significant statistical difference was determined between 2016 and 2017.

Conclusions: Considering the number of children (~50.000) attending public preschools and consuming most of their daily meals in these facilities as well as the fact that early childhood nutrition presents a strong moderator of future food preferences, it is of great importance to take comprehensive approach and joint actions towards reducing salt intake in preschool settings.

Keywords: preschool nutrition, salt intake

13. NUTRITION AND ASTHMA

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Objective: Asthma is a chronic respiratory disorder which is associated with airway inflammation. The influence of nutrition on asthma outcomes is of growing interest, but its importance is still not recognized enough. The objective of this paper is to raise awareness of the importance of nutritional therapy in the prevention and treatment of asthma, as well as about the connection between asthma and adverse reactions to food.

Materials and methods: The used methodology is searching the available scientific literature via google search and google scholar search, updating a database of recent studies, insights and books.

The results are presented by considering nutritional studies on a global scale that address asthma, nutrition and their interconnections.

Medical nutritional therapy of asthma addresses the dietary triggers, corrects energy and nutrient status, educates the patient on a personalized diet that provides optimal levels of nutrients, and watches for food-drug interactions.

Conclusion: A diet rich in antioxidants and monounsaturated fats seems to have a protective and preventive effect. There are also foods that should be avoided. In order to implement a comprehensive approach in the treatment of asthma, it is necessary to apply nutritional protocols as a common asthma management tool.

Keywords: asthma, food allergy, dietary triggers

14. RELATIONSHIP BETWEEN OBESITY AND COLORECTAL CANCER

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Objectives: The number of obese people is increasing. Obesity is associated with many diseases including colorectal cancer. The investigation of relationship between obesity and colorectal cancer is of great importance.

Methods: Results of the studies were searched in the Pub Med database.

Results: There is a positive relationship between obesity and colorectal cancer. Obesity plays a significant role in the development of colorectal cancer. It is shown that higher body mass index is associated with higher risk of colorectal cancer mortality. Mechanisms which link obesity and cancer are positive connection between expansion of the adipose tissue and presumed mediators of the tumor development: elevated triglyceride and low-density lipoprotein, hyperinsulinemia and also increased level of proinflammatory cytokines. Direct relationship between visceral fat and postoperative complications in patients with colorectal cancer were found. There is a positive relationship between obesity and postoperative surgical site infection following surgery for colorectal cancer.

Conclusion: Obesity may be prevented, therefore it is important that people take care of optimal nutrition and adequate physical activity. Preventing obesity the risk for colorectal cancer development may be reduced. Also, obesity prevention may reduce postoperative complications and risk of mortality in patients with colorectal cancer.

Keywords: obesity; colorectal cancer; prevention

15. OBESITY: A RISK FACTOR FOR OSTEOARTHRITIS

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Objectives: Obesity is a serious health problem in the 21st century. According to the World Health Organization the consequences of obesity are increased risk of premature death and reduced quality of life. Osteoarthritis may affect quality of life.

Methods: Search of the results of the studies was performed in Pub Med database.

Results: Obesity and osteoarthritis are positively connected. Obese people have an increased risk to develop osteoarthritis. In obese people an increased load is a mechanical contribution to the pathophysiology of osteoarthritis. In obesity mechanical stress on tibiofemoral cartilage is increased. But, joint overload is not the only risk factor for osteoarthritis. Osteoarthritis may also be present in non-weight-bearing joints such as hand and metabolic factors may have role in its pathogenesis. Adipose tissue is source of adipokines, inflammatory mediators, which have a key role in linking obesity and osteoarthritis and identification of adipokines incriminated the role of adiposity in osteoarthritis.

Conclusion: Osteoarthritis is a significant health problem. Considering that obesity is a risk factor for osteoarthritis, it should have in mind that obesity prevention can significantly contribute to prevention of osteoarthritis. Weight loss, balanced diet and adequate physical activity are of great importance.

Keywords: obesity; risk factor; osteoarthritis

16. PHYSICAL-CHEMICAL PARAMETERS FOR TESTING DIETARY PRODUCTS IN PUBLIC HEALTH INSTITUTE – NIŠ (2014-2018)

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Objectives: Testings as a part of checking physical-chemical parameters of dietary products are conducted on request of Border Sanitary Inspection, Republic Sanitary Inspection for the Nišava and Toplica District or producers. The aim was to look at dietary products health quality based on physical-chemical criteria.

Methods: Results of samples' analyses on physical-chemical quality of dietary products for the period 2014-2018 are presented in the paper. All samples were analyzed in the Public Health Institute, Niš, using accredited methods, and based on the appropriate Rulebook.

Results: For the period 2014-2018, 1337 samples were analyzed in total on the physical-chemical quality. In total, 9 samples were incorrect. Physical-chemical testings include toxicological metal presence analysis and inspection of declaration content and validity. The application for the entry into the Ministry of Health of Republic of Serbia database implies: expert opinion, categorization and approved text of the declaration from the Faculty of Pharmacy in Belgrade or Novi Sad. Great help with control dietary products at import control certainly provide publically available data of the European food safety authority (EFSA).

Conclusion: In five-year period, many samples were analyzed, aiming at the great importance of this laboratory existence.

Keywords: dietary products, physical-chemical parameters

17. MICROBIOLOGICAL CRITERIA FOR THE DIETARY PRODUCTS TESTING IN PUBLIC HEALTH INSTITUTE – NIŠ (2014-2018)

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Objectives: Based on the Law on Food Safety, Official Gazette of RS no. 41/2009, testing of dietary products health safety is conducted in precisely denoted laboratories in different institutions on the territory of the Republic of Serbia. One of them is the accredited laboratory of the Public Health Institute, Niš. The aim was to investigate the health safety based on the dietary products microbiological parameters tested in the Public Health Institute, Niš

Methods: Results of samples' analyses on microbiological quality of dietary products for the period 2014-2018 are presented in this paper. All samples are analyzed using accredited methods, and a database was formed regarding that.

Results: For the period 2014-2018, a microbiological quality was analyzed on 273 samples on average. Microbiological analysis was tested according to the Rulebook about health quality of dietary products (Official Gazette of RS 50/2012). Conducted analyses implied the testing of microbiological parameters and hygienic process criteria.

Conclusion: Among tested samples, there were few invalid results, which presents a statistically negligible incorrectness, and it can be concluded that microbiological quality of dietary products is satisfactory and on the high level.

Keywords: dietary products, microbiological criteria

18. JUSTIFICATION OF RAW PLANT MATERIAL USAGE IN THE PREVENTION AND TREATMENT OF DERMATOLOGICAL DISORDERS

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Objectives: The use of plants in dermatology is constantly increasing. Herbal drug, juices, extracts and isolated active substances are often used in products for the care, protection and treatment of skin and mucous membranes. Consumers of this products believe that they are exceptionally effective and safe because of their natural origin.

Methods: A survey of relevant literature and legal frames was done in order to clarify the modern use of plant materials in prevention and treatment of dermatological complaints.

Results: There is no single legal framework in this area. The European Scientific Cooperative on Phytotherapy recommends the use of 14 herbal drugs for dermatological disorders such as acne, dermatitis, seborrhea, psoriasis, eczema, skin inflammation and wounds. Among the Final European Union monographs on herbal medicinal products prepared by the Committee on Herbal Medicinal Products, 29 are in the therapeutic area of skin disorders and minor wounds. Guidance on essential oils in cosmetic products is published by the European Directorate for the Quality of Medicines and HealthCare of the Council of Europe.

Conclusion: A proper selection of the product is essential for its rational use and it demands an adequate knowledge of the present plant material.

Keywords: herbal drug, ESCOP, EMA/HMPC, legal frame, proper selection

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19. USE OF HERBAL MEDICINAL PRODUCTS IN PREVENTION AND MANAGEMENT OF URINARY COMPLAINTS

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Objectives: Herbal medicinal products have been used for centuries in prevention and treatment of urinary tract disorders. European Medicines Agency recently published *European Union herbal monograph on Species diureticae*. We aimed to review marketed herbal products intended for urinary complaints alongside frequency of their usage.

Methods: The survey was conducted in the local pharmacies in Niš (Serbia) where dispensed products and their ingredients were listed.

Results: There is a variety of different herbal medicinal products used for this therapeutic indication on Serbian market. Apart a few dietary supplements, the most of the products are labeled as herbal tea combinations or herbal drops. All listed products have Ingredients and Posology section in the package leaflet and the most commonly dispensed were poly-herbal teas followed by instant teas and capsules. Beside cranberry fruit and uroantiseptic *Uvae ursi folium*, some of the most frequently used herbal drugs were *Equiseti herba*, *Petroselinii folium* and *Origanum herba*. Around 78% of consumers were women of reproductive age. Beside prevention and self-medication of the symptoms of mild recurrent lower urinary tract infections, these products were often recommended as addition to antibiotic therapy.

Conclusion: Pharmacists could contribute to safe and effective application of herbal medicinal products that must be compliant with the latest scientific knowledge.

Keywords: EMA/HMPC, herbal tea mixtures, package leaflet, self-medication, pharmacists

Acknowledgements. This work was supported by Ministry of Education and Science of the Republic of Serbia (project no. III 41018 and III 46013).

20. THE CONTENTS OF FLAVONOIDS IN SALVIA VERTICILLATA L. EXTRACTS

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Objectives: The plant species of *Salvia* L. genus, have been worldwide known as spices or natural medicines. Their healing properties are mainly attributed to the high content of flavonoids and phenolic acids, compounds with protective effects. *Salvia verticillata* L. is traditionally used in colds and gastrointestinal disorders, but its therapeutic effects have increasingly being examined, lately. The objective of the paper was to determine the content of flavonoids (apigenin, luteolin and their 7-*O*-glucosides) in the *S. verticillata* extracts, collected in the area of Niš.

Methods: The plant material was extracted with concentrated ethanol and absolute methanol by the ultrasound extraction and maceration (EU, EM, MU, MM, respectively). The aqueous extract (A) presented evaporated residue after the isolation of the essential oil from the plant material. The flavonoids contents were determined by high performance liquid chromatography (HPLC).

Results: Apigenin (0.37 ± 0.01 $\mu\text{g}/\text{mg}$) and luteolin-7-*O*-glucoside (7.68 ± 0.11 $\mu\text{g}/\text{mg}$) were predominant in extract MM, while the highest quantity of apigenin-7-*O*-glucoside (9.29 ± 0.26 $\mu\text{g}/\text{mg}$) and luteolin (0.08 ± 0.01 $\mu\text{g}/\text{mg}$) were found in extract MU.

Conclusion: It is believed that *S. verticillata* extracts, especially methanolic, will be increasingly used due to the presence of the flavonoids which have a large number of different pharmacological activities.

Keywords: *Salvia verticillata* L.; extracts; flavonoids; apigenin; luteolin

Acknowledgement: This research was financially supported by the Ministry of Science and Technological Development of Republic of Serbia, grant No III 41018 and III 46013, and Faculty of Medicine, University of Niš, Internal project No MF-INT-25.

21. ANTIOXIDANT ACTIVITY OF CONVENTIONAL AND ORGANICALLY PRODUCED FLOURS

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Objectives: The main product obtained by cereals processing is flour, which is used for production of other products like bread, pastries, pasta, muesli, biscuits, etc. Wheat, corn, rice, barley, oats and rye are the most important and the most cultivated crops. Organic production of cereals is a system of sustainable agriculture designed to produce plants that are not treated with fertilizers and pesticides and have increased biological and nutritive value.

Methods: Two types of flour were obtained from organically cultivated wheat and oat, and two flours (wheat and corn) were bought in the supermarket. The active compounds were extracted by using the 96% ethanol. Total phenolic and tannins content was determined using *Folin-Ciocalteu* method. The antioxidant capacity was estimated in 1,1-diphenyl-2-picrylhydrazyl system.

Results: The highest contents of total phenolic and tannin compounds were determined in the corn flour (5.88 ± 0.71 and 4.27 ± 0.63 mg GAE/g, respectively) while the lowest phenolic compounds content was detected in commercial wheat flour (2.29 ± 0.70 mg and 0.99 ± 0.07 GAE/g, respectively). Wheat flour obtained organically showed the highest antioxidant capacity ($IC_{50} = 11.12 \pm 0.47$ mg/ml), while the lowest antioxidant capacity was found in commercial wheat flour ($IC_{50} = 26.39 \pm 2.13$ mg/ml).

Conclusion: These results can be used as a stimulation towards the usage of organically produced flour in our diet and pinpoint the importance of corn flour as good source of polyphenol compounds.

Keywords: flour, wheat, oat, corn, polyphenols, antioxidant capacity

Acknowledgement: This research was financially supported by the Ministry of Science and Technological Development of Republic of Serbia, grant No III 41018 and III 46013, and Faculty of Medicine, University of Niš, Internal project No MF-INT-25.

22. DETERMINATION THE CONTENTS OF THE SOME MACRO AND MICRO ELEMENTS IN THE LEAVES OF DANDELION (TARAXACUM OFFICINALE WEB.)

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Objectives: The aim of this study was to evaluate the nutritional value of dandelion leaves by determining the content of some macro (Ca, K, Na and Mg) and micro (Cu, Fe, Mn and Zn) elements in this plant species.

Materials and methods: The content of the macro and micro elements in the tested samples was determined using the technique of inductively coupled plasma optical emission spectrometry (ICP-OES).

Results: The detected content of macro elements in the tested samples ranged for Ca 730.97-1690.3 mg/kg, for K 1998.7-3587.1 mg/kg and Na 293.8-504 mg/kg. The content of microelements ranged for Cu 9.25-20.02 mg/kg, Fe 54.52-132.2 mg/kg, Mn 1.55-5.25 mg/kg and Zn 34.08-62.71 mg/kg.

Conclusion: Based on the obtained results of this study, it can be concluded that the leaves of the dandelion contains certain amounts of Ca, K, Na, Mg, Cu, Fe, Mn and Zn. The presence of these nutrients justifies the use of leaves of the dandelion in human nutrition. The analyzed samples contained the highest amount of potassium and iron, of all determined macro and micro elements.

Keywords: dandelion; macroelements; microelements; nutrition

23. ASSESSMENT OF IODINE INTAKE IN PREGNANCY BASED ON FFQ

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Mild to moderate iodine deficiency in pregnancy has a direct impact on children's physical and mental development, on maternal health and the quality of life in affected communities.

Objectives: To assess dietary iodine intake using Food Frequency Questionnaire (FFQ) referring to the frequency of consumption of specific foods and food supplements in pregnancy;

Methods: The designed Self-Administered FFQ was based on a food frequency assessment. Only food products that were sources of iodine were taken into account. Results were compared with median urinary iodine concentration of participants.

Results: Food Frequency Questionnaire (FFQ) was filled out by 300 pregnant women. Pregnancy supplements were used by 163 of them. Pregnant women consuming supplements containing iodine have significantly better iodine intake than the ones who do not do so; $241 \mu\text{gI/l}$ with regard to $125 \mu\text{gI/l}$ ($\chi^2 = 6.73$). Milk and dairy products are a significant source of iodine in pregnancy as they were consumed by 92% of participants. Pregnant women do not consume enough fish, 21% and 26% and they are not an important source of iodine. The 83% of pregnant women are informed of the importance of intake of iodized salt in diet.

Conclusion: Dietary supplements with iodine are important source iodine in pregnancy, especially in iodine-deficient areas with low dietary iodine intake.

Keywords: iodine intake, pregnancy, supplement

SESSION: ENVIRONMENT AND HEALTH

INVITED LECTURES

1. PROTOCOL ON WATER AND HEALTH WITH SPECIAL FOCUS ON EQUITABLE ACCESS TO WATER AND SANITATION WITH EXAMPLE FROM NORTH MACEDONIA

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Under the Protocol on Water and Health, Article 8 stipulates that Parties give prompt and clear notification about outbreaks, incidents or threats. In the event of any imminent threat to public health from water-related disease, Parties shall “disseminate to members of the public who may be affected all information that is held by a public authority and that could help the public to prevent or mitigate harm.” Furthermore, emergency risk communications capacity is a core requirement for countries within the framework of the International Health Regulations. Water related infectious diseases outbreaks, particularly those associated with public water supplies, can potentially cause considerable social and economic disruption and are likely to attract considerable political and media attention. Sustainable development goals 3 and 6 are related to public health and water, sanitation and hygiene. Access to safe drinking water and sanitation is a human right, which is part of the right to an adequate standard of living contained in the appropriate article of the International Covenant on Economic, Social and Cultural Rights. It is clearly recognized by the UN General Assembly and the UN Human Rights Council. According to research on equitable access to water and sanitation done in 2015-2017 in North Macedonia, in Skopje, municipality of Shuto Orizari has the highest percentage of families living in housing without water and sanitation. 95% of Roma are poor, only 16% of Roma living in Skopje have a toilet and a bathroom, while the rest use toilets outside of their homes. Just 26% have access to water. During the investigation have been registered urban/rural disparities in access to water and sanitation, as well higher percentage of improper drinking water samples in rural areas compared with urban ones. One of the worst indicators was menstrual hygiene management with only one school having proper conditions for MHM.

Keywords: public health, drinking water quality, Protocol on Water and Health, equitable access to water and sanitation, sustainable development goals

2. HARDNESS OF DRINKING WATER AS A RISK FACTOR FOR ISCHEMIC HEART DISEASE

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The most prevalent cardiovascular disease is ischemic heart disease (IHD) (MKB10: I20-1, 2), which arises as a consequence of atherosclerosis in the coronary arteries and it is a significant cause of disability, loss of working ability, premature mortality (in Europe, two million people die each year) and rising costs for health services, especially in countries with low population growth dominated by the elderly population.

In our country, rates of mortality from IHD, especially from its most severe form (acute coronary syndrome), are higher in Vojvodina, while in central Serbia it is slightly lower than the average rate (3).

The prevalence of the ischemic heart disease (IHD) differs between populations of different countries(4, 5). Also, among the population in a single country there are geographical variations in the incidence of IHD (6). If we exclude the unchanging risk factors for cardiovascular disease, major changeable risk factors such as smoking, high blood pressure, increased cholesterol levels (total and LDL), diabetes mellitus, have so far not adequately explained the geographical variation in incidence of ischemic heart disease (7-9). The existence of areas with high risk for IHD, especially for acute myocardial infarction, indicate that is very likely that environmental factors are also involved in the pathogenesis of the cardiovascular disease, and it is necessary to consider them carefully (10, 11).

In the last five decades ecological, epidemiological and analytical(anamnestic) data have been accumulated on the protective effect of high values of hardness and Ca and Mg from drinking water on morbidity and mortality from cardiovascular disease (12-14).

The aim of the study was to determine the interdependence between the hardness of drinking water, as a risk factor and morbidity from ischemic heart disease. The research presents an epidemiological and ecological (correlation) study, within which a prospective analytical (anamnestic) small-scale study was performed. The research is based on the analyses of water hardness and the content of Ca and Mg in the drinking water of the Nis water supply system (NIVOS). As a source of data for IHD in the territory of Nis district, the relevant section of the National population register of acute coronary syndrome (REAKS) referring to the Nis district was used. The crude and standardized incidence rates (gender and age) in the territorial units of Nis district formed on the basis of different hardness values of drinking water were calculated. A spatial distribution (map) of the average total crude incidence rate of IHD in the reporting period 2010-2012 was made as well.

Within the anamnestic study, through interviews and using the original structured epidemiological questionnaire, information has been collected on water intake and risk factors for IHD (smoking, physical activity, family history of heart disease and diabetes) in 200 subjects from territorial units which have the highest and lowest values of the hardness of drinking water and the contents of Ca and Mg. To determine the average daily energy intake (which includes the daily intake of fat, protein and carbohydrates), as well as the intake of Mg and Ca in patients, we used the validated semi-quantitative questionnaire on the frequency of food intake in the previous year, Food Frequency Questionnaire (FFQ). Testing of the nutritional status of subjects was carried out by measuring the anthropometric parameters (height, weight) using standard procedures to determine body mass index (BMI) as the ratio of body weight in kilograms and height in meters (kg/m^2). Having reviewed the medical records of patients, data was collected on blood cholesterol, triglycerides and LDL cholesterol levels, and systolic and diastolic blood pressure.

The research has shown that subjects who have consumed soft and medium soft water for drinking (in the area of Niska Banja) for over 10 years have a significantly higher incidence rate of IHD compared to the people of the same sex and age who have consumed hard drinking water (villagers connected to the Moravian-part of the water supply system NIVOS) (table 1).

Table 1. The differences in the incidence rates of IHD

	Niska Banja and nearby villages Water Hardness: Avg: 9,3 °dH Mg:Avg:5,37mg/l, Ca:Avg: 60,05mg/l		Water Supply System of Villages in the Moravian area Water Hardness: Avg: 18,3 °dH Mg:Avg:9,67mg/l, Ca:Avg:104,75mg/l		z-test
Year	The number of newly infected individuals	Crude incidence rate (The number of newly infected individuals /100000)	The number of newly infected individuals	Crude incidence rate (The number of newly infected individuals /100000)	sig
2010	46	198,80	6	84,54	0,000
2011	41	184,15	8	118,64	0,000
2012	32	144,43	3	44,63	0,000

A lot of studies have confirmed that a low level of hardness, especially Mg in drinking water, is a risk factor for ischemic heart disease, especially for acute myocardial infarction among men (15-17).

Although the daily intake of drinking water in the subjects was on average less than 2 l, using an amnesic study it was found that a negative correlation between Ca and Mg from drinking water and its hardness with IHD and risk factors for IHD existed: elevated triglycerides, total and LDL cholesterol, systolic and diastolic blood pressure(table 2).

Table 2. The correlation between different risk factors of IHD

		BMI (kg/m ²)	Ca - food intake (m)	Mg- food intake (mg)	Ca water intake (mg)	Mg – water intake (mg)	Water hardness ⁰ d H	Fats (g)	Smokin g status (duratio n)	Famil y histor y of heart diseas e
IHD	Pearson R	,238**	-	-	-	-	-,250**	,359*	,376**	,430**
	p	,001	,000	,000	,000	,000	,000	,000	,000	,000
Systolic blood pressure	Pearson R	,328**	-	-	-	-	-,141*	,263*	,250**	,362**
	p	,000	,000	,000	,000	,000	,047	,000	,000	,000
Diastolic blood pressure	Pearson R	,274**	-	-	-	-	-,130	,253*	,273**	,312**
	p	,000	,001	,000	,000	,000	,067	,000	,000	,000
triglyceridemmol/l	Pearson R	,283**	,050	-,072	-	-	-,165*	,206*	,306**	,312**
	p	,000	,485	,311	,196**	,196**	,019	,003	,000	,000
cholesterol levelsmmol/l	Pearson R	,369**	-,023	-	-,160*	-,158*	-,104	,172*	,188**	,268**
	p	,000	,746	,001	,024	,025	,145	,015	,008	,000
LDL cholesterol. mmol/l	Pearson R	,331**	-,012	-	-	-	-,251**	,244*	,147*	,202**
	p	,000	,868	,008	,008	,008	,000	,001	,040	,005

* less statistical significance; **higher statistical significance

In his study, Schimatschek states that a relatively low intake of Mg and Ca from drinking water can be of significant importance for the prevention of Mg and Ca deficiencies (18), which was also confirmed by this research and the health effects of average water consumption less than 2 l were also taken into account.

This survey also confirmed the low intake of Ca and Mg in the food as risk factors for IHD as well as known risk factors for cardiovascular disease: a hereditary predisposition to heart disease, smoking and fat intake. Using a binary logistic regression analysis it was shown that the greatest influence on the occurrence of IHD, out of all investigated risk factors, is due to the magnesium from water (equivalent to Ca from the water - a protective factor, $p = 0.000$), magnesium from food (protective factor, $p = 0.000$) and fat (factor risk, $p = 0.000$) (table 3).

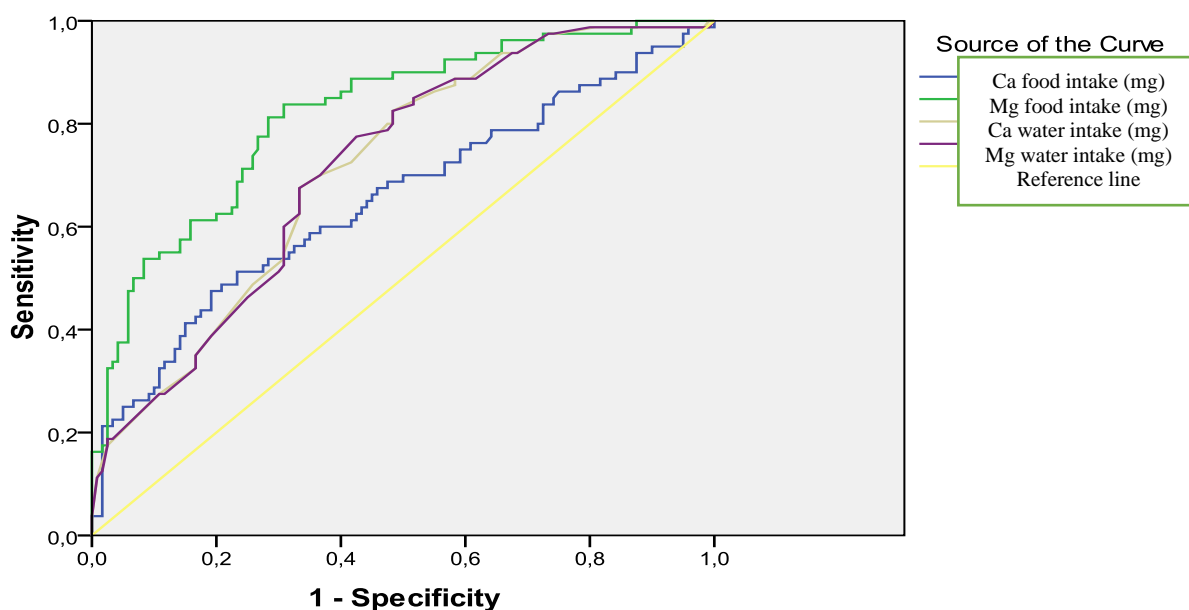
Table 3. The predicative modelling of different risk factors of IHD (binar logistic regression)

Predictors	B	Standard error	Wald	Degree of freedom	p	Exp(B) [OR]	The lowest level 95%CI	The highest level 95%CI
Family history of heart disease	1,928	,599	10,373	1	,001	6,873	2,149	22,554
Smoking status(duration)	,088	,028	9,630	1	,002	1,092	1,033	1,154
Mg -food intake	-,033	,007	21,315	1	,000	,967	,954	,981
Ca –water intake mg	-,040	,010	15,911	1	,000	,961	0,942	0,980
Mg –water intake mg	-,430	,108	15,814	1	,000	,650	,526	,804
Fats g	,057	,014	16,052	1	,000	1,058	1,030	1,088
Proteins g	-,060	,020	9,482	1	,002	,942	,906	,978
Constant	6,004	2,082	8,319	1	,004	404,934		

In the prospective cohort study, in which a large number of subjects with IBS was observed for a relatively long period of time (12 years), the inverse relationship between magnesium intake and IBS risk was confirmed. The negative correlation was determined not only for magnesium from water and food, but also for magnesium supplements (19). The second cohort study which included 13922 men and women who were monitored for 4 to 7 years has confirmed the protective effect of magnesium (20).

Even though many studies have favored Mg (21) as the main protective element of hard water for IHD, Rylander in his most recent study has concluded that Mg and Ca have to be taken into account together, as the analysis of many epidemiological and experimental studies has shown that the risk of death from cardiovascular disease was associated with both the content of Mg and the content of Ca (22).

From the aspect of prevention of IHD, the ROC analysis has shown that it is necessary to add per day for at least 75 mg of Ca and Mg 7 mg from drinking water and 802 mg of calcium and 260 mg of Mg from food intake (graph 1, table 4).



Graph1. The protective amount of Mg and Ca (food and water intake) for IHD

Table No. 47. The protective amount of Mg and Ca (food and water intake) for IHD

Test results	The area below the curve	Standard error	p	The boundary level (IHD is positive if \leq)
Ca –food intake (mg)	,653	,041	,000	802,86
Mg –food intake (mg)	,820	,030	,000	260,33
Ca-water intake (mg)	,715	,036	,000	75,7
Mg –water intake (mg)	,716	,036	,000	6,87

These minimum daily protective amounts of Mg and Ca from drinking water are consistent with the results of many studies (23-25) and can be used to make the final conclusion about the minimum concentrations of these minerals in drinking water in order to prevent IHD.

The results of this study have shown that the degree of hardness of drinking water in the central water supply systems should increase to the optimal 18⁰ dH- 20⁰ dH. The new legislation of laws should include water hardness, Ca and Mg in the regular assessments of drinking water and that would lead to an overall reduction of morbidity and mortality from cardiovascular disease.

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ORAL PRESENTATIONS

1.EFFECT OF AMBIENT AIR QUALITY ON OBESITY

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Objectives. Air pollution is a major adverse risk factor with serious consequences on human health, according to the World Health Organization (WHO). The aim of the paper is to review evidence related to potential impact of exposure to ambient air pollution on the overweight and obesity.

Methods. A literature search was conducted in the PubMed for peer-reviewed articles published until June 2019 that assessed the relationship between air pollution and body weight status.

Results. Nineteen studies, conducted in nine countries (including Serbia), met the selection criteria and were included in the review. In almost half studies (44%) , associations between air pollution and body weight status were reported. The reported associations varied by sex, age and type of air pollutant. Air pollution may lead to unhealthy body weight through metabolic dysfunction like increased oxidative stress and adipose tissue inflammation, elevated risk for chronic disease, and disruption of regular physical activity.

Conclusions. Concurrent evidence regarding the impact of air pollution on body weight status remains mixed. Overall evidence of air pollution being obesogenic remains limited.

Keywords: air pollution, obesity, associations

2.HEALTH EFFECTS OF AMBIENT FINE PARTICULATE MATTER (PM_{2.5}) IN SERBIA

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Objectives: The overall aim of this work is to estimate the health effects of ambient fine particulate matter (PM_{2.5}) in Serbia, specifically, quantify the mortality potentially associated with air pollution.

Methods: Exposure data for Serbia were obtained from European Environmental Agency. The population weighted average exposure in Serbia was 23.9 (SD 5.2) µg/m³. Health effects were assessed using population attributable fraction methods (PAF) for PM_{2.5} at national and district level. Deaths attributable to PM_{2.5} exposures were calculated in national level using WHO Global Health Estimates 2015 data for background natural cause mortality for 30+ years of age for Serbia and Health Statistical Yearbook of Republic of Serbia 2015 for mortality data in district level (not available for Kosovo).

Results: Lowest calculated PAF was in North Banat (10.0%) and the highest was in Kosovo districts (15.4%). Total of 13,600 (PAF=13.4%) deaths in Serbia in 2015 were attributable to air pollution. According to district the range of attributable deaths were from 206 (Toplica) to 2718 (Belgrade).

Conclusion: In total 13,600 deaths were attributable to PM_{2.5} exposure in Serbia. District distribution of PAF shows that the lowest PAF was in the north Serbia while the highest one was in the South.

Keywords: Particulate Matter, Mortality, Serbia

3.SPECIALIST IN PREVENTIVE MEDICINE – BACK TO BATUT AND STAMPAR

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Objectives: To present a new concept of specialization in preventive medicine adapted to the needs of European Union. This is necessary for opening chapter 28 in accessing negotiations of Serbia and EU.

Materials and methods: The basic EU document from 2016 describes specializations in community medicine in EU member states. With no exception, there is only one specialization in community medicine in each state.

Results: We present a new concept of specialization in preventive medicine with a four year training course. This holistic concept is based on the ideas and practice of professor Batut and professor Stampar in the Kingdom of Yugoslavia. One-year sub-specializations would be established in medical ecology, medical dietetics, health management, health education, epidemiology of communicable diseases, epidemiology of non-communicable diseases and medical statistics.

Conclusion: Serbia needs a new specialist in preventive medicine who would be capable of solving all basic public health problems. This is also necessary for a successful opening of the negotiating chapter 28 in Serbia's EU accession negotiations.

Keywords: preventive medicine, specialization, Serbia, EU accession negotiations

4.IMPORTANCE OF A HYGIENE SPECIALIST'S EXPERT OPINION IN AN ACCREDITED LABORATORY

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Objectives: The importance of expert opinion produced by a hygiene specialist is the interpretation of health safety of the analyzed sample.

Methods: The paper analyzes the data on the expert opinions of the specialist of hygiene. A negligible number of samples (less than 5%) are test reports without expert opinions.

Results: Center for Hygiene and Human Ecology IPH Nis, as an accredited testing laboratory according to ISO 17025, annually analyzes over 15000 samples of water and food. All samples were sampled by the Center's staff according to sampling plans prepared by the chief hygiene specialists. After the analyzes are made, the hygiene specialists make an expert opinion. Expert opinion is an integral part of the test report. The hygiene specialist applies an experiential and individual approach in the preparation of interpretations. Problems in the preparation of expert opinions arise when summarizing the health safety of a series of water samples, but also when evaluating facilities that do not have continuous monitoring by an authorized health institution.

Conclusion: Hygiene specialists are the backbone of an accredited laboratory. Expert opinion with the test report is the complete proof of health correctness issued by the authorized health institution.

Keywords: expert, hygiene specialist, accredited laboratory

POSTER PRESENTATIONS

1. RELATIONSHIP BETWEEN THE CHANGES OF ATMOSPHERIC PRESSURE WITH PATHOGENESIS OF DEEP VEIN THROMBOSIS OF THE LOWER EXTREMITIES

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Objectives: The aim of this prospective study was to examine the relationship between the changes of atmospheric pressure with the pathogenesis of deep vein thrombosis (DVT) of lower extremities.

Materials and methods: In this prospective clinical examination, there was a total of 153 consecutive lower limb DVT patients included. They were hospitalized or treated in the Clinic of Vascular Surgery, Clinical Centre of Niš.

Results: The results showed that an increase in atmospheric pressure was associated with an increased risk of developing TDV ($p < 0.05$), with a significant association with the location below the knee ($p < 0.01$) in group of patients under the age of 60.

In group of male respondents, an increase in atmospheric pressure was associated with TDV risk only with a locality above the knee ($p < 0.05$). However, the significant association was found in whole female group ($p < 0.05$) and in group of female respondents with locality above the knee ($p < 0.05$).

Conclusion: It is possible to conclude the connection of the change of atmospheric pressure with the incidence of DVT of lower extremities, as well as the association with age, sex and the localization of the thrombus.

Keywords: deep vein thrombosis, atmospheric pressure, etiopathogenesis

2. MONITORING OF ARSENIC IN ARTESIAN WELLS IN THE SREM AND NORTHERN MAČVA

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Objectives: Arsenic is one of the risk factors responsible for the onset of various diseases and has been shown to be carcinogenic in humans (IARC, 1a). The association between arsenic exposure and non-squamous lung, skin, kidney and bladder cancers has been demonstrated. Ingestion from drinking water, arsenic can lead to skin cancer (even content less than $300 \mu\text{g} / \text{L}$), as well as hyperpigmentation and keratosis (content less than $50 \mu\text{g} / \text{L}$), and arsenic in drinking water $\leq 50 \mu\text{g} / \text{L}$ may be associated with an increased risk of bladder and lung cancer. The determination of arsenic in drinking water in the territory of Srem and Machva has been carried out for the past 15 years. In the last two years from 2017. to 2019., the arsenic content of artesian wells has been continuously monitored in all settlements in Srem and in the northern part of Machva.

Methods: Arsenic content is determined according to the method of SRPS EN ISO 11969: 2009. (EN ISO 11969: 1996) Determination of arsenic content - Atomic absorption spectrometry method (hydration process). Results of arsenic content are expressed in units of $\mu\text{g} / \text{L}$.

Results: The total number of artesian wells in the inhabited places of Srem and Machva during 2017., 2018. and 2019, where the control of safety is performed by the Institute of Public Health Sremska Mitrovica is 67 wells. In the town of Sremska Mitrovica (20 wells), and the remaining 47 artesian wells are located in the following places: Macvanska Mitrovica, Zasavica II, Zasavica I, Ravnje, Radenkovic, Noca, Salas Nocaški, Lacarak, Martinci. Kuzmin, Sremska Raca, Sasinci and Veliki Radinci. At the 12 sites of the analyzed 67 values of arsenic content were exceeded, over $10 \mu\text{g} / \text{L}$. About 18% of the total number of artesian wells have arsenic content above the permitted value. In drinking water from artesian wells where values are elevated, values range from 11 to $120 \mu\text{g} / \text{L}$ arsenic, which is higher than the permitted value of 10% to 109%. The values of arsenic content in the water from other tested wells are from $2-10 \mu\text{g} / \text{L}$ As. WHO recommendations for arsenic in drinking water are, as in the regulations in force in the Republic of Serbia, $10 \mu\text{g} / \text{L}$ ($0,010 \text{ mg} / \text{l}$), Rulebook on the hygienic safety of drinking water, Official Gazette of the Federal Republic of Yugoslavia No.42 / 98 and 44/99.

Conclusion: It is necessary to continue monitoring the content of arsenic in drinking water and to monitor the trend of the population disease in places with high values of arsenic content and to signal if the values are higher than allowed. The suggestion for the next period is also to start, with the analysis of arsenic content in drinking water, the measurement of arsenic content in the urine of the population drinking water from areas with elevated arsenic values as well as the population where arsenic is in quantities below $10 \mu\text{g} / \text{L}$.

Keywords: Arsenic, drinking water, lung cancer, skin cancer

3. EXPOSURE TO ARSENIC IN DRINKING WATER AND BLADDER CANCER

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Introduction: Municipality of Bogatić, part of Mačva district, belongs to the Pannonian Basin, in whose territory were detected high concentrations of arsenic in artesian wells. Numerous epidemiological studies have confirmed the association of exposure to arsenic in drinking water and bladder cancer (C67).

Objectives: Retrospective analysis age-standardized incidence rates (ASRs) and age-specific incidence rates of C67 in Bogatić municipality and rural municipalities of the Mačva district.

Material and methods: The concentration of arsenic in drinking water in Bogatić municipality, was determined by laboratories of Public Health Institute (PHI) Šabac in 2015. ASRs were estimated using data from regional cancer registries the PHI Šabac and compared with Mann-Whitney U test. The control population was from an area, where there were no artesian wells or hydrogeological conditions which would indicate elevated concentrations of arsenic in drinking water.

Results: Arsenic values in all artesian wells in Bogatić municipality were 1.4 to 41 times greater than maximum permissible concentration (average $120\mu\text{g}/\text{l} \pm 165\text{SD}$). Among females ASRs of C67 was higher in Bogatić municipality compared with populations in rural municipalities Mačva district ($p < 0.01$) and bladder cancer incidence was 13% greater than that of the Central Serbia (SIR=113; 95% CI=96.97-131.35). Among males ASRs of C67 was higher in Bogatić municipality, but not statistically significant ($p > 0.05$). Our analyses suggest exposure of arsenic in drinking water can triple the risk of bladder cancer.

Conclusion: These results support the conclusions of previous studies that an association there may be between higher concentrations of arsenic in drinking water and higher ASRs of bladder cancer among males and females.

Keywords: Arsenic, drinking water, bladder cancer

4. WELL WATER ANALYSIS IN 2013-2019 IN ALEKSINAC MUNICIPALITY

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Objectives: Comparison of the Regulations on the healthfulness of swimming pool water (Official Gazette of RS, No. 30/2017), according to which the number of parameters is reduced with the Ordinance on hygienic correctness of drinking water (Official Gazette of FRY, 42/98 and 44/99).

Material and methods: Since the adoption of the new rulebook in the Sanitary Chemistry Division, 484 samples of pool water have been analyzed. For chemical analysis, accredited methods were used and the frequency of monitoring and analysis was once a week during the bathing time period.

Results: Out of 484 samples of pool water, 156 showed chemical defects: 108 at increased pH, 1 at reduced pH, 23 at increased consumption of KMnO_4 , 13 at increased chloride concentration, 7 at increased residual chlorine concentration, 3 at turbidity and one at an increased concentration of Trihalomethane. In 14 samples there were two parameters of chemical malfunction, and in 4 causes 3 chemical defect parameters.

Conclusion: The adoption of the Rulebook on the healthfulness of pool water has diminished the problems that existed in the previous period as a result of inadequate preparation and treatment of water by various disinfectants.

Keywords: Pool water, pH, residual chlorine.

5. PROPER CHOICE OF METHOD FOR AIR POLLUTION ASSESSMENT

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Introduction: For the proper assessment of air pollution, accurate data obtained by precise methods should be available. That is why it is important to choose the right method for analyzing air pollutants.

Aim: District heating was completed in the city center. The aim is to determine which of the two methods shows a more realistic state of air pollution.

Material and methods: During the 14 months of 2017-2018. The ambient air condition was analyzed using two methods. The soot mass concentration was measured reflectometrically and evaluated according to the Regulation on monitoring conditions and air quality requirements. The PM10 particle concentration was measured according to the requirements of standard SRPS EN 12341: 2008.

Results: Test results show that in the downtown district heating conditions, the presence of soot exceeds the allowable concentration in rare sporadic cases. On the other hand, measuring the presence of PM10 particles further results more significantly. These particles are often present in the downtown air for most of the year.

Conclusion: When selecting indicators that show air quality, the correct choice of method to be applied for real-time analysis must be made. Under the conditions of city heating, classic air pollution parameters, such as the presence of soot, do not give a realistic state of air, unlike the new recommended parameters such as PM10 particles.

Keywords: PM10, soot, method selection.

6. OCCUPATIONAL EXPOSURE TO NICKEL IN METALLURGICAL PROCESSES AND ITS ADVERSE HEALTH EFFECTS

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Objectives: In metallurgical processes such as electroplating, alloy production and stainless steel occupational nickel poisoning can occur after long-term exposure to nickel by inhalation or ingestion, which makes it necessary to study its toxic effects. One of the most important route of human exposure to nickel is inhalation which has long been known to cause acute respiratory symptoms, ranging from mild irritation and inflammation of respiratory system to an increased risk of respiratory cancer in workplaces. Given that the exposure to high levels of nickel in biological materials is an important indicator of the toxicological risk, we performed the statistical analysis of the association of age and length of service and nickel concentrations.

Methods: The applied analytical method type is that of retrospective epidemiological cohort study covering the period of ten years. We used data from the annual reports of social medical services and statistics, data from medical records of both primary and specific occupational health care as well as records of the Institute for Workers Health Care and the Public Health Institute in Nis. Using atomic absorption spectrometry, we conducted the analysis of the concentration of nickel in biological material.

Results: The level of nickel in blood and urine of exposed subjects during the time of study was positively correlated with age ($r=0,770$, $p<0,01$ i $r=0,713$, $p<0,01$) and the exposed length of service ($r=0,840$, $p<0,01$ i $r=0,805$, $p<0,01$, respectively).

Conclusion: These data confirm the association between occupational exposure to nickel as well as the age and length of service exposed and point to a response to the consequences of harmful effects. A retrospective cohort epidemiological study showed that the systematic effects of nickel exposure result in an increase of its concentration in biological material, thus confirming the hypothesis of high toxicological risk.

Keywords: nickel, metallurgical processes, occupational exposure, adverse health effects.

7. SIGNIFICANCE OF URBAN GREEN SPACE (UGS) PLANNING FOR COMMUNITY HEALTH

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Objectives: Considering of UGS public health significance and necessity of obtained evidence implementation in practice.

Methods: Literature review, done by search of newer literature in paper and electronic form.

Result and conclusion: There are recent robust evidence about positive influence of high UGS exposition on diabetes, diastolic blood pressure, salivary cortisol, heart rate, HDL cholesterol, all-cause and cardiovascular mortality. Physical activity increases the effects: eg. gardening (individual/community) decreases depression, anxiety, stress and obesity, improves cognitive function, social relations, provides healthier diet.

Main function of UGS: reducing harm (noise, heat, air pollution, seasonal affective disorder), restoring capacities (attention restoration) and building capacities (encouraging physical activity and facilitating social cohesion, synthesis of vitamin D, development of immunological system).

Physical activity in a natural outdoor environment has been associated with reduced negative emotions and fatigue, increased energy and a greater intent to repeat the activity.

There is urgent need to improve the communication and common actions of policy creators, community and public health analysts in evidence-based urban health planning.

It is necessary to animate the health policy creators in order to generate, maintenance and promoting of available UGS.

Keywords: urban green space, community, health, planning

8. NOISE ANNOYANCE IN RESIDENTIAL AREAS IN NOVI SAD, 2012-2016

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Objectives: The aim of paper is to quantify the annoyance of the population in the residential areas in the City of Novi Sad (RA-NS) using environmental noise data, in the first place by road traffic noise. It is important for perceiving the noise impact on the human health.

Methods: Public Health Institute of Vojvodina taken 26 24-hour noise measurements on one measuring spot in RA-NS, during 2012 – 2016.

Results: Daily noise indicator (L_{day}) ranged from 54,6 dB to 70,1 dB, evening noise indicator ($L_{evening}$) from 51,2 dB to 60,0 dB, night noise indicator (L_{night}) from 47,2 dB / 50,7 dB, while total noise indicator (L_{den}) ranged from 58,0 dB to 67,6 dB. Relative to limit values, there were increased 92% of L_{day} , 38% of $L_{evening}$ and 100% of L_{night} . Relative to results, the percentage of highly annoyed population (%HA) amounts 11% during the day and 6% during the night, while prevalence of population highly annoyed (PHA) is 11% - more specifically in the range 9,2-33,9%.

Conclusion: The results confirm that urban noise annoying population in the residential areas. and, in conclusion, that fact is the challenge, the problem and the topic for the public health system.

Keywords: noise, annoyance, population

9. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY ANALYSIS OF OF TRYPTOPHAN STABILITY IN AQUEOUS SOLUTIONS

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Objectives: Tryptophan is an essential amino acid which plays important role in synthesis of proteins and as precursor of many biologically active substances and coenzymes. Its metabolites are involved in the pathogenesis of several neurologic disorders. The human body cannot synthesize tryptophan and its synthesis is dependent on dietary intake. Because of nutritional and toxicological importance of tryptophan, analysis of its stability in aqueous solution is extremely important.

Materials and methods: Tryptophan dissolved in deionized water at the concentration level of 5 ppm was used throughout the study. These solutions were tested at ambient temperature, 8, 37 and 100°C during 15 min, 1 h and 3 days. The remaining tryptophan quantity was measured by high performance liquid chromatography (HPLC) with UV detector at 280 nm wavelength.

Results: The concentration of tryptophan in aqueous solution decreases at temperature of 37 °C and 100°C for from 5 ppm to 3.1 and 2.5 ppm respectively, for 1 h. Further analyses showed the smaller decrease at temperatures of 25 and acceptable stability at 4°C. The obtained results demonstrated continuously increase in the stability of tryptophan with decrease the temperature.

Conclusion: Our results obtained by HPLC method indicate that concentration of tryptophan in aqueous solutions decreases at ambient and much more at higher temperatures. Its storage in refrigerator with control of its concentration are mandatory for further experiments, which are underway.

Keywords: tryptophan, thermal stability, HPLC

10. CAPACITY OF EXTRACTS FROM CHESTNUT LEAVES AND CATKINS TO PROTECT ERYTHROCYTES EXPOSED TO HYDROGEN PEROXIDE FROM HEMOLYSIS

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Objectives: Erythrocytes can be exposed to excessive amounts of hydrogen peroxide under various pathophysiological conditions. In the present study, we examined the chemical composition and the ability of chestnut extracts to protect erythrocytes membrane from hemolysis.

Materials and methods: Leaves and catkins from sweet chestnut (*Castanea sativa* Mill.) were extracted by 50% ethanol as a solvent. The chemical composition of extracts after methanolysis was analyzed using HPLC/DAD and LC/MS. Level of hemolysis provoked by 3 mM H₂O₂ in the presence of chestnut extracts was measured spectrophotometry.

Results: Methyl gallate, dehydrodigallic acid dimethyl ester, ellagic acid, and valoneic acid dilactone methyl ester represented the main compounds in all chestnut extracts after methanolysis. Concentrations of ellagic acid or its derivatives were higher (139.2 mg/g) in leaves extract compared to catkins extract (83.8 mg/g). On the other hand content of gallic acid derivates and flavonoids were higher in catkins extract, 116.9 and 34.9 mg/g respectively. Both extracts protected erythrocytes from hemolysis.

Conclusion: Many of the biological functions, such as antimutagenicity, anticarcinogenic, and antiaging, among others, originate from antioxidant activity. The polyphenol-rich extracts of chestnut can be beneficial in dieth and therapy to decrease negative effects provoked by oxidative stress.

Keywords: Chestnut extracts, catkins, leaves, chemical composition, hemolysis.

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11. ADDITIONAL SOIL TESTING FOR REMEDIATION AND RECULTIVATION PROJECTS

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Objectives: When the values of some parameters in soil exceed limit and remediation values, it is necessary to undertake additional testings to determine the pollution and to decide on the necessity of performing remediation and recultivation projects. This paper presents the results of the basic and additional soil testings on the location of future residential-business complex with historical contamination.

Materials and methods: Sampling and laboratory testing were performed by accredited methods.

Results: The results of 8 tested samples of the 1st serie have shown the exceedance of certain parameteres (lead, cadmium, zink, copper, nickel, cromium, cobalt, barium, polychlorinated byphenils and total carbohydrates C10-C40). Concentrations were above limit values, and only the concentration of zink exceeded remediation value as well, which was confirmed by additional testings.

Conclusion: Although the concentration of zink exceeded remedion value, it was concluded that there is no need for remediation and recultivation projects.

Keywords: soil, additional testings, remediation, recultivation.

12. ELECTRO-OXYGENATED WATER AS A BIOCIDES IN PREVENTIVE MEDICINE

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Electro-oxygenated water (EOW) is new generation disinfectant that works on the basis of withdrawal of electrons from the environment in which microorganisms persist. So it physically destabilizes microorganisms and causes their destruction. Advantages of using electro-oxygenated water as disinfectant is that it does not create resistance, no residue on surfaces, it is not necessary to remove from the surface after disinfection, leaves no residue in the wild and we didn't find any cytotoxic effect on cell culture. Due to its characteristics, this disinfectants can be used in preventive disinfection and in the disinfection related to infectious diseases.

Keywords: electro-oxygenated water, electrolyzed oxidizing water, disinfection, decontamination, bio safety

SESSION: THEORETICAL AND PRACTICAL PROBLEMS OF COMMUNICABLE DISEASES

INVITED LECTURES

1. KNOWLEDGE, ATTITUDES AND BELIEFS OF PARENTS TOWARDS CHILDHOOD VACCINES AND VACCINATION

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Introduction. Childhood vaccinations are the most effective medical interventions to prevent severe complications, disability and death of infectious disease. Despite of all known achievements of vaccinations many parents make a permanent decision not to vaccinate their children with one specific vaccine or with several. Decreasing the vaccine coverage is serious challenge for public health in the 21st century.

The objective of the study was to identify knowledge, attitudes and beliefs of parents towards the uptake of mandatory vaccinations for healthy pre-school children.

Material and Methods. Cross-sectional study was carried out among a randomly selected sample of pre-school children and their parents. Pre-school children aged from 2 to 6 years were from 9 state kindergartens from the area of the city of Niš. Anonymus questionnaire specially prepared for this study was delivered to the parents. The questionnaire was self-administered and had 20 questions about knowledge, attitudes and beliefs towards childhood vaccines and vaccination. The study was done in 2011. Immunization status of pre-school children was assessed by vaccine records.

Results. The total number of 751 of parents completed the questionnaires (751/1100). Response rate was 68.3%. We found that the main sources of vaccine information for parents were magazines 87.2% and the Internet 6.1%. Out of all parents, 4.5% asked their close friends about vaccinations and only 2.2% got information from the medical staff. Good knowledge about mandatory vaccines for pre-school children had 67.0% parents, bad knowledge had 32.2% and only 0.8% didn't know. Good knowledge about side effects of vaccines had 72.0%, bad knowledge had 27.5% and 0.5% didn't know. Opinion that vaccines are always dangerous had 3.0% of parents, opinion that vaccines are sometimes dangerous had 61.0% and 36.0% didn't know. The most resistance and fear of side effects parents showed to the measles-mumps-rubella (MMR) vaccine, more than 50.0% of parents.

Conclusion. Most of parents had good knowledge about mandatory vaccinations of pre-school children and their possible side effects. Better communication with the medical staff in the future is needed. Educational programs for parents are need, too, in aim to increase their knowledge about vaccinations.

Keywords: knowledge, attitudes, beliefs, parents, vaccination

2. INFLUENCE IN THE CENTRAL KOSOVO AND METOHIJA

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Introduction: Flu, or influenza is a contagious disease primarily involving the respiratory tract (RT) and is caused by the family Orthomyxoviridae influenza virus. The new H1N1 strain of type A influenza virus is the most dangerous one since it is a mutation of human, swine and avian flu. The main route of infection of the AH1N1 virus is from an infected person, by airborne droplets during speaking, coughing or sneezing. It can also be transmitted indirectly via contaminated hands caused by touching everyday objects containing droplets and secretion from the nose and throat (1). The symptoms of AH1N1 influenza virus include high body temperature, pain behind the breastbone, runny nose, sore throat, muscle pain, headache, irritating cough, and fatigue. The symptoms develop two days after being exposed to the virus and last less than a week. Cough, however, can last more than two weeks. The warning symptoms of a severe course of the disease include deterioration of mental status, high body temperature during the first three days and low blood pressure as well (2). Influenza-associated complications can be viral and bacterial ones: sinus infections, chronic otitis, viral pneumonia, secondary bacterial pneumonia, deterioration of previous medical problems. This type of influenza may result in other bacterial complications, such as: pneumonia and bronchitis, muscle cramps, septic shock, Reye's syndrome (severe brain inflammation), inflammation of the cardiac muscle, Guillain-Barre syndrome (Neurological disorders) and brain damage (3).

Aim of the paper: the aim of the paper was to examine epidemiological characteristics, clinical course of the disease with the development of complications in patients affected by influenza and living in Serbian enclaves of central Kosovo.

Material and methods: The study enrolled 144 patients, 24.9 % children and 75.1% adults. The study was conducted in the period October 2018 – May 2019. Enclaves are territories with multiethnic populations, including Serbs, Ashkali, Albanians, Gorani, Bosniaks, Turks and other ethnicities. The diagnosis was established according to epidemiological and clinical parameters and laboratory test results as well. In two children transported to the Clinical Hospital Center Kragujevac, and in two adults transported to Clinical Hospital Center Niš, the strain H1N1 type A was isolated in nasopharyngeal swab specimens. The patients were grouped according to gender, age, ethnicity, and complications as well. Numeric and descriptive characteristics are shown. The Student's t-test, the Chi square test X^2 and Fischer's exact test were used for data illustrations.

Results: Mean age for children was 10.52 ± 4.7 , and for adults 51.34 ± 15.73 years. The children were grouped in 5 age groups: younger than 4 years, between 5 and 9, between 10 and 14, and between 15 and 18 years of age. The adults were categorized into 3 age groups: between 40 and 44 years, between 45 and 60, and those over the age of 61. The majority of patients were among the Roma children, 49.1 % of them, and Serbian children, 32.4 %. There were 88.1% of unvaccinated Serbian children. Roma children, as well as children of other ethnicities were 100% unvaccinated. According to ethnicity, unvaccinated adults include 100% of Roma patients, 79.9 % of Serbian patients, and 14.1% of Gorani and other ethnicities. The paper showed that 6.6% of medical professionals were affected by influenza. Roma people were two-fold and five-fold more affected in comparison to Serbs and other ethnicities (X^2 test, $p < 0.05$ %). The majority of patients was recorded in January, February and at the beginning of March. Most of the children presented mild clinical manifestations, 65.9 % of them, while 9.2 % developed complications (T test, $p < 0.05$ %). Complications

were mostly developed in children aged 3 – 10 years. Most common superinfections in children were otorhinolaryngologic ones in 67.5 % of children. Superinfections in children included angina (17.7% of them), sinusitis (19.2%), otitis media (17.2 %) laryngitis (36.7%); interstitial pneumonia and bacterial pneumonia. Statistically significant difference was between the incidence of interstitial pneumonia in 11.7 % and bacterial pneumonia in 5.4 % of children (T test, $p < 0.05$ %). As for the adults, even 69.2% had severe clinical course with the development of complications and superinfections. Superinfections in adults included: angina 13.4%, and tracheobronchitis in 65.7% of patients. They were up to 43 years of age, vaccinated in 13.1 %, and unvaccinated in 2.5 % of cases. Other patients, aged between 44 and 74 years were with comorbidities. There were 21.7% unvaccinated adults aged between 25 and 43 years, with complications developed in otherwise healthy people. The most common complications in adults included pneumonia, in 64.2 % of them, interstitial pneumonia in 16.8 %, and bacterial one in 57.3 % of adult patients (T test, $p < 0.05$ %). Statistically significant difference was between the number of patients with complications of lower (61.1 %) and upper RT (25.3%) (X^2 test, $p < 0.05$). Patients aged 44 - 74 years, with 4 or more co-morbidities, had severe clinical course and complications. Interstitial pneumonia was recorded in 21.3% of adult patients. Encephalitis was developed in 3.1 % of them, and one patient developed transient ischemic attack on the brain and hemiparesis. In 6.1 % of adults, the outcome was lethal due to ARDS and progressive respiratory failure.

Discussion: Our study enrolled 144 subjects affected by influenza. It unofficially revealed that the main cause of influenza outbreak in central Kosovo was attributed to persons from Serbia regularly travelling to Kosovo. There were infected medical professionals among them, as well as people of other occupations. The paper showed that 6.6 % of medical professionals were affected by influenza. A person is infectious before and during the disease. Infectiousness is highest as the symptoms develop and usually lasts 5 days (up to 7 days in children) (4). The greatest concern regarding this virus arises from the fact that it is a new virus and humans have no or minimally developed immune response to it (IR) (5). In 2.7 % of patients the virus was proved at the “Torlak” Institute. Similar to our results, Hsu J et al. showed that one out of every five persons that gets a new strain will have no symptoms, but they will transmit the virus to other people (6).

It means that between 15 and 20 % persons may be infected by this new influenza virus AH1N1, without being aware of it, thus increasing the risk of spreading in a flu season. In 2 children and 2 adults a strain of influenza virus H1N1A was confirmed in large clinical centers. In 1918/19 influenza pandemic was recorded as the deadliest pandemics in mankind. By the end of 20th century there were two more influenza pandemics, but none reached the number of patients, development of complications and lethal outcomes as the one from 1918-1919. Modern living conditions and fast pace of life result in much more rapid transmission of the disease across the world (7). In accordance with this, there was a pandemic infection caused by a new influenza virus A (H1N1) in Vojvodina in 2009. International travelling contribute to the speed and global spreading of the infections. In our study H1N1 strain was isolated in sputum specimens in 4 patients. In 2009 H1N1 was found in the sputum of the patients by using the PCR method, as seen in the paper by Tabla Vo (8). In our study the majority of influenza patients were in the period January-February, influenza outbreak in the territory of Kosovo.

Contrary to our study, the majority of patients was in November and December in other parts of Serbia. There was a statistically significant difference in the number of patients, development of complications and lethal outcomes between the patients from Kosovo in comparison to other regions of Serbia (9). Our study showed that there were 85 children with influenza-like symptoms in that period. The majority of them (38.5%) got affected at the age

3-14, as revealed by our results. According to the data from the “Batut” Institute, there were 3508 (44.3%) affected children on the territory of Serbia in 2018/19. These data revealed that the majority of affected children (465.6 %) were under 4 years of age. Our study showed that 75.1% of adults were affected. Similar to our results from the territory of Serbia, the number of patients monthly increased in the first 3 months. In accordance with the results from other parts of Serbia, the number of adult patients increased with age (9). Our study also revealed that mild respiratory symptoms were noticed in upper RT in children. The study by Wang YH et al had a similar course of the disease in children, just like in our study. Similar to our results, low activity of influenza virus was noticed in children, with mild manifestations of the ENT tract, such as a short-term increase in body temperature and a milder course of the disease (10). Contrary to our results, Wang YH showed in his study that, apart from the virus type A, adenoviruses and parainfluenza viruses were isolated from sputum in children. Children were under health surveillance in this study. Similar results were found in a large study in the USA (11). A paper by Dillatinka Ch revealed that children affected by influenza virus A, along with influenza virus B, and strains H1N1 and H5N1, had gastrointestinal symptoms more frequently, primarily diarrhea syndrome (12).

Contrary to our study, Hammitt LL showed in her paper that children in Great Britain presented severe otorhinolaryngological infections (ENT) and superinfections of upper RT. Manifestations of the ENT tract were caused not only by influenza virus A, but also by adenovirus, influenza coronavirus, parainfluenza virus and syncytial virus. Manifestations in lower RT caused by influenza virus type A, type B and type C, and bacterial (mycoplasma, chlamydia) infections presented severe clinical course in the majority of hospitalized children, with the development of complications. Complications developed in hospitalized children and in children with comorbidities. Superinfections resulted in severe clinical course in most of hospitalized children, with severe central cyanosis as a consequence (13). Children who were affected most belonged to Roma and Serbian populations, compared to other ethnicities. These children were immunocompromised, unvaccinated, and with comorbidities.

There were 69.1 % adult patients in this study. Similar to our results, the number of patients increased in the first three months on the territory of Serbia. Mean age of adult patients was 51.34 ± 15.73 years. Similar results were obtained in a study by Bolotin Sh (14). Mean age was about 40 years and it increased with pandemic spreading among adults. Also, as in other regions in Serbia, the number of adult patients increased with age (9). Among the adult patients there were two-fold and a half more Roma patients, which is statistically significant. Unlike our results which showed respiratory manifestations in 69.1 % of cases, Chien YS showed in his paper that in Taiwan there were manifestations in other systems - cardiologic, neurologic, gastrointestinal. Almost the same number of patients was in Taiwan and in our study. Unlike our results with 44.1 % of otorhinolaryngologic and respiratory manifestations, Chien YS reported in his paper that in Taiwan mild manifestations of RT were recorded, but also severe manifestations of other organ systems: cardiologic, neurologic, gastrointestinal systems. Complications of RT and other systems were caused by H1N1 and H3N2. In the paper of Chien YS, there were 55.1 % lethal outcomes (15). Complications were significantly more developed in adults aged between 54 and 74 years in Roma populations, (56.4 %). Similarly, in a study by Meury S, et al., more complications were noted in adult patients aged over 60 and with comorbidities (16). Pneumonia was registered in 62.7% cases of adult patients aged up to 43 years of age. In older population over 54 years, mostly Roma patients (48.1%), pneumonia developed in 69.3% of them. Unilateral pneumonia was registered in 45.2 % of cases. Bilateral pneumonia developed in 20.1 % of cases. In 6.1 % of cases with bilateral pneumonia, ARDS developed, with progressive respiratory failure. Similar to our study, Yang SG showed that there were a lot of adult patients with pneumonia in China (17).

Lethal outcome was registered in 4.4% of cases. Unlike our study, in a paper by Sellers SA it was shown that there were a lot of extra-pulmonary complications. Hagan RS, Hayden FG, Fischer WA 2nd. In Serbia, medical monitoring of acute respiratory distress syndrome (ARDS) registered a total of 34 cases (35 %) (9). In the paper there were 79.9% unvaccinated Serbian patients, while Roma and patients of other ethnicities were 100% unvaccinated. Fleming DM proved that immunization should be implemented for prevention in children over 3 years of age, in adults with weakened immune response, in pregnant women and new mothers. In accordance with this, the USA, Great Britain (2013/2014), and Finland (2015/2016) developed a universal pediatric influenza vaccination programme (18,19).

Conclusion: In the region of central Kosovo, health-care education regarding vaccination of all ethnic groups should be conducted. In this way a progressive spreading of the disease, clinical course of the disease and the development of complications can be prevented for infections caused by different strains of viruses.

Keywords : influenza, patients, complications, vaccination

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3. VASCULAR ACCESS RELATED INFECTIONS HEMODIALYSIS PATIENTS

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Abstract

Infections are common complications among patients on chronic hemodialysis. Catheter-related bloodstream infections (CRBSIs), exit-site infections, and tunnel infections are common complications related to hemodialysis central venous catheter use. The most common causative pathogens are gram-positive bacteria, with *Staphylococcus aureus* and coagulase-negative staphylococci accounting for 40% to 80% of CRBSIs. Gram-negative organisms cause 20% to 40% CRBSIs, whereas polymicrobial infections (10%-20%) and fungal infections. Catheter-related infections (CRIs) are regarded as the most serious complication of CVCs with a significant increase in morbidity and mortality, and substantial cost implications. CRIs are classified into local infections such as exit-site and tunnel infections, and systemic infections referred to as catheter-related blood stream infections (CRBSI). Clinical manifestations of CRIs are dependent on whether the infection is localised or systemic. The onset of fever and chills, particularly during a HD session, should be considered to be a catheter infection unless proven otherwise. Treatment of CRIs consists of antibiotic treatment with or without catheter removal. antibiotic lock therapy for treatment have varied in the types of antibiotics and concentrations used, the addition of heparin to the solutions, and dwell times in the catheter lumen

Keywords: Hemodialysis, Access, Infection

Introduction

Infection rates in patients on haemodialysis (HD) are more than 26 times higher than that of the general population [1], and more than 100 to 200-fold higher for specific organisms [2]. They are the second leading cause of hospitalisation and mortality in the dialysis population [3–5]. Sepsis-related death is 100 times greater in dialysis patients than in the general population.

For the patients on chronic hemodialysis treatments, a well functioning vascular access is one of the most important conditions for their good quality of life and long term surviving. Vascular access-related infections are one of the major causes of morbidity and mortality second only to cardiovascular disease. [6-9] Mortality rates attributable to vascular access related blood stream infections (VRBSI) among long-term HD patients vary from 12 to 25.9%. [7-9]

The type of vascular access determines the quality of life and the cost of dialysis treatment among end stage renal disease (ESRD) patients. [6-10] There are three principle forms of vascular access available for the treatment with haemodialysis in ESRD. These are arteriovenous fistulae (AVF), arteriovenous grafts (AVG) using prosthetic or biological material and also tunnelled or non tunnelled catheters placed in a central vein.

Many studies have shown the superiority of AVFs compared to the other forms of haemodialysis, but AVF placement should be arranged at least 6 months and AVG at least 6 weeks before the need for dialysis- Central venous catheters (CVCs) are still used in 40% of hemodialysis patients for various reasons, such as waiting for vascular surgery, maturation of fistula, lack of operable vascular anatomy, patient preference, or short life expectancy [12]. A primary barrier to native AVF creation is lack of timely referral. In Europe, 84% of new HD patients had seen a nephrologist for more than 30 days prior to ESRD compared with 74% in the US ($P < 0.0001$) [13].

Epidemiology

The use of central venous catheters as the access for hemodialysis has been associated with much higher blood stream infection (BSI) rates compared with AVG and AVF. The risk of BSI is higher for temporary untunneled catheters (UTCs) compared to permanent tunneled cuffed catheters (TCCs), table 1.

Table 1. **Infection rates according to type of vascular access** [14-20].

Vascular access type	Infection rates
Primary AVF	0.05 episodes/patient-year
AVG	0.2 episodes/patient-year
Untunneled CVCs (Temporary)	5.0 episodes /1000 catheter-days (Range, 3.8-6.5 episodes/1000 catheter-days)
Femoral	7.6 episodes/ 1000 catheter-days (>10% after one week)
Internal Jugular	5.6 episodes/ 1000 catheter-days (>10% after 2-3 weeks)
Subclavian	2.7 episodes/ 1000 catheter-days (>10% after 4 weeks)
Tunneled cuffed CVCs (Permanent)	3.5 episodes/1000 catheter-days (Range, 1.6- 5.5 episodes/1000 catheter-days)

AVF- arteriovenous fistula.,AVG- arteriovenous graft, CVCs-central venous catheters

Pathogenesis and Risk Factors

AVF related infections are uncommon. Infection can occur at anastomosis or cannulation site. The presence of aneurysms, infected thrombi or localized abscess formation increases the risk of fistula rupture and surgical intervention may be required to either salvage or tie off the fistula. There is a higher frequency of AVF associated infection with buttonhole cannulation, however there is no evidence that the use of the buttonhole technique should be discontinued. There is lack of evidence on the duration of antibiotic treatment for AVF infections but a course of antibiotics for six weeks has been suggested [21].

Arteriovenous grafts have the second highest rate of infection in dialysis patients and infection of an arteriovenous graft has a worse prognosis than infection of arteriovenous fistulae. Commonly, may be required surgical exploration, repair, drainage and/or removal together with a prolonged course of antibiotics depending on the extent of infection [22-23]. Failure to recognize graft infection may result in rupture of the graft.

Pathogenesis of vascular catheter-related infection involves interaction between several factors. Primary event is entry of microorganisms with subsequent colonization, multiplication and eventually dissemination in to the blood circulation. Skin and the hubs are the most frequent sources of colonization, and any types of CVCs (temporary TUCs or long-term catheters) may get colonized either through extraluminal (skin-related) or intraluminal (hub-related) routes. The catheter hubs are most often colonized through contaminated hands of dialysis personnel, through luminal colonization of the intravascular segment particularly in long-term catheters that are cuffed and/or surgically planted. For the temporary TUCs, the organisms migrate from the skin insertion site along with the intracutaneous segment, finally reaching the intravascular segment and the tip of the catheter. [24].

Nearly all catheters become colonized shortly following insertion, and the risk of infection is directly related to the quantitative level of organisms multiplying on the surface of the intravascular segment of the catheter. The organisms that adhere to the catheter surface maintain themselves by producing “extracellular slime”, a substance rich in exopolysaccharides, often referred to as fibrous glycocalyx or microbial biofilm. [25]. Bacteria embedded themselves in the biofilm layer, becoming more resistant to the

antimicrobial activity of glycopeptide antibiotics. [26,27]. They are less permeable to phagocytes and antibiotics as antibiotics can act only on the organisms located in the superficial regions of the biofilm.

Therefore, the factors related to immunological status of the host and the virulence of microorganism enhanced by the biofilm environment are the major determinants of the risk of CRBSI among patients on HD. [28].

The patients on long-term HD particularly the elderly and diabetic are at increased risk of *S. aureus* nasal carriage; The intravascular catheters become rapidly coated with some serum constituents such as fibrinogen, fibronectin and laminins that facilitate the attachment of Staphylococci to the foreign material of the catheter through microbial surface components recognizing adhesive matrix molecule (MSCRAMM) mediated mechanisms. [28-30]. Furthermore, *S.aureus* elaborates glycocalices, which promote the bacterial colonization and further spread of infection. CVC placement near the patient's nose and mouth, such as that occurs with subclavian or jugular vein catheters, exposes the patient's catheter exit site to the nasal drainage/discharge and infectious airborne droplets. Methicillin-resistant *S. aureus* (MRSA) may be transmitted in this mode. [31].

ESRD patients are known to suffer from impaired immune defence mechanisms, attributable to the larger proportions of elderly population with comorbid conditions such as diabetes mellitus, malignancy or malnutrition particularly related to uremia and HD treatment. [32-38]. Uremia and inflammation induced by HD filters can cause oxidative stress activation, apoptosis and reduced numbers of T lymphocytes leading to defects in the cell-mediated immunity. [35,36]. In addition, MHC class II analog protein (Map) expressed by *S. aureus* also attenuates the host's cell-mediated immunity by reducing T cell proliferative response to gram-positive bacterial infections. [38].

The high risk HD environment for transmission of nosocomial infections presents a pressing demand for extra skilful nursing care and high levels of hygiene and cleanliness. Understaffing plays a key role in the development of catheter-related blood stream infections CRBSI; the risk of infection has been reported to rise significantly, with nursing staff reduction below a critical level. [39,40].

Clinical manifestations

Patients with chronic kidney disease have impaired immunity and therefore may not mount the full inflammatory response. Mild symptoms include malaise and nausea, in the setting of a normal catheter exit site or tunnel, on physical exam. More-severe symptoms include high fever with rigors, hypotension, vomiting and changes in mental status. Older and more-immunocompromised patients might present with low-grade fever, hypothermia, lethargy, hypoglycemia, or diabetic keto acidosis

Catheter-related infections -CRIs are classified into local infections, such as exit-site and tunnel infections, and systemic infections referred to as catheter-related blood stream infections (CRBSI).

Exit-site infection is manifested by: redness or pain around exit site, purulent discharge at the exit site, and also, fever or rigors may/ may not be present.

Tunnel infection is manifested by redness or pain extending >2cm from exit-site along the subcutaneous tunnel, purulent discharge at exit site fluctuant collection along the subcutaneous tunnel and fever or rigors may be present.

Clinical definitions of *catheter-related blood stream infections* - CRBSIs are those where other sources of infection are excluded by patient examination and review of patient record, and finding of positive catheter tip cultures (if available) with the same organism as that seen on blood cultures.

When CRBSI is present, all or some of these signs may exist: fever with no other obvious source of infection, rigors (especially during dialysis), unexplained hypotension and/or the

patient is unwell or acutely confused. Signs suggestive of exit-site infection is usually present in non-tunnelled catheters but may be absent in patients with tunnelled catheters. Also, signs suggestive of deep seeding infections (endocarditis, osteomyelitis, septic arthritis)

Diagnosis of the Vascular Access-Related Infections

The onset of fever and chills, particularly during a HD session, should be considered to be a catheter infection unless proven otherwise. There are present malaise, fever, rigors, backache, altered consciousness, unexplained hypotension during HD and leucocytosis, and absence of evidence of other sources of BSI such as pneumonia, urinary tract infection and surgical wound infections. Blood culture may be positive for an organism recognized to be a frequent cause of VRBSI such as *S. epidermidis*, *S. aureus* or Gram-negative bacilli etc.⁸¹ Isolation of these microorganisms from the blood culture obtained from peripheral vein and the swab cultures taken from the site of the inflamed vascular access should generally be sufficient to make a working diagnosis of VRBSI. Positive blood cultures obtained from the catheter should be with the quantitative colony count at least four-fold higher than from a peripheral vein,

Bacterial Flora Associated with VRBSI

Gram-positive organisms are responsible for about 80% of catheter-related infections. Staphylococcal infections account for around 60% of infections. The remainder are due to enterococci and gram-negative rods. Rates of pseudomonas, MRSA and fungal infections are low.

Table 2. Bacterial flora commonly associated with vascular access-related blood stream infections.

Bacterial flora	Percentage
Gram positive cocci	52-70
<i>S. aureus</i>	21.9-60
<i>S. epidermidis</i>	8.8-12.6
MRSA	6-8-20.7
<i>Enterococcus faecalis</i>	2.4-8.0
Gram negative bacilli	24-26.7
<i>Ps. Aeruginosa</i>	2.3-15.2
<i>Esch. Coli</i>	10.4
<i>Acinetobacter spp.</i>	12.8
<i>Serratia marcescens</i>	1.2-2.3
<i>Klebsiella pneumonia</i>	6.4
<i>Enterobacter cloacae</i>	8.8
Polymicrobial	16.2-20

MRSA: methicillin-resistant staphylococcus aureus.

Treatment

Treatment of CRIs consists of antibiotic treatment with or without catheter removal. Because of the high prevalence of MRSA and gram negative pathogens, empiric therapy should include Vancomycin and an antibiotic with broad-spectrum gram-negative bacterial coverage. Antibiotic regimen should be modified as soon as the sensitivity reports are available. Linezolid should be reserved for treatment of vancomycin-resistant organisms. With these measures, outpatient management is feasible in greater than 80% of patients with catheter-related bacteremia

Because of the bacterial biofilm formation, treatment of catheter-related bacteremia without catheter removal is relatively ineffective .

Criteria to attempt catheter salvage: difficult to replace catheters, blood sterile in 48–72 h, no sign of tunnel infection, no signs of metastatic infection, microorganisms medically treatable and hemodynamically stable patient

Indications for catheter removal:

Non-tunnelled catheters: catheter has been in situ for ≥ 7 days (femoral catheters), or ≥ 21 days (Jugular or subclavian catheters), pus is present at exit site, patient has signs of systemic infection (Rigors, temperature $\geq 38^{\circ}\text{C}$ with no other obvious source of infection, hypotension, or patient is unwell and microbiology confirmed exit site infection or CRBSI.

Tunnelled catheters: patient is haemodynamically unstable, persistent pyrexia despite treatment with the appropriate antibiotics for >48 hours, tunnel infection with evidence of subcutaneous pus collection, confirmed CRBSI with organisms which are difficult to eradicate (Meticillin-sensitive Staphylococci aureus "MSSA", MRSA, Gram-ve organisms, Fungi). Attempted salvage of tunnelled catheters infected with MSSA or a Gram-ve organism other than Pseudomonas aeruginosa can only be considered if: 1st episode, the patient is responding to treatment, alternative vascular access is difficult, and the decision is authorised by the patient's consultant. Also, evidence of seeding infections such as osteomyelitis, endocarditis, abscess formation, etc., persistent signs of exit site or tunnel infection despite a complete course of antibiotic treatment. relapse of CRI defined as positive exit site culture or positive blood culture with the same organism within 2 weeks after stopping antibiotic treatment. CVC-related infections, recurrent CRI defined as episode CRI with the same organism more than 2 weeks after stopping antibiotic treatment.

Catheter replacement:

Non-tunnelled catheters: assess indication for catheter replacement, catheter replacement should be delayed until the patient is afebrile for ≥ 48 hours, new venotomy site should be used especially if there was an exit site infection, if urgent haemodialysis treatment is required whilst the patient remains febrile, an in/out femoral catheter approach should be adopted.

Recommendation is that never replace infected nor suspected infected catheter over guidewire.

Tunnelled catheters: catheter replacement should be deferred until the patient is afebrile for ≥ 48 hours after commencing treatment, new venotomy site should be used and new tunnel track should be created if the patient had exit site infection, in patients with tunnel infection, a new anatomical site should be used for catheter replacement, if urgent haemodialysis treatment is required whilst the patient remains febrile, an in/out femoral catheter approach should be adopted.

While the formation of a functioning AVF is the preferred vascular access, this is not easily attainable in all individuals, especially elderly patients on HD [41]. Furthermore it remains controversial whether CVCs are superior to AVFs among elderly patients undergoing dialysis with a recent study finding lower rates of catheter-related bacteraemia in elderly patients compared to younger patients [42–46].

Studies that have evaluated antibiotic lock therapy for treatment have varied in the types of antibiotics and concentrations used, the addition of heparin to the solutions, and dwell times in the catheter lumen. Reported success in small series ranged between 40% to 87% depending on the pathogen. Stronger evidence however is available for exchanging catheter over a guidewire

Temporary untunneled catheters can be used as a bridge access device while awaiting maturation of an AVF, and also in patients with severe comorbidities such as congestive heart failure and severe peripheral vascular disease. in those with inadequate vascular anatomy, in those with limited life expectancy, in the very elderly, and as a last resort in patients with multiple access failures.

Conclusion

All patients should have definitive vascular access (AV fistula or graft) before initiation of haemodialysis where possible. The rigorous implementation of standard infection control measures for hygiene and aseptic handling of the vascular accesses at all times would remain a key to minimize the BSI episodes and significantly improve the long-term HD outcomes.

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4. IMMUNIZATIONS, NATIONAL HEALTH, ANTIVACCINALISTS

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Summery

Vaccines have always caused controversy. This is not a new situation in the history of medicine through the ages. In the mid-19th century, after several smallpox outbreaks, the UK government passed a set of laws that introduced mandatory vaccination - first for babies but then for all children up to 14 years of age.

The offenders were subject to increasing penalties. These measures faced firm resistance and caused a series of unrest. This social unrest led to the formation of the Anti-Compulsory Vaccination League in 1867. Its founders were particularly concerned that they considered compulsory vaccination to be a blatant violation of their right to freedom of choice and freedom. Vaccines have made a strong contribution to public health both individually and socially and certainly economically, and therefore represent one of the greatest advances in medicine. What vaccines have achieved can best be illustrated by the following data: Smallpox eradicated, Polio (America, Europe, Western Pacific) - eliminated, measles (America, most of Europe) - controlled, in other diseases dramatically decreased - tetanus, diphtheria, pertussis, rubella, meningitis (caused by *Haemophilus influenzae* type b), meningitis (caused by *Neisseria meningitidis* serogroup C), liver cancer (caused by hepatitis B). Vaccines are also of great importance to the economy, as good organization and quality vaccines reduce hospitalization and the need for costly therapy, while reducing the lasting effects and limiting the long-term effects of the disease.

With the exception of clean drinking water, vaccines are the most effective way to reduce and prevent infectious diseases.

Keywords: immunizations, children, national policy, antivaccinalists

Introduction

Vaccines have always caused controversy. This is not a new situation in the history of medicine through the ages. In the mid-19th century, after several smallpox outbreaks, the UK government passed a set of laws that introduced mandatory vaccination - first for babies but then for all children up to 14 years of age. The offenders were subject to increasing penalties. These measures faced firm resistance and caused a series of unrest. This social unrest led to the formation of the Anti-Compulsory Vaccination League in 1867. Its founders were particularly concerned that they considered compulsory vaccination to be a blatant violation of their right to freedom of choice and freedom.

Vaccines have made a strong contribution to public health both individually and socially and certainly economically, and therefore represent one of the greatest advances in medicine. What vaccines have achieved can best be illustrated by the following data: Smallpox eradicated, Polio (America, Europe, Western Pacific) - eliminated, measles (America, most of Europe) - controlled, in other diseases dramatically decreased - tetanus, diphtheria, pertussis, rubella, meningitis (caused by *Haemophilus influenzae* type b), meningitis (caused by *Neisseria meningitidis* serogroup C), liver cancer (caused by hepatitis B). Vaccination can prevent 27 infectious diseases and group immunity leads to global protection. (1,2,3)

Vaccines are also of great importance to the economy, as good organization and quality vaccines reduce hospitalization and the need for costly therapy, while reducing the lasting effects and limiting the long-term effects of the disease. In addition to reducing epidemics, productivity is reduced (6,7). With the exception of clean drinking water, vaccines are the most effective way to reduce and prevent infectious diseases.

Objectives, methods

The aim of the paper is to determine, on the basis of relevant data and information, the root causes of the partial misunderstanding of the importance of immunizations in the public and the exclusivity of the anti-vaccine lobby. are epidemiologically descriptive, sociopsychological and economic-analytical methods.

Results

Vaccines have always caused controversy. This is not a new situation in the history of medicine through the ages. In the mid-19th century, after several smallpox outbreaks, the UK government passed a set of laws that introduced mandatory vaccination - first for babies but then for all children up to the age of 14. Violators were subject to increasing penalties. These measures faced with firm resistance and caused a series of riots. This social unrest led to the formation of the Anti-Compulsory Vaccination League in 1867. Its founders were particularly concerned that they considered compulsory vaccination to be a blatant violation of the right to choose and to freedom. "Vaccination is the impurity of some virus or poison in the blood, which often leads to serious malignant effects. It has been in fashion for over a hundred years, and most people have received it without question. Yet, there is a time when blind faith will embrace this medical dogma, "(From an essay by John Pitcairn, Jr. - John Pitcairn, Jr. - The Fallacy of Vaccination of 1911. John Pitcairn was a prominent industrialist in Pennsylvania and president of the Anti-Vaccination League of America.

Attitudes on higher quality immunity after natural infections, as well as some ambiguities in scientific settings about vaccines and the immune system, including the application of vaccines according to a strict prescription and the application of a strict protocol, as well as the fight against any objection to vaccines without considering the individuality of the organism and even the disease some of which are ill as well as the current state of the organism, have contributed to the increase in mistrust of vaccines.

The opinion is that in many vaccination cases, the benefit to the individual is small. However, the vaccine is a risk that is always borne by the individual. No one wants to be the person who bears that risk. When they see that there is a risk of the vaccine, many will more tolerate the risk of the disease because the disease is natural. Understanding risk is a strong motive for vaccination support (10). Public distrust of risk assessment and risk perception fueled by the media contribute to this. If we add to this pseudoscience and misinformation as well as evident conflict of interest, then the situation in the last ten years

the area may be seen as chaotic. This was certainly contributed by the lack of information in the general public, although there is scientific evidence in many studies. The evolution of the lack of information has produced misinformation about vaccine safety. More data - scientists reach consensus that data go "in support of hypothesis rejection" - that is, the association is probably accidental. However, parents who are convinced that scientists are wrong are trying to discredit scientists. The media describes the contradiction. Until scientific controversies are rarely reported and parents are confused. It is clear that the disease occurs when vaccine coverage fall (collective immunity reduced) .In the same time in the media and on social media suggests concerns about the unsafe vaccine. The media say there may be a problem. Some parents are confused. Still, because not all relevant and high-quality research has been done on specific situations, scientists will not say that the vaccine did not cause side effects because is insufficient information. It gives the impression of scientific uncertainty. it brings parents into a dilemma (14).

There is a lack of trust in institutions, especially the authorities. Questions to Ask When Reading Newspaper, TV Show, or Vaccine Internet Portal: Who wrote and why? (evaluate expertise and who the author is). To whom is the writing intended? Are the facts confirmed or inaccurate and sensational? Is the information current? Is the information biased, or did the author use the time to represent only one particular view?

When public / public health says - something is safe, what does it mean? How do health officials decide - something is safe? What is the trust in experts? Public health and the public speak different languages. In part because of different understandings of the risks and benefits of vaccination - society and How can we make people believe in scientific explanations? We must learn to speak the same language, or we must believe that the expert knows what the layman does not know. Formation of communication between experts and the public - trust in our own experts (after all, politicians have made us not believe when they speak, so the nation also transfers to experts, but there are few experts among politicians). It is about explaining to the nation what the health goal is. Explaining that every visit to the doctor - consent to a doctor to help us - is not required (12).

So, it appears that resistance to vaccination is primitivism, but it is first and foremost an introduction to new epidemics. Despite the intense pressure of the anti-vaccine lobby, the U.S. Supreme Court ruled in *Jacobson v. Massachusetts* that the need to protect public health outweighs the right to privacy except for religious reasons (13).

The Internet as an opportunity for a communicator on health can be very significant and an opportunity for the health of a communicator. But information seekers seek consequences in the first place. Only half seek the likelihood of information. The advantage is given how something came about and not how likely it is. narrative information. (Betsch & Renkevitz, 2009). Parents want to know how vaccine adverse events are happening and not whether it's likely. People are looking for stories, especially when it is assumed (the story) that the risk of vaccines is high. Tales or narratives are easy accessible through social networks. A output is in need of more exploration of settings that assess the real impact of the information obtained - rather than collecting self-reports of "relevance" on the Internet. As a consequence of internet search information, there is a need for long-term surveys to evaluate the development and change of perceptions of vaccination risk (5).

Conclusion

Recommend as an attitude derived from the doctrine of medical science to all physicians - Get to know preventable infectious diseases.

To develop awareness of additional risk factors for particular diseases, to understand the pathophysiology of the disease and the mechanism of action of vaccines, not to blindly apply protocols and to incorporate into their knowledge the decision to vaccinate a healthy person or patient.

It is necessary to integrate one's own experience with the experience of colleagues. "The safety signal" is not proof that the vaccine is the cause, to look at the facts, to gather evidence and to send it to the experts. and the sit and wait approach increases the theoretical risk, beyond doing anything real, doing nothing means taking the risk.

Finally, we should remind ourselves that medicine rests on the trust between health care staff and citizens. Only strong and flexible vaccination programs are able to meet the challenges of future epidemics or pandemics.

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ORAL PRESENTATIONS

1. TRAVEL-ASSOCIATED LEGIONNAIRES' DISEASE AND PUBLIC HEALTH RESPONSE

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INTRODUCTION: ECDC's estimates indicate that roughly 1000 European tourists a year acquire Legionnaires' disease during their vacation and stay in hotels across the continent.

AIM: Country's public health response to travel-associated Legionnaires' disease review.

MATERIALS AND METHOD: Review of the ECDC technical document of the ELDSNet from 2017 and published data from the scientific and expert literature.

RESULTS: ELDSNet is established with the aim of detection, control and prevention of the cases, clusters and outbreak sources of travel-associated Legionnaires' disease reported in the EU and EEA, as well as assist with detection and response outside these countries. Sharing information enables concrete and timely actions of the ELDSNet Members in order to protect travelers from EU/EEA countries on their travel in and out of Europe. ECDC recommends set of measures that should be conducted by public health authorities of the country that diseased traveler has visited. If the measures are not conducted, the information is publicly announced and large European tour operators can use it for travel arrangements abroad.

CONCLUSION: Operating procedures procure set of common measures that should be followed by all EU/EEA countries involved in protection of their citizens from Legionnaires' disease. Apart from undeniable public health risk, Legionnaires' disease morbidity could compromise the tourism income.

Keywords: Legionellosis, Public health, Montenegro

2. BOTULISM ACTUAL PROBLEM - OUR EXPERIENCES

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Objectives: Botulism is a neuro-intoxication caused by a toxin secreted by *Clostridium botulinum*. Due to extremely high toxicity and lethality, this toxin can be used as an agent in a biological warfare. As the disease is very rarely encountered in clinical practice and may present with non-specific clinical picture, timely diagnosis has a significant impact on the course and outcome of disease. **Method:** We presented ten patients treated at the Clinic for Infectious Diseases of the Clinical Center in Niš, who ate canned food and in whom the diagnosis of disease was made based on the typical clinical picture. **Results:** Predominant symptoms were blurred vision, double vision (diplopia), dry mouth and constipation which were present in all patients. All the patients received antibiotics and nine patients received antitoxin. Neostigmine and enemas were used for the treatment of the disorder of intestinal motility and constipation. **Conclusion:** The diagnosis of botulismus was made based on afebrility, preserved states of consciousness, double vision, dry mouth and history data on consumption of suspicious food; which was particular importance to three patients from same family. Polyvalent serum anti botulinum should be applied as soon as possible because it reduces the occurrence of complications, length of hospital stay and mortality rate.

Keywords: botulism; decontamination; botulinum antitoxin; treatment outcome; bioterrorism.

POSTER PRESENTATIONS

1. INCREASING INCIDENCE OF HAEMORRHAGIC FEVER WITH RENAL SYNDROME COULD BE ASSOCIATED WITH WEATHER CONDITIONS IN VOJVODINA, SERBIA

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Objective: To analyze the correlation between occurrence of haemorrhagic fever with renal syndrome (HFRS) and weather conditions in Vojvodina.

Method: We carried out a descriptive study over a 10-year period (from 2006 to 2015).

Results: During the observed period, a total of 31 HFRS cases were registered. The annual incidence of HFRS in Vojvodina varied, with the highest values (0.51 per 100,000 inhabitants) in 2014, when the floods across the Serbia were registered.

Annual incidence of HFRS obviously increased one month after a heavy precipitation in Vojvodina. During the 2014, average monthly values (AMV) of temperature in January, February and March were 1.3 to 3 times higher and AMV of relative humidity were significantly above the 10-year period average values in Vojvodina.

Conclusion: Our findings indicated possible positive correlation between occurrence of HFRS and meteorological factors in Vojvodina during the months when the reproduction of the HFRS reservoir and the transmission of the virus to humans are most intense. Our study suggests that prevention and control measures of HFRS should be targeted at the sites related to the high density of rodents along with educational campaigns among professionals as well as the general population.

Keywords: Hantavirus, climate, epidemiology, surveillance.

2. EPIDEMIOLOGICAL CHARACTERISTICS OF LEADING ZOOSES IN THE CENTRAL BANAT DISTRICT OF VOJVODINA, SERBIA

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Objective: To determine the epidemiological characteristics of leading zoonoses in the Central Banat District of Vojvodina (CBDV) during 15 consecutive years.

Method: Descriptive study, using the data of the Centres for Disease Control and Prevention of the Institute for Public Health of Vojvodina and Public Health Institute Zrenjanin.

Results: The highest average annual incidence rate was registered for *Salmonellosis*, followed by average incidence rate of *Trichinellosis* and *Q fever*. Apart from the *Q fever*, which showed a stable trend of incidence, other two zoonoses decreased between 2002 and 2016. The *Q fever* was three times more frequently registered in males, while the prevalence of males and females was similar among patients with *Trichinellosis* or *Salmonellosis*. The highest average incidence rate of *Trichinellosis* and *Q fever* was reported in patients aged 20-39 years; *Salmonellosis* predominated among patients aged 0-19 years. The most common source of outbreak of *Trichinellosis* was pork products, while the most common sources of the *Salmonellosis* were both cakes and cookies. Of 92 interviewed patients with *Q fever*, 50 (54.3%) had direct daily contact with their domestic animals during the maximum incubation period.

Conclusion. In order to better evaluate epidemiological characteristics of zoonoses and their control, the prompt sharing of information between the animal and human health sectors along with education of food handlers and the general population in the CBDV are needed.

3. EPIDEMIOLOGICAL CHARACTERISTICS OF LEPTOSPIROSIS IN VOJVODINA PROVINCE, SERBIA, 2009-2018

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Objective

To analyze epidemiological characteristics of leptospirosis in the Autonomous Province of Vojvodina, between 2009 and 2018.

Methods

Chronological, demographic and topographic distribution of leptospirosis in Vojvodina, as well as the mode of transmission of infection and the most isolated serotypes of *Leptospira* were analyzed in the observed period. Descriptive method was used.

Results

Overall 87 cases of leptospirosis and five subsequent deaths (CFR: 5,7%) were recorded in the ten-year period. All cases were hospitalized. The average annual incidence rate was 0,5/100.000 (range: 0,2-1,5/100.000). The disease reveals an extremely seasonal character with a majority of cases reported in August (26,4%), September (23%) and October (17,2%). The disease was more prevalent in men (M/F=15,6:1). The majority of patients (65%) became infected by contact with contaminated water (occupational exposure and recreational fishing were common risk factors). The most frequently isolated serotype was *L. grippityphosa*.

Conclusion

Recognition of only severe forms of the disease that required hospitalization contributed to the underestimation of leptospirosis in the Province. Education of physicians in the primary health care and timely detection of the disease including targeted laboratory confirmation in each case with unclear febrile condition and fulfilled clinical and epidemiological criteria of illness should be carried out.

Keywords: Leptospirosis, zoonosis, epidemiology, Vojvodina.

4. IMPORTED MALARIA ON THE TERRITORY OF BELGRADE, 2014 – 2018

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OBJECTIVES

The aim of the paper was to analyze imported malaria in the Belgrade from 2014 to 2018.

METHODS

A descriptive epidemiological study was applied. Data on the number of patients with imported malaria by gender, age, by region from which malaria was imported for the specified period were taken from the City Institute for Public Health, Belgrade. Proportional, crude and age-specific incidence rates were used in the data analysis.

RESULTS

In the observed period, 77 patients with imported malaria were registered, of which 89.61% were men, and the average crude incidence rate was 0.92/100,000 inhabitants. The highest age-specific rate of imported malaria was registered in the age group of 10-19 years (4,0/100,000). According to the region of arrival, where the imported malaria is from, the number of cases from Asia and Africa, is the highest 34 (44%). The condition is registered throughout the year, with the peak of the disease in August (19.48%). The most dominant serotype is Plasmodium vivax 45% of all imported malaria cases. As a reason for traveling to countries where malaria is endemic, the largest number of patients (44.16%) cited migration, and in 43% of patients symptoms appeared within 30 days of entering Serbia.

CONCLUSION

It is necessary to continuously improve the health education of the population in order to be informed about the manner of transmission of malaria, to apply measures of prevention during their stay in endemic countries.

Keywords: imported malaria; crude incidence rate; Belgrade;

5. HOSPITAL AND COMMUNITY-AQUIRED INFLUENZA IN 2018/19 INFLUENZA SEASON IN A TERTIARY CARE HOSPITAL

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Objective: The aim of this study was to analyze the distribution and epidemiological characteristics of hospital and community-acquired influenza in a tertiary care hospital during.

Material and methods: A retrospective observational study was conducted to identify and characterize cases of hospital and community-acquired (CA) influenza at the Institute for Pulmonary Diseases of Vojvodina, Serbia, during 2018/19 influenza season. Demographic and clinical information was retrieved from the hospital-based information system.

Results: Overall, 203 patients with laboratory-confirmed influenza were registered. A rate of 16.3% of hospital acquired (HA) influenza was observed. Patients with HA influenza had a higher rates of chronic obstructive pulmonary diseases (45.5% vs. 27.1%, $p=0.035$) and malignancy (21.1% vs. 2.9%, $p=0.000$) compared to CA cases.

The time period from symptom onset to starting antiviral therapy was lower (1.48 ± 1.435 vs. 3.75 ± 2.531 , $p<0.001$), a percentage of patients with antiviral therapy within 48 hours was higher (69.7% vs. 36.5%, $p=0.001$) and a total duration of therapy was lower (4.71 ± 1.371 vs. 5.92 ± 2.337 , $p=0.003$) for CA influenza cases.

Patients with HA influenza were more often settled in non-ICU units (87.9% vs. 68.2%, $p=0.038$) and more often had a clinical manifestation of ILI (33.3% vs. 4.7%, $p<0.001$).

A length of hospital stay following confirmation of influenza was lower for HA compared to CA influenza cases (9 vs. 14 days, $p=0.015$). There were no significant differences in lethal outcomes between two groups (9.1% vs. 20.6%, $p=0.15$).

Conclusion: A relatively high prevalence of HA influenza and a significant differences in co-morbidities and clinical course of illness were observed. Improving hospital infection control and vaccination rates for patients with underlying illness and for healthcare workers should be encouraged.

Keywords: influenza, hospital-acquired, community-acquired, co-morbidities, outcome

6. THE IMPORTANCE OF CORRECT HAND HYGIENE PROCEDURE AS A PREVENTION OF HOSPITAL-ACQUIRED INFECTIONS: RESULTS OF COMPLIANCE IN THE CLINICAL CENTER OF SERBIA

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Objectives: Correct hand hygiene procedure of medical staff is one of the most significant measures for the prevention and control of Hospital-acquired infections (HAI). By respecting the 5 moments in the hand hygiene procedure during health care, therapeutic and diagnostic procedures, healthcare professionals can influence significantly on prevention of transmission of hospital infection pathogens in hospital environment. For that reason, proper hand washing technique as well as disinfection, are the most important individual interventions related to activity of a healthcare professional in the prevention of hospital infections. The importance of hand hygiene is indicated by the fact that the World Health Organization (WHO) has designated May 5th as World Hand Hygiene Day. By marking May 5th, World Hand Hygiene Day, we monitored 5 hand hygiene moments of healthcare professionals in the Clinical Center of Serbia (CCS).

Methods: Guideline for Hand Hygiene of the Center for Disease Control and Prevention, Atlanta, <https://www.cdc.gov/HandHygiene/index.html>.

Results: Monitoring from May 6-10, 2019, included 774 health professionals at 22 Clinics of the CCS. In that period, 1642 opportunities and 997 activities were recorded (590 washes and 407 hand disinfection). Compliancy ranged from 61-70%.

Conclusion: With the results shown, we want to motivate healthcare professionals to a higher level of responsibility. Many authors agree and point out that proper technique and hand disinfection can reduce the number of HAI by more than 50%. Prevention and control of the infection spreading in the health care institutions must be part of daily routine practice.

Keywords: hospital-acquired infections, hand hygiene, compliance

7. MEASLES OUTBREAK IN THE CANTON SARAJEVO IN 2019.

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Abstract

Introduction. The current measles outbreak in the Canton Sarajevo in 2019 fits into the picture of the movement of measles in the surrounding countries, as well as in the European region (Italy, Serbia, Romania). Measles has been increasing throughout Europe in the previous years, primarily because of the low vaccination coverage in the most countries. The paper presents the basic characteristics of the measles outbreak in the Canton Sarajevo during the first six months in 2019.

Methods. Descriptive study was done. Data were retrospectively analysed for frequency and distribution of cases in comparison with age, vaccinal status, geographical distribution and date of onset in the Canton Sarajevo has been used. Observed period was for 18 January up to 12 July 2019.

Results. In the observed period a total number of 854 cases of measles was registered, and one fatal case. The largest number of patients was in age group 2 to 5 years, what is the targeted group for vaccination in the Mandatory immunization program in the Federation of BH. Almost 10% of the patients are under the age of one year, suggesting in favor of unvaccinated mothers, or infants have not received passive immunity from vaccinated mothers. The measles incidence in older ages is about generations vaccinated in the previous period with 1 dose of measles vaccine. Outbreak trend in the previous 26 weeks has increasing till to 11th weeks (25 March to 31 March) after that has started to increase.

Conclusion. Insufficient coverage of measles immunization and low community awareness of using the benefits of vaccination as a preventive measure has caused the onset of outbreak.

Keywords: measles, immunization, outbreak

8. MEASLES EPIDEMIC IN REGION OF CENTER FOR PUBLIC HEALTH-BITOLA WITH ACCENT OF DISEASE AMONG HEALTH WORKERS IN PERIOD JANUARY-JUNE 2019

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Center for Public Health Bitola, Macedonia

Objectives:The newest large outbreak of measles in region of CPH-Bitola was associated with Kicevo municipality and occurred from January-June 2019 with a large number of sick people especially among health workers.

Methods:CPH-Bitola reported measles epidemic on 21.03.2019 with 15cases of measles (first case was on January 21,2019). Coordination with health institutions in the region, immunization records control, children and health staff MMR vaccination was the main activity in this period.

Results: Total measles cases number was 77. Immunization status:vaccinated with one dose 19(24.7%); fully vaccinated 27(35.1%); unvaccinated 28(36.3%); no data 3(3.9%). 8(10%) laboratory confirmed measles cases. 57(74%) was over 30 year old people. 9(11.7%)people was hospitalized. 19persons(24.6%) was health staff. CPH-Bitola checked immunization status of 271 health workers in region and 65(23.9%) was vaccinated.

Conclusion: Healthcare workers are a particularly vulnerable group at risk of occupational exposure during measles outbreaks. During the measles outbreak, there's been a lot of focus on unvaccinated children and healthcare personal. MMR vaccine is now mandatory for kids entering kindergarten. Also two doses are recommended for all health staff under 60.

Keywords: measles, immunization, health workers

9. LABORATORY CONFIRMED CASES OF INFLUENZA FROM THE TERRITORY OF NIŠAVA AND TOPLICA DISTRICTS-EPIDEMIOLOGICAL CHARACTERISTICS

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The aim : The aim of this paper is to assess epidemiological characteristics of influenza in Nisava and Toplica District.

Material and methods: Descriptive epidemiological method was used. Data sources were notification records of laboratory confirmed cases of influenza in Nisava and Toplica District in the last five surveillance seasons. Crude incidence rates were calculated per 100,000 inhabitants.

Results: In the observed period 58 cases of laboratory confirmed cases of influenza were registered. The average annual incidence rate was 24.12 ‰. The highest in 2018/19 season (n=45, I= 93.57 ‰). The mean annual lethality rate was 26.19%. In the population, outbreaks were reported in the 2016/17 and 2018/19 seasons. In the hospital and social care facilities, outbreaks were reported in the 2014/15 and 2017/18. The municipality of Nis had the highest incidence rate (17.68 ‰).The most of patients 40-49 yrs of age (32.76%) and male (55,17%). The highest incidence rates were in the age group 0-4 years (52.42 ‰). The highest number of patients were registered in January (44.83%). AH1 P/2009 influenza virus type was isolated in 84.48%. Out of all patients, 87.93% were hospitalized, while 74.14% had pneumonia. Only one patient was vaccinated. Regarding co-morbidity, chronic heart disease present in 18.97% of patients, diabetes in 15.52%, metabolic diseases in 5.17% and obesity in 5.17%. The most common symptoms are: fever (100%), cough (84.48%), shortness of breath (39.66%) and muscle pain (39.66%). Acute respiratory distress syndrome (ARDS) was diagnosed in 18 patients; out of them, 15 with a lethal outcome. 75.86% of patients received antiviral therapy and 94.83% of antibiotics. The median length of hospitalization was 10 days and the disease average length was 15 days (for children 5 and 12.5 days, respectively).

Conclusion: The last flu season has shown that vaccination of high-risk individuals is particularly important in reducing the risk of serious flu illnesses and deaths. Vaccination is highly recommended for healthcare professionals.

Keywords: influenza, epidemiological characteristics, vaccination, outbreaks

10. FACTORS ASSOCIATED WITH TUBERCULOSIS MORTALITY IN SERBIA

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Objective:

The aim of the study was to analyze trends and to identify predictors of tuberculosis (TB) mortality in Serbia during the period 2005-2015.

Methods:

Retrospective analysis of 17441 TB cases registered over the eleven years period in all health facilities in Serbia was performed as well as univariate and multivariable logistic regression analysis to identify independent factors associated with tuberculosis mortality.

Results: Tuberculosis mortality rate for all forms of TB was twice reduced between 2005–2015, from 1.91 per 10⁵ population in 2005 to 0.89 per 10⁵ in 2015 (p value for trend <0.05) due to significant decrease of pulmonary TB (PTB) mortality rate, from 1.70 per 10⁵ population in 2005 to 0.77 per 10⁵ in 2015 (p value for trend < 0.05), while there was no great variations in extra-pulmonary (EPTB) mortality rate (p value for trend >0.05).

Tuberculosis mortality was associated with retreatment (OR=1.39; 95%CI=1.12-1.61), male sex (OR=1.34; 95%CI=1.19-1.52), age 65+ (OR=4.34; 95%CI=4.00-5.00), lower education level (OR=1.63; 95%CI=1.14-2.33), and pulmonary TB (OR=2.24; 95%CI=1.78-2.83).

Conclusion:

In order to further improve performance of TB Program in Serbia, it is necessary to address factors associated with TB mortality by introducing targeted preventive interventions.

Keywords: Tuberculosis; Serbia; mortality;

11. THE CHARACTERISTICS OF INFLUENZA IN ADULTS IN THE TERRITORY OF CENTRAL KOSOVO AND METOHIJA

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Introduction: Influenza or flu is a disease belonging to the group of respiratory tract (RT) viral infections. Influenza virus constantly evolves through mutations and exhibits many types and strains. It enters the body through droplets and secretions from the RT of an infected person or contaminated objects. It starts abruptly, including the following symptoms: high body temperature (T), fever, sneezing, sore throat, extreme fatigue, muscle and joint pain, dry cough, dizziness and headache.

Aim of the paper: the aim of the paper was to examine basic descriptive epidemiological parameters in patients living in the enclaves of central Kosovo.

Material and methods. The study enrolled 69 subjects (70.9% males and 29.1 % females) in the period October 2018-May 2019. They were grouped according to age, gender, ethnicity, risk factors, months of the year, occupation and comorbidities. There are different ethnicities living in the enclaves (Serbs, Ashkali, Gorani, Bosniaks, Turks). The diagnosis was established according to epidemiological and clinical parameters and laboratory test results as well. In two patients hospitalized in the Clinical Hospital Center Niš AH1N1 was isolated. Numeric and descriptive characteristics are shown. The Student's t-test was used to compare numerical means, the Chi square test X^2 for descriptive characteristics, and Fischer's exact test for comparing distribution of descriptive characteristics. Statistically significant difference was acceptable at the risk level of $p < 0.05$.

Results: The mean age of patients was 32.7 years. Their risk factors included obesity (31.4% of them), undernourishment (29.7%), alcoholism (9.8%), smoking (49.5%), comorbidities (57.6%), (T test, $p < 0.05$ %). Statistically significant correlation was found between the undernourished and smokers (X^2 test, $p < 0.05$ %). The number of patients in February (58.5 %) and March (27.1%) was 5 and 3 times (respectively) higher than in January (11.3 %) and April (13.4%) (X^2 test, $p < 0.05$ %), including Serbs (48.5%), Ashkali (8.5%), and other ethnicities (13.4 %). Patients of Serbian ethnicity were affected more than Roma patients by 2-fold (X^2 test, $p < 0.05$ %). The number of patients between 50-54 years of age (19.8%), 55-59 (22.9%), 60-64 (21.7%) and > 65 (17.2 %) is statistically significantly higher (4 and 5 times) in comparison to the patients between 35-39 years of age (5.1%), 40- 44 (5.9%) 45-49 (10.1%) (T test and X^2 test $p < 0.05$ %). In relation to the regions, the greatest incidence was in the municipalities of Gračanica (85.3 %), Dobrotina (33.7 %), Donji Badovac (21.4%), Gušterica (11%) and Brnjice (9.1%). As for occupation, there were farmers (39.2 %), caterers (12.1 %), stokers (12%), butchers (2.1 %), teachers (7.1 %), and health-care professionals (16.7%) (T test, $p < 0.05$ %). Symptoms and clinical signs of patients included: $T > 39.5$ C⁰ (69.8 %), > 38.5 C⁰ (38.1%), > 37.5 C⁰ (22,9 %); fever (59.9%); sore throat (43.2%), fatigue (71.2%), dry cough (66%), muscle and joint pain (77.9 %), dizziness (29.9 %), headache (24.1%). Statistically significant difference (2 and 3 times) was found regarding the number of patients with: $T > 39.5$, sore throat, cough, fatigue and $SPO_2 < 93$ % in comparison to patients with: $T < 39.5$, mild fatigue, no sore throat and $SPO_2 > 93$ % (X^2 and Fischer's test $p < 0.05$ %).

Conclusion: In the region of central Kosovo, health-care education on prevention and seasonal flu vaccination should be conducted each year in all populations in order to prevent rapid spreading of flu outbreaks and development of complications both globally and regionally.

Keywords: influenza, adults, epidemiological and descriptive characteristics, prevention.

12. EPIDEMIOLOGICAL CHARACTERISTICS OF ACUTE VIRAL HEPATITIS C AT CLINIC FOR NEPHROLOGY AND HAEMODYALYSIS OF CLINICAL CENTER NIŠ

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Introduction. Hepatitis C virus (HCV) infection is several times more prevalent among hemodialysis patients than the general population.

The objective of the paper was to investigate and to analyze epidemiological characteristics of the outbreak.

Material and Method. Descriptive study was done. Investigations included interviews of dialysis facility staff, interviews of patients for HCV risk factors, review of patient charts, and review and observation of infection control practices at the facilities. Records of the acute HCV infection and records of the hospital acquired infections were used as well as the laboratory results of all patients and staff. and other medical documentation.

Results. The outbreak was reported on 27 June 2018 with two confirmed patients and one suspected. The total number of registered patients in the outbreak till the end of September 2018 was 25. Males represents 72% of all affected and females accounted for 28%. The youngest patient was 38 and the oldest was 79 years old. All patients were pensioners from the Nišava District. The time of hemodialysis ranges from 4 months to 9 years. Most of affected patients had associated heart or renal chronic diseases. We supposed that incident case and possible source was previously infected patient who was anti-HCV positive from December 2017 and who was dialyzed only in the hall 3. Twice a year in March and in October, the markers of HCV infection in all patients and staff is determined ordinarily plus PCR and HCV RNK test. All patients and staff were HCV negative in March in 2018 except the initial patient. Staff was HCV negative in October, too. The hemodialysis unit has 9 halls and the outbreak of HCV took place only in hall 3. Of all 67 dialyzed patients from the hall 3, 25 dialyzed patients got HCV infection. All of them were asymptomatic and the only sign of infection was laboratory confirmed increase of liver transaminases. Of all 25 infected patients as access to hemodialysis 6 had a temporary catheter, 6 had a permanent catheter and 13 had an arteriovenous fistula. From September 2018 to the present moment there weren't newly infected hemodialyzed patients.

Conclusion. This was the largest outbreak of the HCV infection in the Nišava District ever. Epidemiologic and laboratory data confirmed transmission of HCV among patients at the dialysis units in observed 16 months. Of all infected patients in 8 patients spontaneous seroconversion occurred. Genotypes 2 and 3 of virus C were dominant. A possible way of transmission was the omission in one of the hemodialysis procedures related to the patient's apparatus or preparation. There are no deaths from acute HCV. The measures reported with the outbreak are still in place because the outbreak has not yet been offlined.

Keywords: acute viral hepatitis C, outbreak, hemodialysis

13. CONSULTING, TESTING AND RISK FACTORS OF CLIENTS IN VCT CENTER IN INSTITUTE OF PUBLIC HEALTH OF TUZLA CANTON

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ABSTRAKT

INTRODUCTION Activities at the VCT center include pre-test counseling, HIV testing and post-test counseling. This study was designed to outline the basic principles of VCT counseling, the goals of counseling, testing and controlling HIV infection and to present risk factors and measures to protect against transmission of infection.

METHODS Based on VCT data from the VCT Center of the Public Health Institute of Tuzla Canton, a retrospective analysis of counseling and testing of clients in the period 2013-2017 was performed.

RESULTS During the five-year period, 1,531 clients reported to DPST, 75% of whom were men. Clients are mostly single (77%), and the main reason for visiting VCT is unprotected sexual intercourse (93%) as the leading registered form of risky behavior. Sexual commitment of clients is mostly heterosexual 56%, and they belong to the general population, MSM (male to male) population is 3%, IDU (intravenous drug users) 41%. One HIV positive person is registered during the follow-up period.

CONCLUSION Testing and counseling will certainly help people at risk to face and release fears and doubts about the risks they may have been exposed to in the past. With the expert assistance of a counselor, each individual can find their own way of protecting and managing the risks. Testing enables early detection of infection, timely treatment and care for the sick and prevents the infection from spreading to others inadvertently. Early treatment is more successful and eliminates or reduces the potential complications of the disease.

Keywords: VCT center, risk factors, HIV counseling and testing

14. SEXUAL BEHAVIOR OF USERS OF SERVICES OF THE CENTER FOR VOLUNTARY AND CONFIDENT COUNSELING AND TESTING FOR HIV/AIDS IN ŠUMADIJA DISTRICT

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Abstract

Introduction. HIV infection is one of the main problems of public health in the world.

The objective of the paper was to analysis sexual behavior of users of the services of the Center for voluntary and confidential counseling and testing (VCCT) for HIV in Šumadija District.

Methods. The retrospective cohort study involved users of the services of the Institute of Public Health of Kragujevac in the period from 1st of January 2013 until 31st of December, 2017. The standardized HIV counseling client questionnaire was used.

Results. The total number of visitors was 1495 (1070 males and 425 females). The average age was 29.7±10.6. This was a first testing for HIV in 71.1% of females and 59.3% of males (p<0.05). Multiple partners are the most common risk factor for HIV infection, and unprotected sexual intercourse is the most common form of risky behavior in both sexes. In the past 12 months, condom was never used by 12.4% of males and 6.9% of females (p<0.01). It is more common for men to enter homosexual relationships (p<0.01). More than 90% of VCCT visitors were at risk of having HIV infection.

Conclusion. VCCT services are most commonly used by unmarried males, who have multiple partners, unprotected homosexual or heterosexual relationships.

Keywords: HIV/AIDS, MSM population, unprotected sex

15. 3RD HEALTH PROGRAMME-EU HEALTHY GATEWAYS JOINT ACTION 04-2017 - PREPAREDNESS AND ACTION AT POINTS OF ENTRY (PORTS, AIRPORTS, GROUND CROSSINGS)

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Objectives: Dissemination of implementation and actions undertaken to ensure that the results and deliverables of the action will be made available to the target groups.

Methods: The activities have been divided among nine Work Packages, as Management of the action, Dissemination, Evaluation of the action, Integration in National Policies and Sustainability, Ground crossings, Air transport, Maritime transport, Chemical threats and Capacity building – Training.

Results: All actions are performed in order to improve capacities at points of entry (PoE) – including ports, airports and ground crossings – in preventing and combating cross-border health threats. In this way, all activities are contributing to a high level of public health protection.

The Joint Action will move from the inter-epidemic mode to an emergency mode, in the case of public health emergencies of international concern (PHEIC), according to the International Health Regulations (IHR) and *Decision No 1082/2013/EU*. The starting date of the Joint Action was 1st May 2018. The Joint Action will run for a period of 36 months.

Conclusion: Underlining and performing multisectoral approach and cross sector collaboration and cooperation is crucial in terms of fulfilment of Joint Action milestones and deliverables. Setting up of multisectoral Working group as the main core for coordination and performing activities related to designation of airport is priority.

Keywords: Joint Action, Preparedness, Ports, Airports, Ground crossings, IHR

16. INCIDENCE AND PREVALENCE OF SYPHILIS IN VOJVODINA (SERBIA), 2009-2018

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Abstract

Objective: To analyse the incidence and prevalence of syphilis in Vojvodina as well as distribution of disease among certain population.

Method: The incidence of syphilis was analysed using notification records of syphilis cases in Vojvodina between 2009 and 2018. The prevalence, of syphilis in men who have sex with men (MSM), heterosexual men and women, was analysed using the data with anonymous and voluntary laboratory testing which was conducted between 2013 and 2018.

Results: Although the average incidence of syphilis in Vojvodina in the last decade was low, trend of this infectious disease increased especially among men. The average incidence of syphilis among men ranged from <1/100.000 in 2011 to 5.0/100.000 in 2016, while the average incidence of syphilis among women was <1/100.000. The male to female sex ratio for infection increased and ranged from 1:1 (in 2011) to 18:1 (in 2013). Prevalence of syphilis among MSM (9.4%) was almost 8 times higher than prevalence among heterosexual men (1.2%) and 47 times higher than prevalence among women (0.2%).

Conclusion: Increased trend of incidence of syphilis and higher prevalence among MSM population highlighted the need for an innovative approach, with target control and improved monitoring of syphilis in vulnerable population.

Keywords: Syphilis, incidence, prevalence, MSM

17. THE FIRST POINT PREVALENCE SURVEY OF HEALTHCARE-ASSOCIATED INFECTIONS IN LONG-TERM CARE FACILITY IN KRAGUJEVAC, 2017

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Objectives. The healthcare-associated infections (HAIs) are marked as the important problem in hospital but their significance is not considered in long-term care facilities. Serbia was invited to conduct its first HAI prevalence study in these institutions, together with the countries of the European Union. The aim of this study was to assess the prevalence of HAIs and determine their basic characteristics.

Methods: This prevalence study was conducted in Gerontological Center (GC) in Kragujevac, in May 2017. ECDC (European Centre for Disease Prevention and Control) HAIs definitions and methodology were applied.

Results: A total of 234 residents were eligible population, i.e. they living full-time (24 hours a day) in this GC, present at 8:00 AM on the day of the study and not discharged at the time of the survey. A total 8 inhabitants fulfilled the surveillance case definition for 8 HAIs. The prevalence of residents with an HAI was 3.4% (95%CI: 1.08-5.72), as well as the prevalence HAIs. The most commonly were registered urinary tract infections (n=5) followed by pneumonia (n=2) and unexplained fever (n=1). The causative agents of HAIs were: *Proteus mirabilis* (n=2) and *Klebsiella* spp (n=1), while other results of the microbiological examination were not available at the time of the study or not done.

Conclusion: The results obtained should help determine the rates HAIs in long-term care facilities in Serbia, determining priorities for improving the situation and made HAI preventative strategies.

Keywords: healthcare-associated infections, prevalence study, long-term care facilities

18. THE APPROACH AND DEVELOPMENT OF THE TOOL FOR ACTIONS DURING THE OUTBREAK OF THE BACTERIA *LEGIONELLA SPP.* IN THE INTERNAL WATER SUPPLY SYSTEM OF THE HOSPITAL X

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Objectives: In case of an outbreak of bacteria *Legionella spp.* infection in a hospital environment, the primary task of all stakeholders in the process is to take care of the patient's health and to prevent further development and reproduction of bacteria in the internal water supply system of the presented hospital. Due to the awareness of the complexity of the problem, we decided to describe the modern method of selecting suitable measures and thus help decision-makers.

Materials and methods: Firstly, the literature overview of the presented topic has been done. Secondly, we developed, implemented, and maintained a pilot model for the prevention and control of bacteria *Legionella spp.* in the internal water supply system of hospital X.

Results: To eliminate and control the occurrence of *Legionella spp.* in the internal water supply system, an innovative holistic approach through the prism of the discourse of Dialectical Systems Theory was used. It is complex but essential to success in the long term.

Conclusion: The tool should be accepted by the relevant national authorities, taken into account mostly in healthcare facilities. The tool should be included as up-to-date to Water Safety Plans (WSP) for the prevention of infections caused by *Legionella spp.*

Keywords: water supply system, hospital X, *Legionella spp.*, approach, dialectical and system theory

SESSION: THEORETICAL AND PRACTICAL PROBLEMS OF NON-COMMUNICABLE DISEASES

INVITED LECTURES

1. INCIDENCE AND PREVALENCE OF COLORECTAL CARCINOMA IN THE NIŠAVA DISTRICT

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Introduction. Colorectal cancer (CRC) is the third most commonly occurring cancer in men and the second most commonly occurring cancer in women. It represents about 9.4% of all incident cancer in men and 10.1% in women. The objective of the paper was to assess changes in colorectal cancer incidence in Nišava District from 1999 to 2015.

Material and Method. Descriptive study was done. The data about CRC (codes C18 to C21 according to the 10th Revision of International Classification of Diseases) were obtained from the Serbian Cancer Registry. The data were analyzed for the population of the Nišava District from 1999 to 2015. Age-standardized rates (ASRs) of incidence were calculated by direct method and population of the World was used as a standard. Data about population was used from Censuses 1998, 2002 and 2011. Trend lines were estimated.

Results. The total number of new registered cases of CRC in the observed period was 3455 (2110 in males and 1345 in females). The average annual standardized incidence rate was 53.2/100,000 (66.1 /100,000 in men and 40.8/100,000 in women). In the observed period, male to female new cases ratio was 1.6. The lowest age-standardized incidence rate in men was 24.8/100,000 (in 2007) and the highest was 40.4/100,000 (in 2005). The lowest age-incidence rate in women was 15.3/100,000 (in 1999) and the highest was 29.7/100,000 (in 2012). Non significant increase of incidence trend of CRC was determined both in men ($y = -0.1184x + 34.46$ $R^2 = 0.0189$) and in women ($y = 0.0456x + 20.178$, $R^2 = 0.0032$). The highest age-standardized incidence rates were registered in the city of Niš (50.9/100,000) and in the municipality of Aleksinac (35.9/100,000) and the lowest was in municipality of Merošina (25.6/100,000). In the observed period, in all municipalities, age-standardized incidence rates of CRC were higher in male than in female.

Conclusion. Trend of CRC incidence increased in the observed period both in men and in women. New cases of CRC were registered after thirty years of age and the incidence was higher in men than in women. Measures of primary and secondary prevention are urgent.

Keywords: colorectal cancer, incidence, prevalence, trend

Introduction

Colorectal cancer (CRC) is the third most commonly occurring cancer in men and the second most commonly occurring cancer in women (1). It represents about 9.4% of all incident cancer in men and 10.1% in women (2). According to GLOBOCAN the 5-year prevalence of CRC, is estimated to be 43.8 million. Countries with the highest age-standardized incidence rates of CRC in 2018 were Hungary (51.2/100,000), South Korea (44.5/100,000), Slovakia (43.8/100,000), Slovenia (58.9/100,000), Portugal (54.0/100,000), Japan (49.1/100,000), Australia, New Zealand, The United States of America (USA) (3).

According to the World Cancer Research Fund there were over 1.8 million new cases in 2018 (4). Countries with the lowest incidence rates are in Africa (except the South African Republic) and in South and in Central Asia. Countries with middle incidence rate are in middle Latin America.

Serbia was on the 13rd place in 2018 with age-standardized incidence rate of 36.7/100,000 (2) and men was on the 8th place with age-standardized incidence rate of 49.0 while women wasn't in the first 20th places according to the incidence of CRC in the observed year (3,4). CRC incidence rates are approximately 30% higher in men than in women and reasons for this gender disparity are not fully understood yet (5). The gender disparity reflects differences in exposures to risk factors for CRC and sex hormones (6). Nearly 4.6% of men (1 in 22) and 4.2% of women (1 in 24) will be diagnosed with CRC in their lifetime. Lifetime risk is similar in men and women despite higher incidence rates in men because women have longer life expectancy (6,7).

It is estimated that the number of newly CRC cases will increase by more than 60% by 2030, or more than 2.2 million people worldwide will get CRC (8).

The incidence of CRC increases with aging and is most commonly diagnosed in people over 50 (9). CRC is predominantly a disease of developed world with a Western culture and developed world accounts for over 63% of all CRC registered cases. The incidence rates of CRC vary greatly from country to country and about 60% of new cases of CRC have been diagnosed in the most developed parts of the world (10).

An increase in the incidence of CRC has been identified in Eastern Europe, Asia and South America (9). Hungary had the highest rate of CRC in men (70.6/100,000) followed by Slovakia (60.7) and South Korea (59.5/100,000). Norway had the highest rate of CRC in women (39.3/100,000) followed by Hungary (36.8/100,000) and Denmark (36.6/100,000) and the lowest was in sub Saharan Africa, in Ghana and Mozambique, (in both countries rates were 1.5/ 100,000) (11).

Risk factors associated with the incidence of CRC age-over 40 years of age, hereditary factors, obesity, physical inactivity, cigarette smoking, the regular daily alcohol consumption diet high in animal fat, high meat consumption, consumption of red meat, low fibers intake (12).

The objective of this paper was to assess temporal changes in colorectal cancer incidence in Nišava District in the period 1999-2015.

Material and Method

Descriptive study was done. The data about CRC (codes C18 to C21 according to the 10th Revision of International Classification of Diseases) were obtained from the Serbian Cancer Registry (13,14). The data were analyzed for the population of the Nišava District from 1999 to 2015. Age-standardized rates (ASRs) of incidence were calculated by direct method and population of the World was used as a standard. Data about population was used from Censuses 1998, 2002 and 2011. Trend lines were estimated.

Results

The total number of new registered cases of CRC in the observed period was 3455 (2110 in males and 1345 in females). The average annual standardized incidence rate was 53.2/100,000 (66.1 /100,000 in men and 40.8/100,000 in women). There were 1.6 more men than women.

Table 1. The number of new cases, crude and standardized incidence rates of colorectal cancer in Nišava District from 1999 up to 2015.

Year	Men			Women		
	No. of cases	Crude rate	Standardized rate	No. of cases	Crude rate	Standardized rate
1999	123	64.7	36.0	61.0	31.2	15.5
2000	107	56.6	30.0	78.0	40.0	26.4
2001	110	58.4	31.1	79.0	40.7	19.5
2002	111	59.1	31.2	81.0	41.8	19.9
2003	126	67.3	35.6	22.0	42.4	18.3

2004	145	77.6	38.7	113.0	58.6	28.6
2005	142	76.1	40.4	89.0	46.2	20.9
2006	126	67.7	34.6	71.0	37.0	16.5
2007	92	49.6	24.8	72.0	37.6	18.2
2008	136	73.6	34.9	93.0	48.8	22.2
2009	132	71.7	37.9	80.0	42.1	17.8
2010	107	57.1	28.8	70.0	37.8	17.0
2011	135	74.0	35.2	76.0	40.3	18.4
2012	141	76.6	34.8	105.0	68.0	29.7
2013	138	75.5	35.0	85.0	44.9	19.4
2014	102	56.1	25.3	77.0	40.9	19.7
2015	137	75.8	33.4	93.0	49.6	22.0

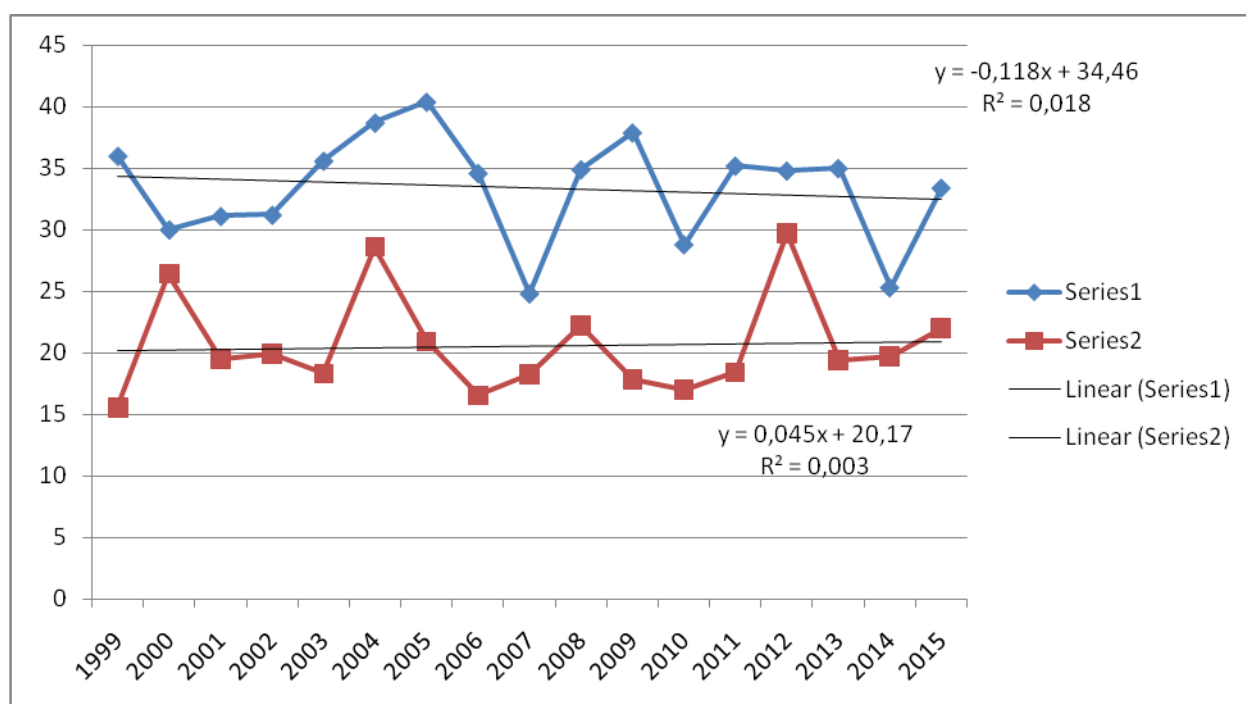


Figure 1. Incidence trend based on standardized-incidence rates of colorectal cancer in Nišava District from 1999 up to 2015

The lowest age-standardized incidence rate in men was 24.8/100,000 (in 2007) and the highest was 40.4/100,000 (in 2005). The lowest age-incidence rate in women was 15.3/100,000 (in 1999) and the highest was 29.7/100,000 (in 2012) (Figure 1).

Non significant increase of incidence trend of CRC was determined both in men ($y = -0.1184x + 34.46$ $R^2 = 0.0189$) and in women ($y = 0.0456x + 20.178$, $R^2 = 0.0032$).

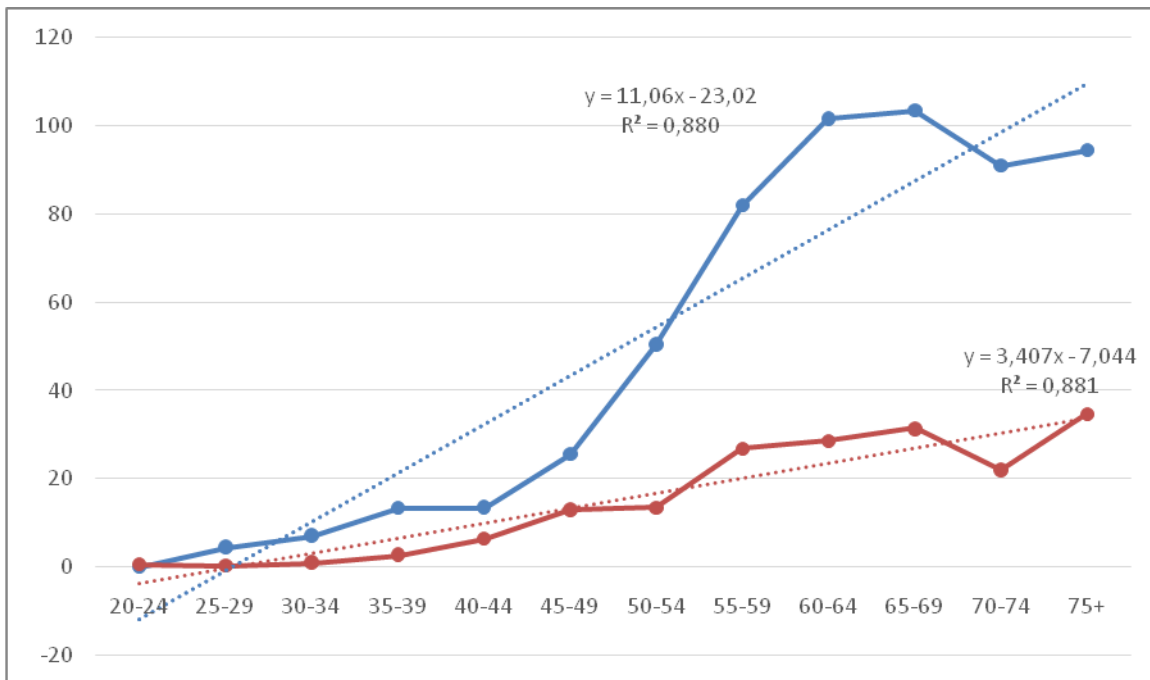


Figure 2. Incidence trend based by age and sex in Nišava District from 1999 up to 2015
 The highest age-incidence rates both in men (103.4/100,000) and in women (31.4/100,000) was registered in the age group of 65-69 years of age. The highest increase of incidence rates was recorded from 45 to 65 years of age, both in men and in women.
 The highest age-standardized incidence rates were registered in the city of Niš (50.9/100,000) and in the municipality of Aleksinac (35.9/100,000) and the lowest was in municipality of Merošina (25.6/100,000).

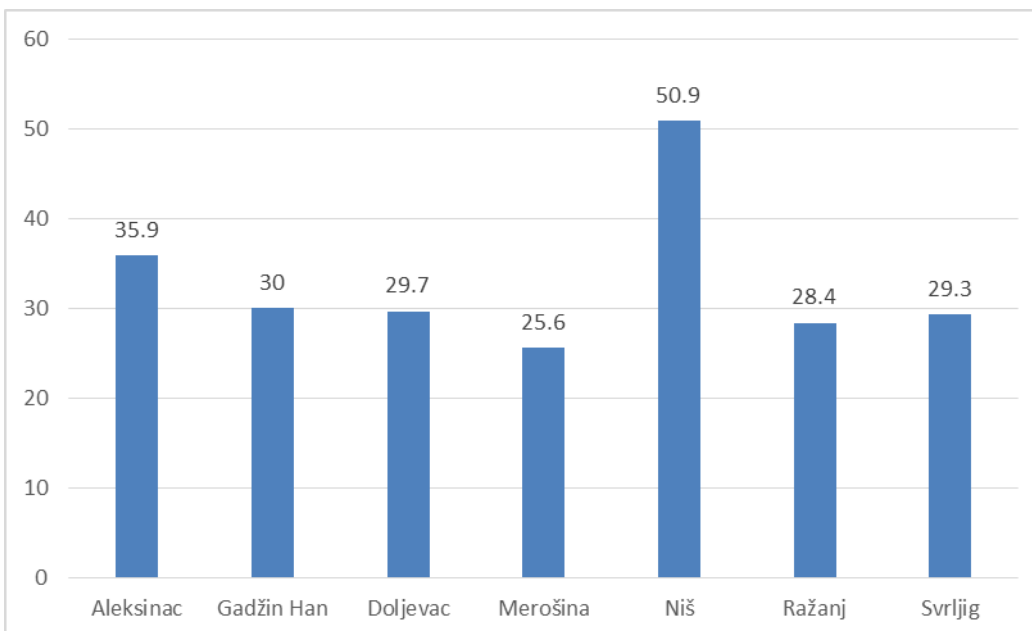


Figure 3. Incidence trend based on standardized-incidence rates of colorectal cancer in municipalities of Nišava District from 1999 up to 2015
 In men the highest age-standardized incidence rate was in the city of Niš (65.6/100,000), municipality of Merošina (58.7/100,000) and municipality of Aleksinac (45.2/100,000).
 In women the age-standardized incidence rate was recorded in the city of Niš (36.6/100,000), municipality of Merošina (33.5/100,000) and in Ražanj (31.4/100,000). The lowest in women was in municipality in Doljevac (19.7/100,000) and Svrljig (20.5/100,000).

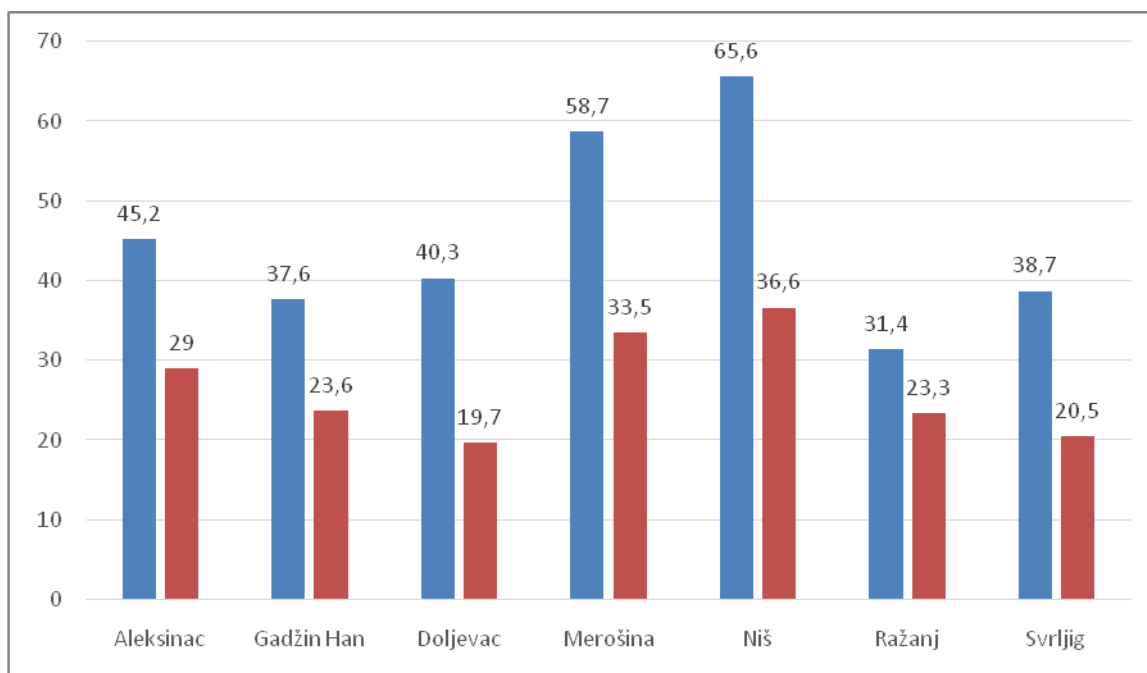


Figure 4. Age-standardized incidence by age and sex in municipalities of Nišava District from 1999 up to 2015

In all municipalities in the observed period age-standardized incidence rates of CRC men had higher than women (Figure 4).

Discussion

Colorectal cancer (CRC) is important malignant disease in the world and in Central Serbia, as the third most commonly occurring cancer in men and the second most commonly occurring cancer in women (12).

In the observed period, in Nišava District, standardized incidence rate was 53.2/100,000. In both sexes, the highest age-standardized incidence rate was registered in the age group of 65-69 years. In both sexes, the first new cases was registered very early; the youngest female case was 20 years old, and male case was 25 years of age. Increase of incidence trend of CRC was determined both in men and in women. In 2010, Central Serbia, standardized incidence rate was 40.4/100,000, similar to high incidence rates observed in other countries (14).

In Central Serbia, low standardized rates were registered in the southeastern part of the country (less developed parts), while high rates were found in Zaječar District (39/100,000), Beograd District (31.6/100,000) and Pirot District (30/100,000). In 2010, the lowest registered rate was found in Toplica District (17,8/100,000) and represented the lowest rate in Europe and world (2).

CRC incidence is increasing rapidly with economic development in many parts of the world. High incidence rate, observed in eastern and central European countries, as Slovakia and Hungary, was influenced by several life style factors, as high prevalence of physical inactivity and being overweight, as well as consumption of high-fat food (14, 15).

Traditionally low CRC incidence rates were registered in Asia but not in Japan, Singapore and Israel. Economic development with western habits had resulted in increasing incidence (15,16). High prevalence of obesity was observed in Japan (16).

Stagnating and decreasing trend of incidence were observed in USA, Australia, New Zealand and several north and western European countries (6-9). Declines in CRC incidence and mortality could be result of early uptake and effective screening, early detection of the disease and polyps (3,6, 17,18). From 2013, National program for early detection of colorectal cancer is implemented in Serbia and includes men and women aged 50 to 74 years.

In the observed period, in Nišava District, male to female new cases ratio was 1.6, which is in accordance with data from many other countries across the world. According to these results, incidence rate in female was lower than in male, and might be the result of strongly associated risk factors, such as cigarette smoking habits and CRC risk in men (11). Also, obesity is an important risk factor with specific gender characteristics including fat distribution and metabolism (14, 15).

Conclusion

Trend of CRC incidence increased in the observed period both in men and in women. New cases of CRC were registered after thirty years of age and the incidence was higher in men than in women. Measures of primary and secondary prevention are urgent.

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2. PREVENTION OF COLORECTAL CANCER

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Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second most common cause of cancer mortality worldwide. CRC is both one of the most common and one of the most preventable cancers globally, with powerful potential for primary, secondary and tertiary prevention. CRC incidence is now increasing rapidly with economic development in many parts of the world. The risk of developing CRC is influenced by both environmental and genetic factors. CRC shares several main risk factors, such as excessive alcohol consumption, smoking, physical inactivity and being overweight, with other common diseases; therefore, primary prevention efforts to reduce these risk factors are expected to have multiple beneficial effects that extend beyond CRC prevention, and should have high public health impact. A sizeable reduction in the incidence and mortality of CRC can also be achieved by offering effective screening tests in organised screening programmes which have been implemented in an increasing number of countries. Stool-based screening tests and intervals are as follows: Guaiac-based fecal occult blood test (FOBT), every year; Fecal immunochemical test (FIT), every year, FIT-DNA, every 1 or 3 years. Direct visualization screening tests and intervals are as follows: colonoscopy, every 10 years, computed tomographic colonography, every 5 years, flexible sigmoidoscopy, every 5 years, flexible sigmoidoscopy with FIT; sigmoidoscopy every 10 years, with FIT every year. Countries with early and high uptake rates of effective screening have exhibited major declines in CRC incidence and mortality, in contrast to most other countries. Increasing evidence shows that the prognosis and quality of life of CRC patients can be substantially improved by tertiary prevention measures, such as the administration of low-dose aspirin and the promotion of physical activity.

Keywords: colorectal cancer, prevention, screening

3. RISK FACTORS AND PREVENTION OF MYOPIA

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Myopia remained one of the most important problems in ophthalmology. It is present worldwide, and is a common cause of blindness in young active persons. In the past decades the prevalence of myopia in young adolescents has been rising and accounts for 10-25% and 60-80% in industrialized Western and Eastern societies. 1.6 billion people worldwide are estimated to have myopic refractive error and this number is expected to have increased to approximately 2.5 billion by the year 2020. This indicates that myopia is becoming a significant global health problem. The invalidity of the person caused by high myopia and the worldwide appearance of myopia needs studying the etiology and pathogenesis of this refractive error in the course of better profilax.

The real nature of genetic and no genetic factors, as well as their interactions in etiology and pathogenesis of myopia is still unknown. Primarily genetic factors are responsible for the development of a refractive error and contribute to 84%-86% of the cases of myopia and hypermetropia and 50% and 60% of the cases of total and corneal astigmatism respectively. There is an opinion that high myopia is inherited on dominant manner, and small myopia may be inherited poligenetic or autosom dominant way of inheritance.

Anyway if both parents are myopic there are 50% to 100% chance that children will be myopic. Environmental risk factors that may have an influence on myopia are: near work may be presented as studying, reading, watching TV, playing play station, lack of sports activities, working at computer, amount of light, working conditions, weakened accommodation, activities muscles bulb motors and eyelids, uncoordinated relationship intraocular pressure and rigidity of sclera, the overall condition of the organism, the activity of the endocrine system, increasing anthropometric measures, level of education and urbanization .

The refraction of the eye may change in the course of life. In the first months of life preterm children more frequently suffer from myopia, astigmatism, anisometropia, mainly anisomyopia compared to full-term infants. Hypermetropia and astigmatism can be found in newborns and suckling, but these two disorders are noted to rapidly decrease in the first year of life, while myopic refraction is extremely rare (about 1%) at this age.

A general hygienic dietetic regime which includes appropriate nutrition, physical activity, children staying in fresh air, suitable regime of work, at school and at home, together with fulfilling the hygienic standards as well as periodical controls children at the systematic examinations in the responsible health. Children with high myopia need to avoid hard exercise, professions. It is also indicate to have a periodical control on six months. The first ophthalmological exam is best to be at 3 to 5 years of life. On this way the refractive error will be diagnosed in appropriate time. The complete ophthalmological exam must be performed in case that the child may have same optic disc abnormality that can be involved with myopia.

Key words: Myopia , Risk factors, prevention of myopia

Introduce. Myopia is a global and increasing problem. The results of meta-regression analysis showed that the prevalence of myopia increased from 10.4% (1993) to 34.2% (2016). [1] It is expected that 49.8% of the world population will have been myopic by 2050, while 9.8% of the world population are expected to suffer from high myopia. In addition to the economic and social burdens, associated ocular complications may lead to visual impairment [2]. Myopia is influenced by both genetic and environmental factors. [3]

According to the World Health Organization, it is not equally distributed among different countries and age groups. [1]

History. The first observation of axial myopia dates back to ancient times. There is a record of Aristotle (384-322) that animals with protruding eyes see poorly from a distance (Duke Elder, Abrams, 1970). From the XVII and XVIII centuries observations were made on optical changes, as well as anatomical confirmation of the existence of a greater axial length of the myopic eye. In the second half of the XIX and early XX centuries, mechanical and biological theories (near work) were marketed explaining the onset of myopia [4]. Today, the importance of genetic research in this area.

Types of myopia. Axial myopia, as a typical and common type, whether simplex ($\leq -6,0$ D) formed by a random combination of the basic elements of the refractive system of the eye or pathological (progressive, degenerative) ($\geq -9,25$ D) which is much more serious, defined by inheritance, but also by post-natal factors, is the subject of numerous theories and analysis centuries back. There is a positive correlation between the ocular biometric parameters, particularly axial length and vitreous body length, and the degree of myopia (*axial myopia*). [3-5]

Examination. In the past years, various techniques had been used to study ocular blood in myopia, such as fluorescein angiography (FA), indocyanine green angiography (ICGA), color Doppler imaging (CDI), optical coherence tomography (OCT), and optical coherence tomography angiography (OCTA). These tools provide a noninvasive and quantitative approach for monitoring choroidal and retinal changes in pathologic myopia. Especially, OCTA is an imaging technique that enables high-speed, high-resolution, and depth-resolved imaging of the retinal and choroidal vasculatures in myopia-related complications diagnosis such as chorioretinal atrophy and choroidal neovascularization (CNV). [6]

Treatment. Most nearsighted patients observe marked improvement with treatment including corrective lenses, corneal refractive therapy, and refractive surgery. [1-6]

Uncorrected refractive error is a leading cause of visual loss in the population, and high myopia increases the risk of pathologic ocular changes such as cataract, glaucoma, retinal detachment, and myopic macular degeneration, all of which can cause irreversible vision loss. [7]

Risk factors for myopia. The refraction of the eye may change in the course of life.

Hypermetropia and astigmatism can be found in *full term children*, but these two disorders are noted to rapidly decrease in the first year of life, while myopic refraction is extremely rare (about 1%) at this age. During the preschool period, hypermetropia from +3.0 to +4.0 D at birth decreases to +0.50, emmetropia that may even turn into myopia. In the first months of life *preterm children* more frequently suffer from myopia, astigmatism, anisometropia, mainly anisomyopia compared to full-term infants.[5]

Astigmatism relatively rarely occurs as an isolated refractive error (simple, compound and mixed astigmatism make up about 20% of all astigmatisms). Over 80% of astigmatism combines with hypermetropia/myopia and can change in the course of life. *Anisometropia*, an unequal refraction of both eyes, can cause amblyopia. The prevalence of anisometropia varies depending on the definition and ranges from 20 to 80% of the total population. Anisohypermetropia more commonly causes *anisometropic amblyopia* than anisomyopia. Anisometropia between the two eyes >2.50 D is present in 20% of people with myopia ≥ 6 D. Scientific studies have reported anisometropia between the two eyes >10 D (unilateral myopia) and familial anisometropia, >20 D in a mother, her sisters and daughters. [5,8].

A special problem are identical twins with “mirror image” astigmatism with or without esotropia. Identical twins account for 0.2% of the world population and 8% of all twins. In the so-called “*mirror-image*” *twins* variants there are potential phenotypic differences between the right and left sides of individuals (Spemann, 1920), and they can be found in

25% of identical twins. Refraction anomalies (myopia, hypermetropia and astigmatism) are complex heterogeneous disorders and ideal for genetic investigation. Studies of *twins* take a special place in human genetics due to the possibility of comparing genetic and environmental factors [8].

Retinopathy of prematurity (ROP) is an important cause of potentially preventable blindness in children. The incidence of blindness varies between 15% in developed countries, and 60% in middle - income countries. The economic development of the country determines the possibility of ROP screening and treatment as well as consecutive ROP induced blindness. The sequels of ROP are important too. Approximately 20% of all premature babies can develop some form of strabismus or refractive error over time. [9] The refractive error abnormalities of ROP patients have been found to appear early in infancy and persist well into adulthood. The prevalence of myopia is 90.7% among adults with premature retinopathy, compared with 25% in the adult population without premature retinopathy. [10]

Emmetropization process of ocular development in the postnatal stage. In a normal development, most eye growth takes place in the first year of life: the refractive state changes as the axial length increases and the cornea and lens flatten. However, prematurity may affect the emmetropization process of ocular development in the postnatal stage, the so-called *myopia of prematurity (MOP)*. This myopia is non-axial, consisting of the steeper cornea, shallower anterior chamber and increased lenticular thickness. This suggests that severe ROP and/or its treatment may result in the arrested development of the anterior segment. The true nature of myopia in preterm infants, as well as its progression, is not well-understood. It is believed that it results from the influence of three etiological factors: prematurity, severity of ROP, and changes due to the different therapies applied (laser or anti VEGF).[11]

Recommendations for follow-up examinations for preterm infants must include all aspects of the visual function, i.e., visual acuity, contrast sensitivity, visual fields, refraction, strabismus, and perceptual problems.[9] Premature retinopathy screening at the Eye Clinic in Niš (started in 2008) creates conditions for further follow-up of the refractive state of children's eyes in general (especially in twins). [8]

The complete ophthalmological exam must be performed in case that the child may have same *optic disc abnormality* that can be involved with myopia, or in case the adults may *have retinal pathology associated with severe forms of myopia* [12]

Myopia has a diverse etiology, with both environmental and genetic factors believed to be involved in the myopia's development and progression.

Genetic factors. Primarily genetic factors are responsible for the development of refractive error and contribute up to 84-86% of the cases of myopia (35% AD and 50% AR) and hypermetropia and 50% and 60% of the cases of total and corneal astigmatism, respectively.

If both parents are myopic, the chances of the child being myopic are 42%. If one parent is short-sighted, the possibility of the child being myopic is about 22.5% and if the parents are not short-sighted, the possibility of developing myopia is 8%. [8]

New genetic studies have shown an association of myopia and loci on chromosome 8q12, as well as loci on chromosome 15q14 with high hypermetropia. Genetic linkage studies have mapped the dozen loci, while association studies have found more than 70 different genes. Many of these genes are involved in common biological pathways known to mediate extracellular matrix composition and regulate connective tissue remodeling. Other associated genomic regions suggest novel mechanisms in the etiology of high myopia, such as mitochondrial-mediated cell death and photo receptor mediated visual signal transmission. [3]

The emphasis has also been placed on the influence of genetic/non genetic factors on myopia prevalence in different ethnic groups, sex, ages and with *the association of myopia and genetic disorders* like Marfan's syndrome.

Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder, with mutation of the fibrillin gene on chromosome 15q. Involving the cardiovascular, skeletal and ocular systems.

It was first described by *Antoine – Bernard Marfan* in an 1896 case report of a young girl with unusual musculoskeletal features, while *Bürger* first described ophthalmological features of MFS in 1914. *Ocular features of MFS* include bilateral ectopia lentis (40–56 %), myopia (28%), retinal detachment (0,78%), anisometropia, glaucoma. Early detection and correction of refractive errors prevents amblyopia – correction after the age of 12 years is unlikely to restore visual acuity, as well as early integral and update management by a multidisciplinary group, to obtain the best quality of life and survival. [13]

Environmental factors. It has been concluded that environmental factors such as “near work”, light exposure, lack of physical activity, scoliosis, growing anthropometric measures, higher education, urbanization, race, region, age, sex contribute to the development of myopia. [1-7,14-17]

“*Near work*”, The educational level is a strong predictor for myopia, which was thought to be mediated through the effects of prolonged amounts of near work, especially in childhood. In Asia, where a perceived “epidemic” of myopia has been observed, Chinese children have been reported to have higher prevalence of myopia compared with other racial groups. The discrepancies in cultural backgrounds may explain the ethnic differences observed in the pediatric population, because Chinese culture emphasizes very early educational achievements and passing examinations. It is still impossible to conclude that near work is an independent risk factor for myopia. [16]

Deformities of the spinal column and refractive errors deserve a special attention and follow-up in the period of adolescence. Scoliosis is the commonest among spinal column deformities, and usually starts as a poor posturing of the body. Adolescent idiopathic scoliosis (AIS) is the most common form of scoliosis (90 %), four to six times more frequent in girls (5) and a leading orthopedic problem in children. Preventive measures against deformities of the spinal column and refractive errors are necessary for an adequate therapeutic treatment.

The significance of systematic examinations is to be emphasized, as it is the best way of early revealing and diagnosing refractive errors, any disease or body deformities. In addition, a full cooperation of parents, children, teachers, and all the subjects involved in the treatment is needed. [14]

Myopia prevalence in different ethnic and age groups. Myopia is the most common cause of correctable visual impairment in the developed world and a leading cause of preventable blindness in developing countries. Poor vision as a consequence of uncorrected refractive error has been identified as a priority area by the World Health Organization’s global initiative to eliminate avoidable blindness by the year 2020. Geographic variations in myopia prevalence are marked in both child and adult populations with the highest levels of myopia in East Asia, where approximately 80% of young adults are myopic. Compared to East Asian children the prevalence of myopia is lower in children from South Asia. The lowest prevalence appears to be in white children, with similarly low levels of myopia in children of African Caribbean origin. These variations together with the recent rapid increases in the prevalence of myopia (especially among children in Asia and in higher income countries) suggest that environmental factors are important determinants of myopia and hence of reduced unaided distance vision [15] .

The reasons for the observed racial differences in myopia prevalence are poorly understood. Race may be a surrogate for differences in both genetic biomarkers and environmental exposures such as the intensity of schooling, near work, outdoor activity and lifestyle factors. [16]

Sex-related differences have been reported later in childhood and adolescence, with higher levels of myopia in girls. The reason for sex-related differences remains unclear but it may reflect differences between the sexes in response to environmentally determined factors, such as educational demand. [15]

The projected increases in myopia and high myopia are widely considered to be driven by environmental factors (nurture), principally lifestyle changes resulting from a combination of decreased time outdoors and increased near work activities, among other factors.[16] So-called high pressure educational systems, especially at very young ages in countries such as Singapore, Korea, Taiwan, and China, may be a causative lifestyle change, as may the excessive use of near electronic devices. Other proposed causes include *light levels*, which may be directly related to time outdoors. The global myopia in the year 2000, with the bulk of myopia in age groups younger than 40 years, reflects the significant lifestyle changes for children and young people over the past 10 to 25 years, especially in the large population centers of Asia. These lifestyle changes will continue to spread with increasing *urbanisation* and development. [17]

Higher amounts of myopia have the potential to cause vision impairment by *myopic macular degeneration* or *its comorbidities*, cataract, retinal detachment, and glaucoma, the risk of which increase in myopia. [17]

Prevention of myopia. In 2010, it was estimated that uncorrected refractive error was the most common cause of distance vision impairment, affecting 108 million persons, and the second most common cause of blindness globally. But, myopia and high myopia will show a significant increase in prevalence globally, affecting nearly 5 billion people and 1 billion people, respectively, by 2050. 1 billion people with high myopia by 2050, 7.5 times more than in 2000. Myopia and high myopia estimates from 2000 to 2050 suggest significant increases in prevalence globally, with implications for planning services, including managing and preventing myopia related ocular complications and vision loss among almost 1 billion people with high myopia. [17]

Uncorrected refractive error is a leading cause of visual loss in the population.

The screening of refractive errors in the premature babies, especially with some of the sROP should be done earlier in the pre-verbal period, at the age of nine months.

As the refractive error of ROP patients has been found to be present early in infancy and to persist into adulthood, it is necessary to follow up these patients even later as they are growing up. The screening of refractive errors in the full term children is important too. The first ophthalmological exam is best to be at 3 to 5 years of life. On this way the refractive error will be diagnosed in appropriate time. The significance of systematic examinations is to be emphasized, as it is the best way of early revealing and diagnosing refractive errors, any disease or body deformities. The complete ophthalmological exam must be performed in case that the child may have same optic disc abnormality that can be involved with myopia or in case that the adults' who may have myopic macular degeneration or its comorbidities. A general hygienic dietetic regime for myopic children which includes appropriate nutrition, physical activity, children staying in fresh air, suitable regime of work, at school and at home, together with fulfilling the hygienic standards as well as periodical controls children at the systematic examinations in the responsible health. Children with high myopia need to avoid hard exercise, professions. It is also indicate to have a periodical control on six months. Early treatment of myopia can prevent social and academic difficulties that can accompany poor vision.

Conclusion. Myopia has a diverse etiology, with both environmental and genetic factors believed to be involved in the myopia's development and progression.

Uncorrected refractive error is a leading cause of visual loss in the population.

High myopia is associated with higher risks of cataract, glaucoma, and retinal diseases.

Early treatment of myopia can prevent social and academic difficulties that can accompany poor vision.

The uptake of myopia control, however, requires a strong evidence base and a concerted effort by government, education, and health systems.

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4. THE APPLICATION OF MODERN SOFTWARE PACKAGES IN THE DIAGNOSIS OF DIABETIC RETINOPATHY

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Diabetic retinopathy is a microvascular complication of diabetes mellitus which damage the retinal blood vessels, reduce perfusion, induce ischemia, and damage to the function of the retina. It is the leading cause of visual acuity and blindness of working population. At the time of diagnosis of type 2 diabetes, often there are already initial changes on the retina. The first 20 years, 60% of patients with diabetes develop some form of diabetic retinopathy.

Modern imaging methods, such as optical coherence tomography (OCT) and optical coherence angiography (OCTA) it is possible to spot early changes in the structure of the macula in patients with diabetes and before the first clear manifestation of diabetic maculopathy.

Mentioned imaging techniques and the analysis of digital images of the fundus, are important in an early detection of changes in diabetes and their monitoring.

Optical coherence tomography is a noninvasive method of recording layers of the retina, the macula accurately processed. This method is also known as optical biopsy retinal tissue. It allows consideration of all the layers of the retina and the initial layers choriocapilaris.

Optical coherence angiography is noninvasive method of recording the blood vessels of the retina and choroid. Various software systems such as:

-Optovue AngioVue (AngioAnalytics)

-Carl Zeiss Meditec AngioPlex

-Nidek RS-3000 Advance Optical Coherence Tomography

-Topcon DRI OCT Triton

-Spectralis OCTA Heidelberg

-Canon Angio eXpert

enable an analysis of retinal blood vessels, superficial, deep layer, retinal pigment epithelium and choriocapilaris.

Analysis of blood vessels involves an assessment of the density of the vascular network and determining diameters of retinal vessel, and the analysis of abnormal blood vessels resulting such as choroidal neovascularization.

A digital image of the fundus, it is possible to analyze the morphological, typical changes of diabetic retinopathy (microaneurysms, hemorrhages, different forms of ischemic changes, IRMA) After morphological analysis digital images can be quantitatively analyzed by using the system for processing and analyzing digital image ImageJ (<http://rsbweb.nih.gov/ij/>).

Using these modern non-invasive methods, with software system which enable an analysis of blood vessels, and their correlation with the results of the analysis of digital images of the ocular fundus to detect early changes, can be important for early detection of changes, monitoring of process, and use of appropriate therapy as well as following its effects.

Diabetic retinopathy is a microvascular complication of diabetes mellitus which damage the retinal blood vessels, reduce perfusion, induce ischemia, and damage the function of the retina. It is the leading cause of low visual acuity and blindness in working population (1,2). At the time of diagnosis of type 2 diabetes, often there are already initial changes on the retina. Twenty years after diagnosis, 60% of patients with diabetes develop some form of diabetic retinopathy (3).

Modern imaging methods, such as optical coherence tomography (OCT) and optical coherence angiography (OCTA) are used to spot early changes in the structure of the macula in patients with diabetes, even before the first clear manifestation of diabetic maculopathy(3,4).

Mentioned imaging techniques and the analysis of digital images of the fundus, are important in early detection of changes in diabetes and their monitoring.

OCT is also known as optical biopsy of retinal tissue. It is a noninvasive method of recording layers of the retina as well as an initial layer of choriocapilaris (fig.1)(1).

OCTA is noninvasive method of recording the blood vessels of the retina and choroid. Various software systems such as:

-Optovue AngioVue (AngioAnalytics)

-Carl Zeiss Meditec AngioPlex

-Nidek RS-3000 Advance Optical Coherence Tomography

-Topcon DRI OCT Triton

-Spectralis OCTA Heidelberg

-Canon Angio eXpert

These systems enable analysis of retinal blood vessels, superficial, deep layer, retinal pigment epithelium and choriocapilaris (fig 2).

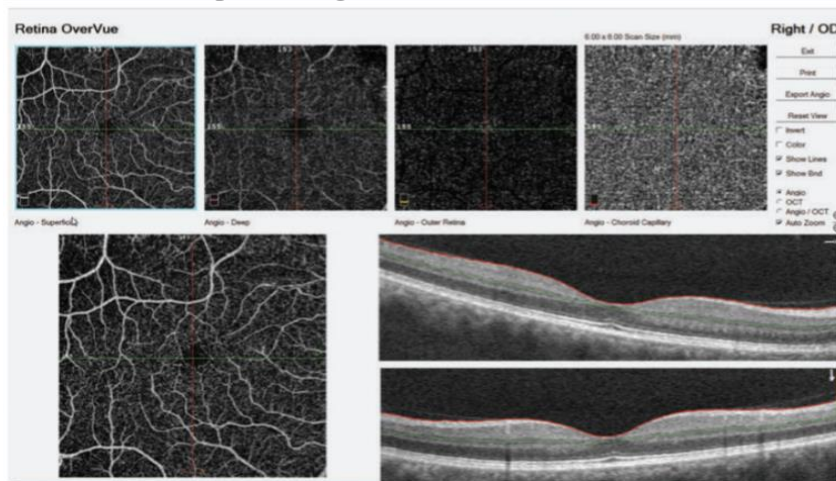


Figure 2. Angio OCT and presented layers

Analysis of blood vessels involves an assessment of the density of the vascular network and determines diameters of retinal vessel, and provides analysis of abnormal blood vessels such as choroidal neovascularization (fig3).

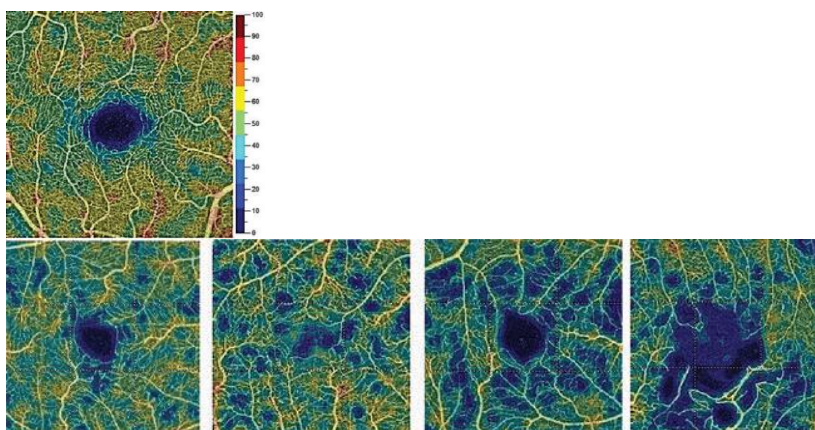


Figure 2. Appearance of vascular network in normal person and in patients with diabetic retinopathy

Using a digital image of the fundus, it is possible to analyze the morphological, typical changes of diabetic retinopathy (microaneurysms, hemorrhages, different forms of ischemic changes, IRMA)(fig.6). After morphological analysis digital images can be quantitatively analyzed by using the system for processing and analyzing digital image ImageJ (<http://rsbweb.nih.gov/ij/>)(5).

The quantitative analyze of diameters and area of avascular macular zone (FAZ) is presented in table 1.

Groups	FAZ diameter μm Superficial layer	FAZ diameter μm Deep layer	FAZ area μm Superficial layer	FAZ površina μm Deep layer
Healty	573-578	659	0,25-0,38	0,38-0,43
DM without NP	370-696		0,348-0,38	0,49-0,54
NPDR	370-813		0,38-0,40	
NPDR mild			0,46	
NPDR advanced			0,45	
NPDR severe			0,46	
RDP	410-1150		0,47-0,51	
DME			0,34	0,76
DMI			0,58	
DR in general	370-753	1009	0,20-0,58	0,56-0,81

Table 1.FAZ OCTA funding from literature

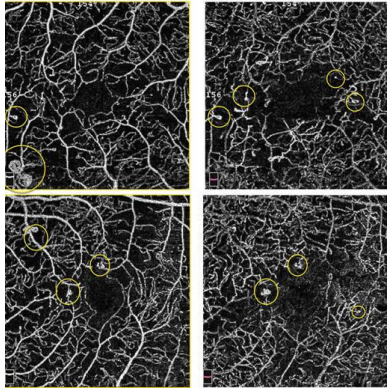


Figure 6. Microaneurysms detected by OCTA

Using these modern non-invasive methods, with software system which enable an analysis of blood vessels, and their correlation with the results of the analysis of digital images of the ocular fundus, can be important for early detection of changes, monitoring of process, and use of appropriate therapy as well as following its effects (5,6).

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POSTER PRESENTATIONS

1. CANCER SCREENING PROGRAM IN MONTENEGRO

Ostojić Đurđica, Nikčević Kovačević I., Samardžić I., Vuković- Leković J., Čampar A., Mugoša B.

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Objective: The aim of this research was to report period of six years (01 June 2013 – 01 June 2019) of conducting the National Colorectal Cancer Screening Program (NCCSP) in Montenegro.

Method: The data are collected from the integral electronic information system and pathohistological findings from Department of Pathology, Clinical Centre of Montenegro.

Results: Group contained 217.157 individuals, age 50-74, registered at chosen doctors for adults (CD). CD teams invited, by phone, 168.433 (77,56%) individuals. The uptake rate was 78,14% (range 70,94-81,75%, 131.614 participants).

Immunochemical Fecal Test (FIT) was positive in 6.135 participants (average 8,59%). A total of 4.060 colonoscopies (complete colonoscopy 92,70%), and 716 (17,64%) biopsies were performed.

In observed period 48 (6,7%) colorectal cancers were found.

In 532 cases of adenomas: 335 (46,79%) low grade dysplasia, 23 (3,21%) intermediate grade dysplasia and 174 (24,30%) high grade dysplasia, were found. Hyperplastic polyps and colitis were found in 136 (19,00%) cases.

Conclusion: According to European Guidelines for quality assurance in colorectal cancer screening and diagnosis, uptake rate in NCCSP is higher than desirable level. The NCCSP implemented in Montenegro is well accepted approach for colorectal cancer prevention.

Keywords: colorectal cancer, screening, Immunochemical Fecal Test, colonoscopy, biopsy

2. BURNOUT SYNDROME AMONG WORKERS IN THE PRIVATE SECURITY SECTOR

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² Institute of Public Health, Nis

³ Institute of Public Health, Kraljevo

Objectives: Burnout syndrome at work is a prolonged response to chronic emotional and interpersonal stressors that are associated with the workplace. It is characterized by emotional exhaustion, depersonalization and low personal accomplishment. The aim of the study was to determine the prevalence of the workplace burnout syndrome in the private security sector.

Materials and methods: The research was conducted in the form of a multicentric cross-sectional study in the period from January to April 2019 in private security agencies in Kraljevo, Čačak and Kruševac. The study included 122 employees who voluntarily agreed to participate in the research. The data was collected using Maslach Burnout Inventory to evaluate the workplace burnout syndrome (engl. Maslach Burnout Inventory Human Services Survey-MBI-HSS).

Results: While considering the results of each subscale, burnout syndrome of a significant degree was detected in the sample examined: emotional exhaustion (high 4.9%, moderate 13.9%); depersonalization (high 3.3%, moderate 12.3%); personal accomplishment (low 23.8%, moderate 35.2%). The prevalence of the burnout syndrome in the sample was 15.6%.

Conclusion: Our study has confirmed that the burnout syndrome of employees working in the private security sector is present in all of the three defined areas. Unlike the total workplace burnout syndrome, speaking in terms of percentages, a significantly larger number of workers developed symptoms in moderate or high degrees in their individual domains.

Keywords: private security, burnout, emotional exhaustion, depersonalization, personal accomplishment

3. PREVALENCE OF DIABETES AMONG THE HOSPITALIZED PATIENTS FROM ACUTE ISCHEMIC STROKE IN MONTENEGRO 2013

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Objectives: To determine the prevalence of diabetes, as one of the leading risk factors for stroke, among men and women hospitalized due to acute ischemic stroke (AIS).

Methods: Data from medical history discharge notes of hospitalized cases from the 2013 Population Stroke Registry in Montenegro have been used in the paper. Proportions have been used as structure of the disease indicators.

Results and Conclusion: During 2013, 1252 hospitalized cases of stroke were registered in Montenegro, of which 111 (8.9%) had diabetes. Of these, 1004 cases were AIS, of which 97 (9.7%) had diabetes (47% men and 53% women).

The average age of diabetic AIS cases was 70 years. There is no statistically significant difference in the age structure of diabetic and non-diabetic AIS cases. We expected that diabetic AIS cases are younger than non-diabetic cases, as well as higher prevalence of diabetes in stroke, taking into account that in the literature it is around one-third of all stroke patients with diabetes.

Possible explanation for why the expected values were not obtained was that a significant number of stroke cases have not been hospitalized (outpatient and fatal non-hospital cases, for which we do not have reliable data if they had diabetes).

Keywords: stroke, diabetes, prevalence

4. SIGNIFICANCE OF NEGATIVE SYMPTOMS IN THE ONSET AND OUTCOME OF SCHIZOPHRENIA AND THEIR SECONDARY AND TERTIARY PREVENTION BY PSYCHOSOCIAL METHODS

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Eugen Bleuler, a Swiss psychiatrist, who coined the term schizophrenia (1908) singled out the essential symptoms of schizophrenia known for its famous 4 A (autism, association disorder, loss of affectivity, ambivalence). In this way, he defined the negative symptoms of schizophrenia, whose essential importance was expressed in the onset of the first schizophrenic episode, as well as in the functional and social wellbeing recovery after the same. Based on the analogy with Bleuler, Stahl singles out 5A as a set of negative symptoms and classifies them as: alogia, affective numbness or flattening, asociality, anhedonia, and avolition. In DSM-5, a manual for mental disorders, as a special dimension of the definition of schizophrenia, negative symptoms are distinguished, with two primary symptoms: being reduced emotional expression and avolition, and three additional symptoms are alogia, anhedonia and asociality. There has been intense research into negative symptoms over the last two decades with the formation of subgroups of negative symptoms and their association with cognitive symptoms. Numerous biological studies address the isolation of new drug groups whose mechanism of action is different from the dopaminergic hypothesis of schizophrenia. Although negative symptoms in schizophrenia are clearly anatomically determined and organic brain changes and dysfunction of certain brain regions precede the onset of negative symptoms, their severity and residual lag after the first schizophrenic episode, there are opinions that they are primarily socially conditioned and that psychosocial interventions are important for their early treatment, as well as to prevent patients deterioration after the first episode and their rehabilitation. These interventions must be managed integratively by the persons who manage the monitoring centers for the high-risk population for the onset of psychosis, as well as the early intervention centers for the first psychosis. These interventions are divided into psychosocial, psychotherapy (modified cognitively behavioral methods), other alternative methods, creative methods, cultural methods and work with the patient's family.

Keywords: negative symptoms, schizophrenia, prevention, integrative approach

5. THE LEADING CAUSE OF CANCER DEATHS AMONG MEN IN BRANICEVO DISTRICT, 2001-2015

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²Institute of Public Health Požarevac

Objectives: Examining the structure of cancer mortality can contribute to better planning and management of population health care.

Materials and methods: Based on the deaths data from the Republic Statistical office, an epidemiological analysis of the mortality structure of leading cancer sites among men in the Branicevo district from 2001 to 2015 was conducted. Proportions, non-standardized and standardized mortality rates on world population were used in the analysis.

Results: In Branicevo district, men most commonly died of malignant tumors of lung (30.4%), colo-rectum (12.2%), prostate (9.6%), stomach (4.8%), and pancreas (4.2%). Standardized cancer mortality rates were for lung 50.2, colo-rectum 16.2, prostate 11.1, stomach 6.7, and pancreas 6.6 per 100.000. During this period, all cancer localizations recorded an increase in dying, except for stomach cancer. The highest increases in mortality rates were recorded from colo-rectal cancer ($y=2.6512x+74.665$) and lung cancer ($y=1.4646x+26.697$). Although the average cancer mortality structures in the district and in Serbia were similar, a higher increase in deaths from colorectal and lung cancers was observed in Branicevo than the average in our country.

Conclusion: The increase in cancer mortality rates imposes the need to redefine the role of prevention in the Branicevo district, primarily for colo-rectal cancer screening and smoking prevention.

Keywords: mortality, cancer, leading cause, man

6. PHARMACOECONOMIC ASPECTS OF TREATING COXARTHROSIS – COST-OF- ILLNESS STUDY BASED ON DATA FROM SERBIA

Kostić J. Marina¹, Janković S.¹, Cvetković L.², Stanojević-Pirković M.³, Milovanović J.¹, Milovanović O.², Parezanović Ilić K.⁴

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Objective: The aim of this study was to estimate the total costs of the treating patients with coxarthrosis in medical facilities in Central part of Serbia, to structure them and to analyse the main determinants of these costs.

Methods: For purpose of this survey we conducted pharmacoeconomic, retrospective, cost-of- illness study with a "bottom to the top" approach from societal perspective. Study population included 52 patients with a confirmed diagnosis of coxarthrosis who were treated as at the Clinical Centre in Kragujevac as also in outpatient medical facilities during 2018th. Median values and ranges were reported to avoid potential distortions associated with mean costs.

Results: Total costs of treating coxarthrosis were estimated about 198.117 RSD (58.130-526.729) per patient per year, where direct costs were the main key drivers with value of 76.063 RSD (28.503-352.298). The main determinants among direct costs were costs due to hospitalization (25,33%), surgical (14,96%) and physical procedures (7,71%).

Conclusion: The structure of total costs of treating coxarthrosis in pharmacoeconomic sphere of Serbia are in line with other published studies but with significant differences in absolute values of these costs due to low prices for medical services in Serbia.

Keywords: Cost of illness study; coxarthrosis; societal perspective

7. TREND IN LUNG CANCER INCIDENCE IN BRANICEVO AND DANUBE DISTRICT, 2001-2015.

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¹Institute of Public Health of Serbia

²Institute of Public Health Požarevac

Objectives: Presenting increasing trend of lung cancer incidence in men and women in the Branicevo and Danube district between 2001 and 2015.

Materials and methods: The source of incidence data was the Cancer Registry of the Institute of Public Health of Serbia. The incidence rates were standardized and the trend of lung cancer incidence from 2001 to 2015 was shown as a linear trend.

Results: During the observed period, there was an increase in incidence rates of lung cancer in both men and women in the Branicevo and the Danube district. A cumulative increase in the incidence rate for men was registered in the Branicevo district (19.2% or 1.3% per year ($y = 49.98 + 0.592x$)). Also, a cumulative increase in the incidence rate for women was 55.2% or 3.7% per year ($y = 12.32 + 0.399x$). An increase in the lung cancer incidence rates was also registered in the Danube District. In men, a cumulative increase in incidence rates was 9.0% or 0.6% per year ($y = 70.00 + 0.229x$) and in women a cumulative increase in incidence rates was 34.7% or 2.3% per year ($y = 14.94 + 0.813x$).

Conclusion: During the observed period, the rates of lung cancer in both sexes and in the both districts increased on average by 0.87% annually in men and by 2.84% annually in women. This trend will continue in the future.

Keywords: lung cancer, incidence, trend

8. INCIDENCE OF ACUTE MYOCARDIAL INFARCTION IN POPULATION OF NIŠAVA DISTRICT FROM 2008 TO 2017

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²University of Niš, Faculty of Medicine Niš, Serbia

Introduction. Acute myocardial infarction (AIM) is the first cause of disease and premature death in the world and in our country.

Our paper aimed to determine the trend of incidence of AIM in the Nisava District in the period 2008-2017.

Method. A descriptive study was applied. Data were obtained from the Population registry for acute coronary syndrome (AKS) of Serbia. Incidence rates were calculated per 100,000 population standardized by the direct method according to the standard population of the world. A linear trend was calculated.

The results. A total of 6073 new patients were registered. There was (63%) men and (37%) women. AIM is most commonly registered after the age of 25. The incidence of AIM increases with aging and the highest standardized rates of AIM incidence have been reported in the age group 65-69. The trend of increasing incidence with aging is statistically significant $y = 12.854x - 0.80455$, $R^2 = 0.8369$. The most common AIM in the Nisava District was ST elevation myocardial infarction (STEMI) (67.1%). AIM without ST elevation (NSTEMI) (31.6%) was significantly less represented, while AIM with left branch block (1.3%) was least represented.

Conclusion. AIM is a significant disease in the population of Nisava district. The highest incidence rates were registered in the 65-69 age group. The incidence trend is showing an increase.

Keywords: acute myocardial infarction, trend, incidence

9. INCIDENCE OF THYROID CANCER IN NIŠAVA DISTRICT 2007-2016

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Introduction: Thyroid cancer (TC) is one of the most common malignant diseases of the endocrine system. It represents about 5% of all cancers in females and less than 2% in males.

The objective of the paper was to determine the incidence trend of TC in the population of the Nišava District from 2007 to 2016.

Material and Methods: Descriptive study was done. Data about all new cases TC were obtained from the Cancer Registry of Serbia. Crude incidence rates were calculated per 100.000 inhabitants. Direct method of standardization was performed with the World population as a standard. Trend lines were estimated using linear regression. Data about population of the Niš District were obtained from 2002 and 2011 Censuses. The trend was considered to be significant when the p-value was below 0.05 ($p < 0.05$).

Results: The total number of 167 new cases of TC were registered (43 in males and 124 in females). The average annual standardized rate (ASR) of incidence in males was 1,4/ 100, 000 and in female it was 4.7/100, 000. Females had higher annual ASR of incidence and female to male ratio of incidence was 2.8:1. The first new cases of TC in males was registered after 25 years of age and in females above 15. Trend of incidence in males stagnant: $y = -0.110x + 1.98$, $R^2 = 0.113$ and in females: $y = -0.130x + 5.46$, $R^2 = 0,144$ it showed insignificant decreasing.

Conclusion: Trend of TC incidence in males stagnant and in females incidence trend showed insignificant decreasing. Female to male incidence ratio was 2.8:1.

Keywords: thyroid cancer; incidence, trend

10. SCREENING OF DEPRESSIVE SYMPTOMS AMONG IN MEDICAL STUDENTS

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Introduction. Depressive symptoms are common in medical students. The objective of the paper was to assess the prevalence of depressive symptoms in the first-year medical students. **Methods.** The cross-sectional study based on the Patient Health Questionnaire-9 (PHQ-9) was done. **Results.** The response rate was 83% (331 of 400). Overall, 48% of the students had symptoms of depression. The average PHQ-9 score in first-year students was 6.75 ± 4.60 . The most prevalent were mild depressive symptoms and they were observed in almost every third medical student. The female students had significantly higher average PHQ-9 score compared with the male students 6.37 ± 4.88 vs 4.89 ± 4.27 , $p < 0.01$. The significant negative correlation between depressive symptoms in medical students and their everyday achievement was observed ($\rho = 0.610$; $p < 0.001$). **Conclusion.** More than a half of all the examined students didn't have signs of depressive symptoms and 48% of them did. Depressive symptoms were more prevalent among the female compared with the male students. Depressive symptoms had a significantly negative impact on daily activities of the students. During medical studies students experience high levels of stress and they should be screened for the symptoms of depression.

Keywords: depressive symptoms, prevalence, medical students, PHQ-9 questionnaire

11. INCIDENCE OF DIABETES MELLITUS IN MUNICIPALITY OF ALEKSINAC FROM 2008 TO 2017

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Introduction. Diabetes mellitus (DM) is the most common chronic metabolic disease today. An increase in the incidence trend of type 1 diabetes mellitus (T1DM) and type 2 (T2DM) was observed worldwide.

The objective of the paper was to determine the incidence of DM in the population of municipality of Aleksinac from 2008 to 2017.

Material and Method. Descriptive study was done. Data about all new cases DM were obtained from the Population Diabetes Registry of Serbia for the period 2008-2017 only for the municipality of Aleksinac. Crude incidence rates were calculated per 100,000 inhabitants. Incidence rates per 100,000 population were calculated, standardized by the direct method according to the standard population of the World. Data about population of the municipality of Aleksinac were obtained from 2002 and 2011 Censuses.

Results. A total of 1.149 new cases of T1DM and 1030 of T2DM was registered. Regarding gender, T1DM occurs slightly more frequently in women, 56.3%, while in men 43.8%. T2DM also occurs slightly more frequently in women 55.8%, while in men 44.2%. Age-standardized incidence rate of T1DM shows an increase in the age groups (for age group 5-9 row incidence is 221,95 and for age group 10-14 row incidence is 170,95) and a decrease in the older age groups. Age-standardized incidence rate of T2DM shows an increase in the age groups 55-59 years and was the highest in the 60-64 age group.

Conclusion. There has been an increase in the number of patients with both types of diabetes mellitus, and that both types of diabetes mellitus in female are slightly more frequent. T1DM is registering much more in persons under 20 years of age and slightly more frequently in women. The increase of incidence rate of T2DM was registered in older persons, above 55 years of age. Further researches is needed.

Keywords: diabetes mellitus, type 1 diabetes, type 2 diabetes

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